Neuroprotective effect of a brain-targeting form of docosahexaenoic acid after stroke: an MRI-based study

Fabien Chauveau, Tae-Hee Cho, Magali Perez, Michel Guichardant, Adrien Riou, Pierre Aguettaz, Madeleine Picq, Michel Lagarde, Yves Berthezène, Norbert Nighoghossian, et al.

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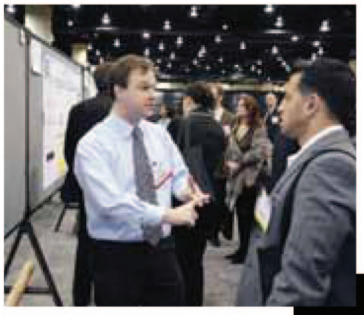

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W MP1

Selection for Delayed Intravenous Alteplase Treatment Based on Prognostic Score

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Background: Approved use of intravenous alteplase for ischemic stroke offers net benefit. Pooled analysis of RCT suggests that additional patients could benefit but others may be harmed with initiation of alteplase beyond 4.5 hours after stroke onset. We proposed prognostic scoring methods to identify a strategy for patient selection to be applied first to an existing trial dataset and then validated in the pooled RCT 4.5-6h data. **Methods:** We selected 500 patients treated by iv alteplase and 500 controls from VISTA, matching Rankin (mRS) outcomes to those from pooled RCT 4.5-6h data. We ranked patients by prognostic score (from age and NIHSS). We iteratively chose lower and upper score limits to exclude patients with extreme predicted outcomes. We generated odds ratios for alteplase treatment effects on mRS distribution within these populations of patients with intermediate prognostic scores; and examined proportions attaining mRS 0-1, and surviving. We chose prognostic score limits to optimise our sample for a net treatment benefit significant at p=0.01 by Cochran-Mantel-Haenszel test and by ordinal logistic regression. We also defined more inclusive limits based on p=0.05 criteria. After finalising prognostic score limits, for validation we had these applied by an independent statistician to the pooled RCT data for 4.5-6h, testing for net benefit by CMH test, ordinal regression and also by dichotomised outcomes: mRS 0-1, mortality and PH2 bleeds at 5% significance. All analyses were adjusted for age and NIHSS. **Results:** In the VISTA training dataset, limits of 56-95 on a prognostic score based on 145-0.46*age-2.5*NIHSS retained a population of 714 patients in whom there was net benefit significant at p=0.01; limits of 47-104 gave net benefit in 937 patients at p=0.05. When applied to the 1120 patients in the pooled RCT 4.5-6h dataset, score limits of 56-95 retained 711 patients and gave OR for improved mRS distribution of 1.13, 95% CI 0.87-1.47, CMH p=0.89. More patients achieved mRS 0-1 (OR 1.44, 1.02-2.05, p=0.04) but mortality and PH2 bleeds were increased: OR 1.56, 1.01-2.40, p=0.04; OR 15.6, 3.7-65.8, p=0.0002 respectively. The wider limits of 47-104 gave ordinal OR 1.13 (0.90-1.41, CMH p=0.40, n=988). **Conclusion:** Selection of patients between 4.5 and 6h based on simple clinical measures failed to deliver a population in whom the alteplase effect would be safe and effective.

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W MP2

Higher rCBV Values In The PWI/DWI Mismatch Area Predict Favorable Clinical Outcome In Acute Ischemic Stroke

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Introduction: Regional cerebral blood volume (rCBV) on perfusion weighted MRI (PWI) reflects the degree of collateral circulation and reactive vasodilatation in acute ischemic stroke. **Hypothesis:** We hypothesized that higher rCBV values in the PWI/DWI mismatch area would predict favorable clinical outcome in acute ischemic stroke. **Methods:** We included Target Mismatch profile patients (n=34) from the DEFUSE study and performed standardized processing of DWI and PWI images (RAPID software). Target Mismatch profile was defined as mismatch profile ($PWI_{Tmax>6s}$/DWI ratio>1.2 and an absolute mismatch >10 mL) without Malignant profile (DWI or $PWI_{Tmax>8s}$ lesion >100 mL). The baseline $PWI_{Tmax>6sec}$ images and baseline DWI images were chosen as the common space to define the mismatch area. CBV and ADC values were estimated in the mismatch areas on co-registered images. Relative rCBV was defined as the absolute rCBV value in the mismatch area on the lesion side / the absolute rCBV value in the mirrored contralateral side. Relative regional ADC (rADC) was defined as the absolute rADC value in the mismatch area on the lesion side/ absolute rADC value in the mirrored contralateral area. Favorable clinical response (FCR) defined as an improvement of 8 or more points on the NIHSS between baseline and 90 days or a score 0 or 1 on the NIHSS at 90 days, was the primary outcome parameter. **Results:** Significant differences in relative rCBV were present in the mismatch region in patients with FCR vs. no FCR [1.09 (IQR 1.03, 1.27) vs. 1.01 (IQR 0.89, 1.09); p=0.02]. There were no significant differences in relative rADC, absolute rCBV values, or absolute rADC values in the mismatch region in patients with FCR vs. no FCR. An ROC curve analysis identified relative rCBV>1.16 as the optimal threshold to predict FCR (sensitivity=0.36, specificity=1.0). This threshold was valid for both patients with and without reperfusion. After adjusting for reperfusion status, the odds ratio for FCR with relative rCBV>1.16 was 9.0 (95%CI, 0.9 to 89.5; p=0.061). Multivariate analysis was performed in 29 patients who had adequate data for reperfusion status. Relative rCBV was the only independent predictor of FCR [odds ratio 2.08 (95%CI, 1.04 to 4.19) per 0.1 relative rCBV increase]. **Conclusions:** Our study demonstrates that patients with high relative rCBV ratios in the acute mismatch region have more favorable clinical outcomes, irrespective of reperfusion. These results suggest that high levels of rCBV reflect good collateral circulation and favorable prognosis even if reperfusion does not occur.

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W MP3

FLAIR/DWI Ratio in Wake-up Strokes Patients: A Comparative Study With Known Onset Patients.

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Background: One quarter of ischemic strokes occur during sleep, in many, shortly before or after awaking. FDA approval for the use of IV tPA excludes patients who awaken with stroke, unless they were proven normal within 3 hours. Brain MRI with negative Fluid Attenuated Inversion Recovery (FLAIR) and positive Diffusion Weighted Imaging (DWI) is a possible surrogate for time from stroke onset. We aim to compare the FLAIR/DWI signal between patients who wake-up with stroke versus those with known onset. **Methods:** We use a prospectively collected stroke database including patients from 2004 to 2009 who had brain MRI as initial imaging screening. Wake-up stroke was defined as ischemic stroke, "last seen normal" more than 6hours ago, with ED arrival between 4 and 10am with brain MRI within 3 hours from ED arrival. We chose 2 controls groups with known time from stroke onset: 1) patients who received brain MRI within 6 hours from stroke onset (Control A) or between 6 and 12 hours (Control B). DWI and FLAIR signal was rated as normal or abnormal. Lesion volume and FLAIR/DWI ratios were obtained using automatic maximal entropy threshold (Image J v1.42). Associations were assessed using the Kruskal Wallis (KW) test with Holm-adjusted pair wise Wilcoxon Rank Sum for continuous data and Fisher-Freeman-Halton (FFH) test for multiple pair comparisons. **Results:** We identified 19 wake-up patients, 22 Control A patients and 19 Control B patients. Admission NIHSS was higher in controls (8.5±6.8 vs. 17.1± 9.4 vs. 11.2±9.4; p=0.003) and hypertension was higher in the wake up group (84.2% vs. 59% vs. 36.8%; p=0.012). Abnormal FLAIR signal were significantly different among groups (wake-up group 47.3%, control A 36.1%, control B 89.5%; FFH p=0.0012). There were statistically significant differences in FLAIR/DWI ratio among the 3 groups (wake-up group 0.04±0.06; Control A: 0.05±0.12, Control B: 0.17±0.15; KW p=0.0005). Post-hoc pair wise comparisons showed that Control group B was statistically significant different from the wake-up group (p=0.0045) and Control group A (p=0.0015). DWI volumes were not different among the 3 groups (wake-up group 19.83±34.72ml; Control A: 33.31±42.15ml, Control B: 26.33±39.14ml; KW p=0.086). **Conclusion:** Abnormal FLAIR signal and FLAIR/DWI ratio were similar in patients with wake-up strokes and AIS patients imaging within 6 hours from the stroke onset, but dissimilar from patients imaged between 6 to 12 hours. This supports the notion that ischemia may begin shortly before or after awaking.

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W MP4

Safety And Efficacy Of Intravenous Thrombolysis Beyond 4.5 Hours In Acute Ischemic Stroke Patients Selected By Perfusion Computed Tomography

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Background and objectives: Several ongoing clinical trials are testing the hypothesis that multiparametric MRI can select stroke patients for reperfusion therapies in delayed time windows. Previously, large case series showed that MRI-guided intravenous thrombolysis in the 3-6 hour window was safe and effective. However, whether the more available perfusion computed tomography (PCT) is useful to extend the therapeutic window for stroke thrombolysis, remains largely unknown. We aimed to study the safety and efficacy of i.v. alteplase (tPA) beyond 4.5 hours in stroke patients selected with PCT. **Subjects and Methods:** We studied all consecutive hyperacute ischemic stroke patients admitted to our stroke unit and treated with i.v. tPA between January 2008 and May 2010. Patients within 0-4.5 h (group A) were treated according to non-contrast computed

tomography (NCCT) criteria. Beyond 4.5 hours (group B), patients received i.v. tPA when the following PCT criteria were met: (1) absence of established hypodensity on NCCT, (2) infarct core occupying chemic tissue, (3) ischemic penumbra exceeding infarct core by >20%. The following outcome variables were assessed in both groups: (1) rate of symptomatic hemorrhagic transformation during admission, (2) rate of complete arterial recanalization 1 hour after tPA bolus as defined by transcranial Doppler thrombolysis in brain ischemia (TIBI) criteria, and (3) favorable long-term outcome defined as a modified Rankin scale score ≤2 at day 90. **Results:** A total of 175 patients received i.v. tPA. Of them, 21 (12%) were treated beyond 4.5 h using PCT criteria. All patients in group B had an acute non-lacunar middle cerebral artery (MCA) ischemic stroke. Mean onset-to-treatment time was 143 ± 47 min for group A and 421.4 ± 250 min for group B. Both groups were comparable regarding risk factor profile and stroke severity, the only significant difference was found in prebolus glycemia, which was lower in group B (127 mg/dl vs 104 mg/dl, p=0.017). Rates of symptomatic hemorrhagic transformation (A: 5.2%, B: 4.8%, p=0.9), complete 1h recanalization (A: 30.8%, B: 33%, p=0.4) and good long-term outcome (A: 58.4%, B: 61.9%, p=0.7) did not differ significantly among both groups. **Conclusion:** Our results suggest that intravenous thrombolysis may be safely and efficaciously administered beyond 4.5 hours in MCA ischemic stroke patients selected by PCT criteria. PCT-based detection of tissue-at-risk could be used in clinical trials testing reperfusion therapies.

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W MP5

FLAIR Signal as a Surrogate Of Time In Acute Ischemic Stroke: An Inter Rater Validation Study

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Background: Many patients with acute ischemic stroke are denied thrombolytic therapy because the time from stroke is unknown. Brain MRI with negative Fluid Attenuated Inversion Recovery (FLAIR) and positive Diffusion Weighted Imaging (DWI) lesion has been suggested as a surrogate for acute stroke within 6 hours or less. We studied the inter-rater reliability of FLAIR negative and DWI positive MRI over time from onset with the aim to validate this surrogate marker for time from stroke onset. **Methods:** A prospectively collected acute stroke database was used and included patients from 2004 to 2009 who had brain MRI as initial imaging screening. Four examiners, blinded to patient information, rated the DWI and FLAIR as positive or negative for early ischemic changes. Additional identification of the lesion on FLAIR and DWI were obtained using automatic maximal entropy threshold (Image J v1.42). The final agreement of the lesion score was obtained by agreement between at least 3 raters or 2 raters plus the imaging software. Final FLAIR signal agreement was plotted over time of stroke onset and the association was calculated using Spearman correlation. Percentage of agreement and Fleiss Kappa was used obtain the concordance and interrater agreement between the 4 raters. **Results:** Sixty FLAIR and 63 DWI images from 63 patients were available for the interpretation. There was a strong correlation from time of stroke onset to FLAIR signal ($r = 0.61$; $p < 0.0001$). Inter rater agreement was better for the DWI sequence than FLAIR. DWI positive signal agreement was 86% with a ê coefficient of 0.57, FLAIR positive signal agreement was 50% with a ê coefficient of 0.45 and FLAIR/DWI mismatch agreement was 53% with a ê coefficient of 0.46. **Conclusion:** There is a strong correlation of time of onset with FLAIR signal on brain MRI in ischemic stroke patients w. However, fair inter rater reliability precludes the use of such approach to reliably estimate time of onset.

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W MP6

Patient and Hospital Characteristics Associated with Use of IV tPA among Acute Ischemic Stroke Patients Arriving within 2 hours of Symptom Onset

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Background: We have previously reported increased use of IV tPA at GWTG-Stroke hospitals, but little is known about the factors associated with greater likelihood of treatment in the program. Patient and hospital characteristics among those patients arriving within 2 hours of symptom onset and without documented contraindications to IV tPA treatment were analyzed. **Methods:** After excluding 56,477 patients with documented contraindications to IV tPA, data on 37401 eligible acute ischemic stroke (AIS) patients who arrived at 1172 hospitals within 2 hours from last known well between April 2003 to June 2009 were included. Patient and hospital characteristics independently associated with IV tPA treatment were determined by multivariable GEE models. Because NIHSS was missing in 13006 patients (34.8%), multivariate regression models that included (N=22245) or did not include (N=33097) initial NIHSS score were built. **Results:** Among eligible AIS patients arriving within 2 hours, 63.2% (2364/37401) received IV tPA. The median time to treatment from last known well was 140 min (IQR 115-165), from arrival was 81 min (IQR 63-103) and almost all (92.4%) were treated within 180 min. In a model without NIHSS, patient factors most strongly associated with tPA treatment included younger age; white race; no prior stroke/TIA, PVD, diabetes or prosthetic heart valve; use of EMS and earlier arrival and imaging times. Hospital factors included bed size, teaching hospital status, region and percentage of all stroke patients at that hospital with an NIHSS recorded. When NIHSS was added to the model, it emerged as the most powerful predictor with other findings similar (Table 1 and 2).

Table 1. Patient Characteristics Associated with IV tPA Use in Eligible Patients Arriving <=2 hr of Symptom Onset

	Adjusted Model with NIHSS		
Variables	**Adjusted OR**	**95% CI**	**P-value**
Patient Characteristics			
Age, per 10 year increase	0.86	0.84, 0.89	<.0001
Black race	0.85	0.73, 0.98	0.02
Stroke/TIA	0.65	0.60, 0.71	<.0001
PVD	0.73	0.62, 0.87	0.0003
Diabetes Mellitus	0.85	0.78, 0.93	0.0001
Prosthetic Heart valve	0.63	0.47, 0.86	0.0029
Onset to Arrival, per 10 minutes increase	0.88	0.86, 0.89	<.0001
Arrival to CT, per 10 minutes increase	0.86	0.83, 0.89	<.0001
Arrival Via EMS	1.59	1.42, 1.78	<.0001
NIH Stroke Scale 10-14, (Reference 0-9)	2.63	2.36, 2.92	<.0001
NIH Stroke Scale 15-20, (Reference 0-9)	3.55	3.12, 4.03	<.0001
NIH Stroke Scale 21-42, (Reference 0-9)	2.76	2.41, 3.16	<.0001

Table 2. Hospital Characteristics Associated with IV tPA Use In Eligible Patients Arriving <=2 hr of Symptom Onset

	Adjusted Model with NIHSS		
Variables,	**Adjusted OR**	**Lower 95% CI, Upper 95% CI**	**P-value**
Hospital Characteristics			
Hospital Beds, per 200 increase	1.13	1.05, 1.22	0.0012
Teaching hospital	1.45	1.16, 1.80	0.0011
Hospital Region, South, (Reference Northeast)	0.54	0.42, 0.69	<.0001
% patients w/ NIHSS recorded, per 10% increase	1.08	1.04, 1.12	0.0001

Discussion: Patient predictors of IV tPA in eligible AIS patients include increased stroke severity, younger age, later arrival within the first 2 hours, use of EMS, white race, and absence of prior stroke/TIA. Hospital predictors include larger size, teaching status, and location outside the South. Health officials should emphasize use of 911 as early as possible after symptom recognition, and implementation of protocols to obtain rapid imaging and document NIHSS and specific tPA contraindications systematically. Further research is needed to better understand the reasons for non-treatment among patients without documented contraindications.

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W MP8

Myocardial Infarctions Following Carotid Stenting and Endarterectomy: Results from the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST)

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Background: CREST showed no difference in the primary composite endpoint. However, a higher risk of stroke following carotid artery stenting (CAS) and a higher risk of myocardial infarction (MI) following carotid endarterectomy (CEA) underscore the need for analysis of the individual components of the endpoint. Herein we analyze the amplitude of and outcomes from periprocedural MI and biomarker positivity. **Methods:** Cardiac biomarkers were measured before and 6-8 hours after the procedure; ECG was performed prior to and 6-48 hours post and 1 month. Additional biomarkers and ECGs were obtained for evidence of elevation of biomarkers, ECG change, or chest pain lasting >15 minutes or for other ischemic symptoms. ECGs were reviewed at a reading center and biomarkers were measured locally. MI was defined as a CK-MB or troponin 2 or more times the site's upper limit of normal(ULN) plus chest pain or equivalent symptoms or ECG evidence of ischemia. **Results:** Among 2502 subjects, 14 MIs occurred in the CAS group and 28 MIs occurred in the CEA group (HR=0.50; 95% CI: 0.26-0.94; p=0.032), and the median biomarker ratio (peak/ULN) was 40X ULN (intermediate risk biomarker ratio for non ST elevation < 10X ULN, expected ratios with ST elevation MI are ~ 500X ULN). Twenty additional patients had biomarker evidence of MI without either chest pain or ECG changes (bio+only), 8 CAS and 12 CEA. MI occurred on day 0-1 in 77% of MI and bio+only; only 3 occurred beyond the 1st week. Biomarker elevations and ratios were higher in the 27 MI patients with chest pain compared to the 15 MI patients without chest pain or to the 20 bio+only patients (Table). The hazard ratio for mortality up to 4 years was 3.40 (95% CI: 1.67-6.92) times greater for those with MI (n=42) and 3.57 (95% CI: 1.46-8.68) times greater for bio+only (n=20) compared to those with neither MI nor bio+only (n=2440) (p≤0.001 for a significant difference among the groups). Adjustment for age had little impact on the estimated risk differences. **Conclusions:** MI and biomarker positivity without symptoms or ECG changes were infrequent in CREST, and by comparison to MI in other settings were relatively small. MI with chest pain had higher biomarker levels compared to those biomarker abnormalities in isolation or in combination with ECG changes. Increased mortality after the periprocedural period is associated with periprocedural MI or bio+only.

Table. Infarct size estimated by biomarkers. Values are median (interquartile range).

	Biomarker ratio	Peak CK	Death
MI (n=42)	40 (12-116)	238 (132-460) IU	8
MI with chest pain (n=27)	69 (26-142)**	188 (126-382) IU	3
MI, no chest pain (n=15)	28 (10-63)	375 (217-698) IU	5
Bio +only (n=20)	14 (9-27)*	298 (119-353) IU	5

*p<0.05 compared to MI with chest pain.
**p<0.04 compared to MI, no chest pain.

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W MP10

Is There an Age Differential Between Outcomes of Carotid Angioplasty and Stent Placement and Carotid Endarterectomy in General Practice?

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Background/Objective: Recently Carotid Revascularization Endarterectomy versus Stenting Trial (CREST) suggested that carotid angioplasty and stent placement (CAS) may provide greater benefit than carotid endarterectomy (CEA) in younger patients (aged less than 70 years) with carotid artery stenosis. We wanted to identify if such differential results in age strata are observed in general practice among patients undergoing CEA and CAS. **Methods:** We analyzed the data from the Nationwide Inpatient Sample (NIS) which is representative of all admissions in the United States from 2004-2007. The primary composite end point was stroke, cardiac complications, or death during the post procedural period, similar to CREST study. Our secondary outcomes were comparison of length of stay and hospital charges. We used a multivariate model, adjusting for patients' age, hospital characteristics, and co-morbid conditions between <70 years (group I) and those aged ≥70 years (group II). **Results:** Of the total 183278 estimated patients, who received treatment for carotid artery disease during the study period, 91% underwent CEA and the remaining 9% underwent CAS. Of the total procedures, 41 % were performed among patients aged <70 years (group I). CAS was more often performed in large volume hospitals (p< 0.0001) in both groups. There was no statistically significant difference in the composite end points of post operative stroke, cardiac complications and in-hospital mortality in either group (<70 years: OR: 1.2; 95%CI: 0.97-1.52, and ≥70: OR:1.1; 95%CI 0.94-1.29). In both groups, patients who underwent CAS had about 1.5 times higher hospital charges (<0.0001) despite a minimally shorter length of stay (p<0.0001). These results were similar when we restricted the analysis for patients seen at teaching hospitals. **Conclusion:** We did not identify any significant differences between CEA and CAS in the composite of post procedure stroke, cardiac events, or death at the national level in either age group. In addition, prominently higher hospital charges even in the younger patients may limit widespread acceptance of CAS in United States.

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W MP11

C-reactive Protein and Cerebral Embolism in Carotid Stenting: a New Marker of Risk

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Introduction: Carotid artery stenting (CAS) is a possible method of carotid revascularization for stroke prevention; however cerebral embolism may occur during the procedure. Hypothesis. Cerebral embolism during CAS could be associated with specific morphological and serological patterns. **Methods:** Consecutive patients with carotid artery stenosis undergoing filter-protected CAS were preoperatively evaluated to identify carotid unstable plaque at duplex ultrasound, complicated aortic plaque at trans-esophageal echocardiography and flogistic status with high sensitivity C-reactive proteins (hs-CRP) serum levels. Aortic arch type, carotid artery tortuosity index, and complexity of the procedure were considered. Cerebral embolism was evaluated by comparing at diffusion weight resonance magnetic imaging (DW-RMI) preoperative and postoperative cerebral lesions (number and volume in mm^3 of total, ipsilateral and contralateral cerebral lesions) and through the analysis of cerebral protection filters obtained from CAS by light and scanning electron microscopy. **Results:** From January to December 2009, 20 consecutive patients were submitted to CAS with no complications. At least 1 asymptomatic cerebral lesion on DW-MRI was present in 18 (90%) patients. Female gender was associated with higher total and ipsilateral number of cerebral lesions at DW-RMI (18.2±10.9 vs. 8.3±8.8 p=0.03 and 11.0±6.9 vs.4.0±5.3 p=0.02 respectively); presence of complicated aortic plaque was associated with higher volume of contralateral cerebral lesions (2350±2593 vs. 636±632 mm^3 p=0.02). Hs-CRP >5mg/l was correlated with higher number of total, ipsilateral and contralateral cerebral lesions (16.2±10.7 vs. 4.3±3.4 p=0.02, 9.3±6.6 vs. 1.5±2.3 p=0.01 and 6.8±4.7 vs. 2.8±1.1 p=0.04 respectively). HsCRP >5mg/l gives an OR 2.6 (C.I. 1.005-6.8) of elevated total number (n>5) of cerebral lesions and an OR 3.9 (C.I. 1.1-13.7) of elevated volume (>1000 mm3) of cerebral lesions. Hs-CRP>5 mg/l was also correlated with greater surface involvement by embolic materials in the cerebral protection filters at microscopic analysis (37.0±5.7 vs. 26.9±2.5 p=0.004). Neither the morphological characteristics of the plaque and of the supraortic vessels, nor the complexity of the procedure correlated with number or volume of new cerebral lesions at DW-RMI. **Conclusions:** Rather than morphological and technical aspects of the procedure, high levels of Hs-CRP are associated with higher embolic risk during CAS. These results are important in the definition of embolic potential of carotid plaques.

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W MP12

Identifying High-Risk Asymptomatic Carotid Stenosis: Ulceration on 3D Carotid Ultrasound Vs. TCD Microemboli

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Background: With more intensive medical therapy, the 2-year risk of stroke in patients with asymptomatic carotid stenosis is now less than 1%; i.e. well below the risk of carotid

endarterectomy or stenting. Microemboli on transcranial Doppler (TCD) identify the small proportion of patients with asymptomatic carotid stenosis who can benefit from endarterectomy or stenting . In this study we compared microemboli with carotid ulceration on three-dimensional ultrasound (3D U/S) as an additional method for identifying ACS patients at sufficiently high risk to benefit from revascularization. **Methods and Results:** ACS Patients (n=253) with carotid stenosis >60% by Doppler ultrasound were studied prospectively with TCD embolus detection and 3D U/S to detect ulcers, and followed for 3 years. Mean age was 69.66 (SD 8.51) years; 46.2% had at least 1 ulcer and 16.6% had 2 or more ulcers (Ulcer+). Ulcer + patients had higher levels of LDL cholesterol (P=0.02), and were more likely to have microemboli (14.3% versus 4.3%; P=0.02), a stroke (7.1% versus 1.4%; P<0.049), or any stroke, death or TIA in 3 years (14.3% versus 3.3%; P=0.01). In this cohort, the 3-year stroke risk associated with microemboli was 13%. **Conclusion:** ACS Patients with 2 or more ulcers detected by 3D U/S are at increased risk of stroke (about half that with microemboli) and may benefit from endarterectomy or stenting. Until complication rates of endarterectomy or stenting are below 2%, patients without ulcers or microemboli would be better treated medically until they develop symptoms, ulcers or emboli.

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W MP13

Blacks are Less Likely than Whites to Receive Intravenous Tissue Plasminogen Activator for Acute Ischemic Stroke in Cook County, Illinois

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Objective: To assess if ethnic disparities exist in the use of intravenous tissue plasminogen activator (tPA) for acute ischemic stroke (AIS) in Cook County, Illinois. **Background:** Ethnic disparities in stroke care include observed differences in stroke incidence, severity, mortality, acute management, and rehabilitation. There are less data regarding ethnic disparities in the acute stroke management and use of tPA. Cook County, Illinois is a large metropolitan region with an ethnically diverse population. **Methods:** A retrospective analysis of the Illinois Hospital Association CompData® was performed, specifically, identifying those patients with primary discharge diagnosis of ischemic stroke based on ICD-9 codes (433.01, 433.11, 433.21, 433.31, 433.81, 433.91, 434.01, 434.11, 434.91, or 436) and who were hospitalized in Cook County, Illinois. We analyzed the utilization of tPA based on its ICD-9 procedure code (99.10) and tested the association between ethnicity and tPA use while controlling for relevant and available covariates. Univariable and multivariable logistic regression analyses were employed to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for independent predictors of tPA use. **Results:** Between January 1, 2008 and September 30, 2009, there were 13,033 AIS discharges from Cook County hospitals. The mean age was 70 years with 54% women, 50.5% white, 35.6% black, and 7.0% Hispanic. Overall, 3.3% of AIS patients received tPA but this differed by ethnicity (4.3% in whites, 2.1% in blacks, and 3.2% in Hispanics; $p < 0.001$). In multivariable analysis adjusting for age, gender, insurance level, primary stroke center status, hospital bed size, and urban/suburban location, ethnicity remained strongly associated with tPA use ($p < 0.001$). Specifically, blacks were half as likely to receive tPA (adj. OR 0.53, 95% CI 0.42-0.68, $p < 0.001$) compared to whites while tPA use in Hispanics (adj. OR 0.87, 95% CI 0.56-1.23, $p = 0.348$) compared to whites was not different. **Conclusions:** In Illinois' Cook County, blacks are half as likely as whites to receive tPA for treatment of AIS. A variety of reasons may account for the ethnic disparity including poor knowledge of stroke symptoms causing delays in presentation, limited access to certified stroke centers, and possibly treatment biases and delays in the hospital. Further study into ethnic disparities in acute stroke care is warranted.

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W MP14

Poorer Patients Have More Severe Ischemic Strokes

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Introduction: Initial stroke severity is one of the strongest predictors of eventual stroke outcome. However, predictors of initial stroke severity have not been well-described within a population. We hypothesized that poorer patients would have a higher initial stroke severity upon presentation, even after controlling for other known predictors of stroke outcome. **Methods:** Using previously published surveillance methodology, we identified all cases of hospital-ascertained ischemic stroke (IS) occurring in 2005 within a biracial population of 1.3 million. "Community" socioecomic status (SES), a well-validated aggregate variable for estimating individual SES, was determined for each patient based on the % below poverty in the census tract in which the patient resided (determined through geocoding) Community SES for the 346 census tracts in the region was collapsed into 4 categories: % below poverty of 0%-5% (richest), 6%-10%, 11%-25%, and >25% (poorest). Patients who lived in institutions were excluded. Severity of stroke was estimated with a retrospective NIH Stroke Scale Score. Linear regression was used to model the effect of SES on stroke severity. Models were adjusted for race, gender, age, pre-stroke disability, and history of medical comorbidities (see table). **Results:** There were 2264 ischemic stroke events detected in 2005; 25 were excluded due to missing data or age <18, and 306 were excluded due to residence within institutions. Among 1933 remaining cases, 21.9% were black, 52.3% were female, and the mean age was 71 years (range 19-104). The median NIHSSS was 3 (range 0-40). The poorest community SES was associated with a significantly increased initial NIHSSS by 1.6 points (95% CI 0.5-2.6 P<0.001) compared with the richest category in the univariate analysis, which remained significant even after adjustment for demographics and comorbidities (Table). **Conclusion:** We found that increasing community poverty was associated with worse stroke severity at presentation, independent of other known factors associated with stroke outcomes. In fact, the magnitude of change in the NIHSSS severity for the poorest patients was similar to the effect seen for a history of coronary artery disease or hypertension. SES may impact stroke severity via medication compliance, access to care, cultural factors, or may be a proxy measure for undiagnosed disease states. Understanding how socioeconomic factors contribute to initial stroke severity is critical to improving outcomes among stroke patients in the U.S.

Table: Multivariable Model of Change in Initial NIHSSS Associated with SES, Demographics, and Medical Co-Morbidities

	Change in NIHSSS Points (95% C.I.); p-value
% below poverty within census tract: poorest vs. richest category	2.4 (1.2-3.7);p<0.001
Age (by year)	0.01 (-0.02- 0.04);p=0.422
Race (Non-black vs. black)	0.7 (-0.2 – 1.6);p=0.138
Gender F vs. M	-0.02 (-0.6 – 0.6); p=0.957
Pre-stroke disability mRS (per point)	0.5 (0.5 – 1.0);p<0.001
History of prior stroke	-0.4 (-1.2-0.4), p=0.255
History of CAD/afib	1.3 (0.6 – 1.9); p<0.001
History of HTN	-1.3 (-2.1 - -0.5);p=0.001
History DM	-0.03 (-0.7 – 0.6);p=0.931
Current smoking (vs. non-smoker)	-0.1 (-0.8 – 0.5);p=0.653
BMI (per point)	-0.04 (-0.09 – 0.01);p=0.081

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W MP15

Forty-year Stroke Burden in Mexican Americans and Non-Hispanic Whites

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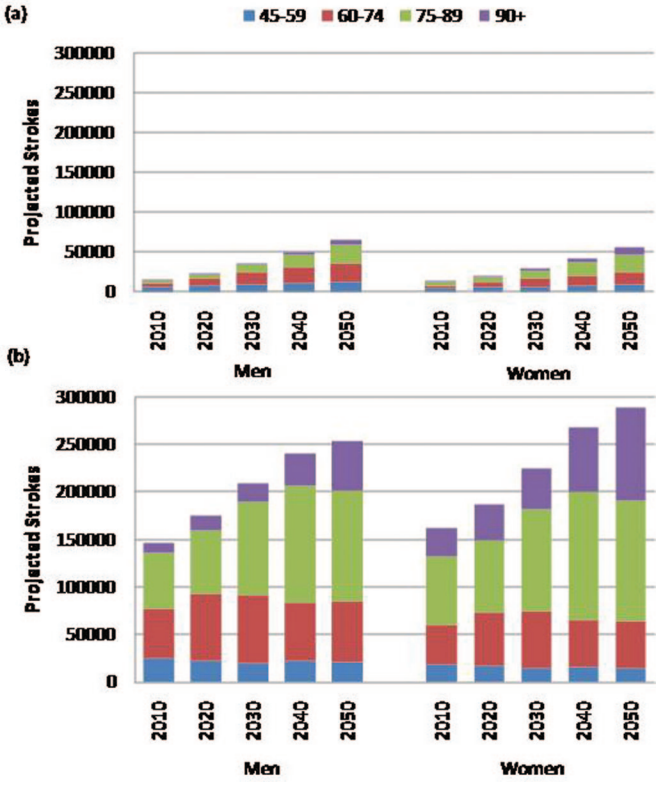
Background: The number of strokes in the US will increase dramatically over subsequent decades with the aging population. Mexican Americans (MAs) are a fast growing population with an increased stroke burden. The objective was to estimate and compare 40-year stroke burden, by decade from 2010-2050, in MA and non-Hispanic white (NHW) men and women, using population projections from the US Census and data from the Brain Attack Surveillance in Corpus Christi (BASIC) Project. **Methods:** Stroke surveillance data from the BASIC Project for 2000-2008 and 2000 US Census data were used to calculate annual stroke (ischemic and hemorrhagic) incidence rates by ethnicity (MA, NHW), age (45-59, 60-74, 75-89, 90+), and sex. To calculate projected numbers of strokes, annual incidence rates were multiplied by corresponding ethnic, age, and sex-specific projected population counts by decade. MA projected population counts were estimated by multiplying Hispanic projections by proportion MA in 2000. Incidence rates were assumed to remain constant over time. **Results:** The figure displays projected strokes by decade for MA (a) and NHW (b) men and women. Both ethnic groups will experience large increases in the number of strokes over time. NHWs will increase from ~300,000 strokes in 2010 to over half a million in 2050, a ~75% increase. MAs will increase from ~26,000 strokes in 2010 to >120,000 in 2050, a >350% increase. In both ethnic groups, an increasing number of strokes will occur in those 90+ over time. Among NHWs, women have a greater stroke burden than men in all years due to a greater number of strokes among those 90+ years. Among MAs, men have a greater stroke burden than women in all years due to a greater number of strokes among those <75 years. **Conclusions:** Strokes will increase dramatically over the coming decades, with increases being considerably steeper in MAs compared with NHWs. Many of these strokes will be in the elderly which has huge social

and economic consequences. Efforts to prevent stroke and reduce stroke-related disability in aging populations are critical.



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W MP16

Recent Trends in Sex-Specific Stroke Incidence amongst 35-64 Year-Olds in the United States

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Background: The overwhelming majority of strokes occur in persons older than 65 years; therefore, stroke among younger individuals is relatively understudied. Furthermore, information on the potential influences of sex on stroke in this latter demographic are limited, despite the unique stroke risk factors harbored by women younger than 65 years. Recent nationwide studies have shown an emerging sex disparity in stroke prevalence in the United States (US) amongst middle-aged individuals; women aged 45-54 are now twice as likely as men to report previous stroke. It is unknown whether this sex disparity in stroke prevalence is due to an increase in stroke incidence or improved survival after stroke amongst young/middle-aged women. This study aimed to assess temporal trends from 1997 to 2006 in hospitalizations for stroke among men and women aged 35-64 years in the United States (US). **Methods:** Data were obtained from all states within the US that contributed to the Nationwide Inpatient Sample. All patients (identified by the International Classification of Diseases, Ninth Revision procedure codes) admitted to hospitals between 1997 and 2006 with a primary or secondary discharge diagnosis of stroke (n= 3,161,752) were included. We analyzed age-adjusted rates of stroke hospitalizations per 100,000 persons among men and women aged 35-44, 45-54, and 55-64. **Results:** From 1997 to 2006, age-adjusted stroke incidence among individuals aged 35-64 years decreased by 10% from 66.7 to 60.3 stroke hospitalizations per 100,000 (curvilinear trend: $P<0.01$) in men, and 8% from 52.7 to 48.3 stroke hospitalizations per 100,000 (linear trend: $P<0.001$) in women. The 55-64 year age group highly accounted for the reductions in stroke incidence: slope=-12.3, $P<0.001$ for men and slope=-8.9, $P<0.001$ for women. Among those aged 45-54 years, stroke hospitalization rates remained unchanged, whereas for those aged 35-44 years, hospitalization rates increased slightly in both men (slope=0.71; $p=0.008$) and women (slope=0.89, $P<0.001$). Although the rate of increase in stroke hospitalization rates was higher in women compared to men aged 35-44, the difference was not significant. **Conclusion:** From 1997 to 2006, age-adjusted hospitalization rates for stroke have declined in individuals aged 55-64 years. However, stroke hospitalization rates have remained stable amongst individuals aged 45-54, and increased amongst individuals aged 35-44 years, suggesting that younger individuals perhaps warrant more aggressive stroke prevention efforts.

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W MP17

Race-Ethnic Disparities in Ideal Cardiovascular Health in the Northern Manhattan Study (NOMAS)

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Background and Purpose: The 2020 American Heart Association impact goal is to improve the cardiovascular health of all Americans by 20% while reducing deaths from cardiovascular disease and stroke by 20%. The newly defined national goals for ideal cardiovascular health are based on 7 health factors ('Life's Simple 7'). Our aim was to evaluate for race-ethnic disparities in the prevalence of these 7 factors in an elderly urban cohort. **Methods:** The Northern Manhattan Study is a community-based prospective cohort study designed to examine the incidence and risk factors for stroke and cardiovascular disease among different race-ethnic groups. Stroke-free subjects over age 40 had a complete baseline interview, exam, and fasting bloods. We classified 7 cardiovascular health factors (smoking, body mass index (BMI), physical activity, diet, total cholesterol, blood pressure, and fasting glucose) into ideal, intermediate, or poor according to the new AHA definitions. Multiple logistic regression analysis was performed to investigate the race/ethnic differences in prevalence of individual ideal health factors after adjusting for demographics, socioeconomic status, health behaviors and history of vascular disease. **Results:** Among the 3219 participants (mean age 69 $\pm$10 years), 63% were female, 54% Hispanic (H), 25% non-Hispanic Black (NH-B), and 21% non-Hispanic White (NH-W). Overall, only 0.5% had 7 or 6 ideal factors, 4% had 5, 14% had 4, 30% had 3, 32% had 2, and 19.5% had $\leq$1 ideal factor; 18% had 4 or more ideal factors. Age and sex-adjusted prevalence of having 4 or more ideal factors varied across race-ethnic groups (H 15%, NH-B 19%, NH-W 29%, $P<0.0001$). Even after adjustment, Hispanics and NH-Blacks were less likely than NH-Whites to have 4 or more ideal factors (H vs. NH-W: OR 0.60, 95%CI 0.46-0.80; NH-B vs. NH-W: OR 0.69, 0.53-0.89). Compared to NH-Whites, Hispanics had lower odds of ideal physical activity (0.55, 0.43-0.70), BMI (0.59, 0.46-0.75), and blood pressure (0.56, 0.36-0.88); whereas NH-Blacks had lower odds of non-smoking (0.55, 0.41-0.73), ideal physical activity (0.75, 0.60-0.94), BMI (0.56, 0.45-0.71), and blood pressure (0.58, 0.37-0.89). NH-Blacks, however, had higher odds of ideal cholesterol compared to NH-W (1.57, 1.24-1.98) and H (1.39, 1.13-1.71). All 3 groups were similar in terms of very low prevalence of ideal diet. **Conclusions:** Only 18% of this elderly cohort had 4 or more of Life's Simple 7 ideal cardiovascular health factors. Substantial racial-ethnic disparities in the prevalence of ideal cardiovascular health exist even after adjustment for multiple socioeconomic variables. Improvement of cardiovascular health to achieve the 2020 AHA Impact Goal represents a great challenge, and will require intensive efforts among Hispanics and Blacks.

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W MP18

Effect of Diabetes (DM) on Ischemic Stroke Incidence and Case Fatality

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Introduction: DM is known to be an important risk factor for ischemic stroke. DM has been proven to be a potent risk factor in the young, with risk ratios for ischemic stroke in one metropolitan area as high as 6-10 for those less than age 55, but without any increase in case fatality. We examined whether similar effects are seen in the geographically distributed Reasons for Geographic and Racial Differences in Stroke (REGARDS) study. **Methods:** Participants were recruited between 2003-2007 and include 30,239 black and white community dwellers age >45 at baseline. The cohort was designed to be balanced on race and sex, and region; the final sample was 41% black, 55% female, and 56% reside in the "stroke belt" in the southeastern US. Participants in this ongoing study are surveyed every 6 months to ascertain incident strokes which are physician adjudicated based on medical record review. Confirmed ischemic stroke events were included in this analysis and participants missing covariates or reporting stroke before baseline were excluded (N=3464). DM status was defined by self report. Incidence rates and risk ratios were calculated for those with and without DM and stratified by age and race. **Results:** Of 26775 eligible subjects, 5931 were defined as having DM. Mean follow-up was 4.4 years. Subjects with DM were older and more likely to be black; they had higher BMI, less education, lower income, and were more likely to have hypertension, hypercholesterolemia, heart disease, and atrial fibrillation. There were 394 incident ischemic strokes. Ischemic stroke was significantly more common among those with DM than without (1.8% vs. 1.4%, $p = 0.01$). Incidence rates and rate ratios are presented in the table. Risk for ischemic stroke was significantly higher in younger individuals with DM in both races and becomes non-significant beyond age 75. This association was still present after adjustment for region, sex, income and education. There was a trend towards higher 30-day case fatality in those with DM (12.7% vs. 7.0%, $p=0.07$). **Conclusions:** This confirms

significant risk for ischemic stroke in those with DM, especially in those < age 55 (4.5-5.5 fold increased risk). As seen in other work, ischemic stroke risk attributable to DM declines with age but our results again show that diabetes is a very potent risk factor for ischemic stroke in the young. Importantly, no effect of region was seen, so this effect is relevant to all patients with DM and not exclusive to the stroke belt or any one region. Finally, there was a trend towards higher case fatality rates in those with DM and further study is needed.

Incidence Rates per 100,000 person years, and DM:NDM Incidence Rate Ratios (IRR)

Age-group	No DM	DM	IRR
Black			
<55	95 (36,253)	438 (182,1053)	4.58 (1.23,17.0)
55-64	255 (183,355)	607 (440,839)	2.39 (1.50,3.79)
65-74	486 (368,641)	783 (577,1063)	1.58 (1.04,2.39)
≥75	981 (732,1314)	633 (375,1069)	0.65 (0.36,1.18)
White			
<55	49 (16,152)	275 (69,1100)	5.54 (0.92,33.2)
55-64	166 (121,266)	480 (312,736)	2.88 (1.70,4.90)
65-74	404 (325,503)	697 (496,981)	1.72 (1.15,2.59)
≥75	922 (759,1119)	991 (646,1520)	1.07 (0.67,1.72)

Presented are age and race specific incidence rates with IRR (obtained by dividing incidence rate in DM by NDM)

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W MP19

Accurate and Fast Perfusion Lesion Segmentation Tool for Clinical Settings

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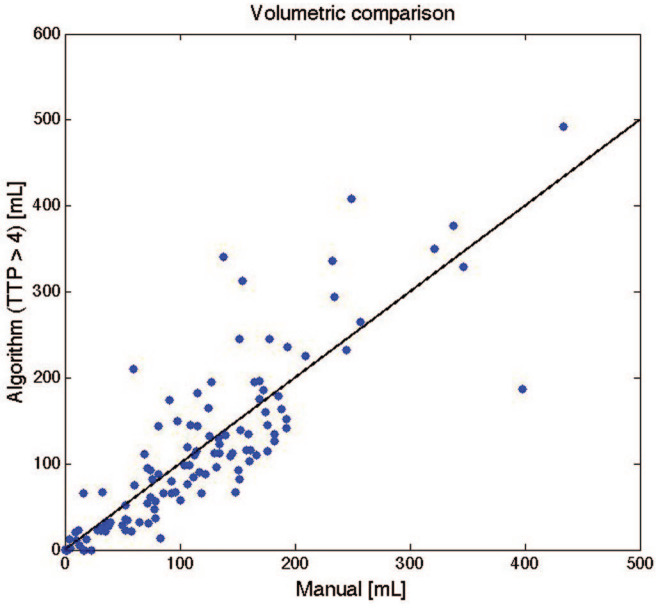
Introduction: Perfusion- and diffusion weighted MRI (PWI/MRI) is widely used to select stroke patients who are likely to benefit from reperfusion therapies. This prompts a need for clinical software, which estimates PWI and DWI lesion volumes, quickly and accurately. We present a novel semi-automatic algorithm to segment PWI lesion on maps of time to peak (TTP). We compare our results to manually outlined PWI lesions and thresholded maps in 120 patients. **Method:** Initially, CSF and left-right hemisphere masks were generated automatically and were applied to remove artifacts and contra-lateral hemisphere. A connected components labeling algorithm examines an image to find clusters of voxels, which are connected in the sense that neighboring voxels have similar perfusion values. The ipsi-lateral hemisphere was converted to binary maps at TTP >2, >4, >6 and >8 seconds, and the manually outlined lesions were used to establish an optimum threshold. The connected components labeling algorithm examined the binary maps and returned label maps containing the regions fulfilling the thresholds. The PWI lesion was selected in order to the user chosen seed point on the label maps. We quantify the agreement between algorithm and manual outlining using correlation, sensitivity and specificity. **Results:** Optimal agreement between algorithm and manual and outlining is obtained using a TTP threshold of 4 seconds as input to the algorithm ($R2 = 0.74$). The median volume difference was 3 mL with inter-quartile range [-17.6, 23.5] mL with a 4s threshold, the median sensitivity is significantly higher for the algorithm (74 %) than for the thresholded maps (55 %), $p < 0.05$. The median specificity was also higher using the algorithm (96%) compared to thresholding (93%), although this was not significant. **Conclusion:** Our algorithm demonstrates excellent agreement with manual lesion volumes, and produces a 19% increase in sensitivity compared to simple thresholding. Requiring minimal user intervention, this algorithm may be a clinically relevant tool for fast identification of PWI lesions on TTP maps with high accuracy. We speculate that the semi-automatic outlining software may be used as decision support in emergency settings.



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W MP20

Standardized regional Perfusion Parameters in Dynamic Whole Brain Perfusion CT

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Introduction: Dynamic CT-perfusion (CTP) is frequently used in acute stroke imaging, however there is need for further standardization and harmonization of this technique for reliable quantification of tissue at risk. Perfusion thresholds applied to the entire brain to identify salvageable tissue have been established, but there is evidence for significantly different regional ischemic vulnerability. The purpose of this study was to assess and standardize human regional blood flow parameters in a large sample of non-stroke patients using whole brain dynamic CTP. **Methods:** Within 30 months, whole brain dynamic CTP was performed in 1050 patients admitted for new-onset acute stroke. In 135 cases, there was no evidence for any perfusion abnormality, persistent symptoms or infarction on follow up imaging. In these cases, CTP maps (cerebral blood- flow [CBF], -volume [CBV], time to peak [TTP] and mean transit time) were calculated and co-registered to standard MNI-152 space (FLIRT5.5). In all normalized CTP maps, a weighted average perfusion value (mean and SD) was calculated for each perfusion parameter in a priori brain regions defined by the anatomical probability distribution in the standardized Harvard Oxford cortical/subcortical atlases (significant differences $P < 0.05$ adjusted for multiple comparisons). **Results:** A total of 68 defined regions in 135 normal brains were evaluated. There were significantly different normalized values of regional perfusion parameters in cortex, subcortical grey matter and white matter. In cortical grey matter the highest mean perfusion values were observed in the Insula, Heschl's gyrus, calcarine gyrus and opercular cortex, the lowest in the temporal and frontal cortex. In subcortical grey matter the highest perfusion values were found in the Putamen, Thalamus, and Hippocampus (Figure 1). **Discussion:** This study demonstrates the variability of regional perfusion parameters derived from whole brain dynamic CTP in a large population. There are significantly different regional perfusion parameters in cortical and subcortical grey- and white matter and the results are in accord with gold standard PET studies in the past. Regional blood flow thresholds may be a more precise measure of tissue at risk to account for significant variability in regional ischemic vulnerability. **Conclusion:** A normalized map of dynamic CTP parameters of the whole brain is presented for the first time to target the need for standardization of stroke evaluation and to improve assessment of regional tissue at risk.

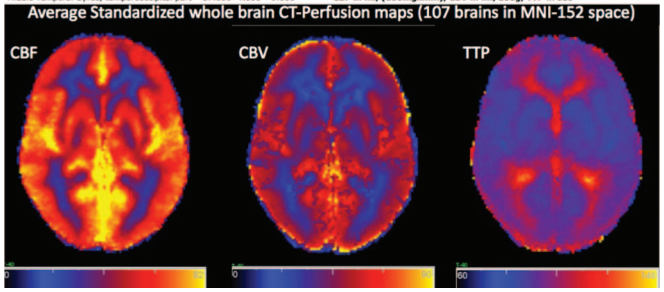
Average Standardized regional brain CT-Perfusion parameters (68 brain regions in MNI-152 space)

Harvard Oxford subcortical regions	CBF	CBV	TTP
Left Cerebral White Matter	42.286	3.520	9.885
Left Cerebral Cortex	56.488	4.442	9.470
Left Lateral Ventrical	43.355	3.918	10.884
Left Thalamus	63.305	5.072	9.700
Left Caudate	50.811	3.806	9.120
Left Putamen	59.032	4.621	8.803
Left Pallidum	47.804	3.893	8.979
Brain-Stem	43.930	3.869	9.925
Left Hippocampus	66.107	5.453	9.702
Left Amygdala	49.231	4.787	9.424
Left Accumbens	48.405	4.083	9.026
Right Cerebral White Matter	45.817	3.718	9.842
Right Cerebral Cortex	56.644	4.513	9.485
Right Lateral Ventricle	46.174	4.074	10.965
Right Thalamus	64.549	5.019	9.766
Right Caudate	49.646	3.620	9.205
Right Putamen	57.848	4.577	8.924
Right Pallidum	49.022	3.980	9.009
Right Hippocampus	66.360	5.565	9.818
Right Amygdala	54.450	5.323	9.645
Right Accumbens	46.297	4.008	9.169

Harvard Oxford cortical regions	CBF	CBV	TTP
Frontal Pole	48.521	4.994	9.722
Insular Cortex	52.447	4.323	9.121
Superior Frontal Gyrus	52.912	3.517	9.210
Middle Frontal Gyrus	53.236	3.896	9.399
Inferior Frontal Gyrus, pars triangularis	57.360	4.609	9.127
Inferior Frontal Gyrus, pars opercularis	58.623	4.585	9.091
Precentral Gyrus	57.247	3.855	9.188
Temporal Pole	35.036	3.566	9.315
Superior Temporal Gyrus, anterior division	56.924	4.419	9.379
Superior Temporal Gyrus, posterior division	60.097	4.650	9.367
Middle Temporal Gyrus, anterior division	49.576	4.884	9.858
Middle Temporal Gyrus, posterior division	55.862	4.583	9.600
Middle Temporal Gyrus, temporooccipital part	57.606	4.606	9.661

contd. Harvard Oxford cortical regions	CBF	CBV	TTP
Inferior Temporal Gyrus, anterior division	28.488	2.878	10.241
Inferior Temporal Gyrus, posterior division	41.563	4.549	10.012
Inferior Temporal Gyrus, temporooccipital part	53.200	4.578	9.932
Postcentral Gyrus	56.854	3.759	9.241
Superior Parietal Lobule	54.113	3.377	9.553
Supramarginal Gyrus, anterior division	58.316	3.970	9.197
Supramarginal Gyrus, posterior division	57.308	3.996	9.338
Angular Gyrus	57.920	4.069	9.421
Lateral Occipital Cortex, superoir division	58.124	3.979	9.780
Lateral Occipital Cortex, inferior division	61.034	4.915	9.911
Intracalcarine Cortex	73.817	5.575	9.439
Frontal Medial Cortex	49.826	5.795	9.791
Juxtapositional Lobule Cortex	66.281	4.087	8.921
Subcallosal Cortex	45.153	4.966	9.655
Paracingulate Gyrus	64.692	4.888	9.014
Cingulate Gyrus, anterior division	61.214	4.545	9.051
Cingulate Gyrus, posterior division	68.889	4.830	9.376
Precuneous Cortex	69.010	4.547	9.420
Cuneal Cortex	71.969	4.880	9.532
Frontal Orbital Cortex	49.910	6.036	9.590
Parahippocampal Gyrus, anterior division	41.395	5.202	10.330
Parahippocampal Gyrus, posterior division	64.455	5.418	9.492
Lingual Gyrus	73.380	5.621	9.600
Temporal Fusiform Cortex, anterior division	20.524	2.153	9.401
Temporal Fusiform Cortex, posterior division	44.242	4.771	9.714
Temporal Occipital Fusiform Cortex	61.011	4.964	9.669
Occipital Fusiform Gyrus	64.158	5.041	9.810
Frontal Operculum Cortex	63.668	4.900	8.938
Central Opercular Cortex	66.369	4.972	8.895
Parietal Operculum Cortex	62.761	4.757	9.027
Planum Polare	67.942	5.308	9.141
Heschl's Gyrus (includes H1 and H2)	72.759	5.326	8.939
Planum Temporale	64.776	4.832	9.128
Supracalcarine Cortex	72.622	5.417	9.474
Occipital Pole	63.782	5.196	10.110

CBF in ml/(100mgxmin), CBV in ml/100g, TTP in sec



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W MP21

High Tmax Values on Perfusion MRI Often Reflect Low CBV - A Pathophysiological Link Between the Malignant Perfusion Profile and Poor Outcome?

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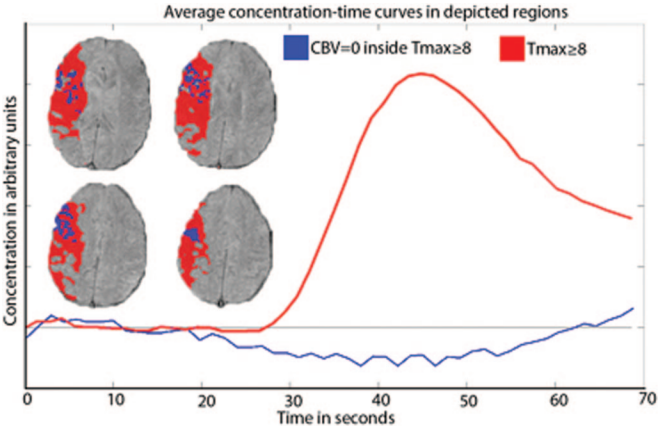
Background: Patients with very large regions of severe Tmax delay on MR-perfusion imaging have been shown to be at increased risk of poor outcome in several studies, at least partly due to increased risk of hemorrhage. Recently it was also shown that patients with areas of very low cerebral blood volume (CBV) are at increased risk of hemorrhage. Both very low CBV and severe Tmax delay may reflect severe ischemia and this may compromise vessel wall integrity leading to hemorrhage. We hypothesized that the very large regions of severe Tmax delay and very low CBV may be closely interrelated and aimed to investigate the relationship between these two perfusion parameters. **Methods:** We used data from the EPITHET study database in which 99 patients with ischemic stroke and perfusion imaging data obtained within 6 hours of stroke onset were randomized to tPA and placebo regardless of MRI profile. 1) Simulations were used to measure the effect of low CBV on Tmax. We simulated CBV of 4%,2%,1%,0.05%,0.01% and 0% with a constant MTT of 6 s and arrival delay of 2s to measure the influence of CBV on Tmax. 2) We then measured the volume of Tmax>=8 for each patient in the EPITHET dataset and the fraction of this volume that had CBVzero (CBV 0). CBV was calculated by integration of the contrast concentration time curve. **Results:** 1) Simulations showed that Tmax values increase as CBV decrease, Spearmans rho=-0.61, p=8 was 51 mL (27-139). A median of 4% (1-17%) of the Tmax lesions were made up of CBV=0. Thus, a significant portion of a Tmax>=8 lesion often reflects not just severely delayed perfusion, but a complete absence of perfusion (CBV=0). **Conclusion:** Tmax can be prolonged both by (i) prolonged delays in bolus arrival or (ii) by complete absence of tracer (CBV=0). Tissue fate for these two scenarios is likely to differ markedly and complimentary consideration of regions with CBV=0 may assist risk management. This finding indicates that high Tmax values can reflect very low CBV and offers a pathophysiological explanation for why high Tmax values indicate risk of hemorrhage.



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W MP22

Optimized Use Of Perfusion Weighted Images In Stroke: Flow Thresholds, Choice Of Maps And Calibration

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Background and Purpose: Perfusion weighted (PW) magnet resonance imaging (MRI) is used to identify the tissue at risk in stroke imaging. However, current obstacles are (i) the choice of the best PW map, (ii) the adequate threshold and (iii) the adequate quantification. We evaluated a simple MR based and positron emission tomography (PET) validated calibration of different PW maps for clinical use. **Methods:** PW-MRI and quantitative PET (15O-water) were performed in acute stroke patients (<24h). In a region of interest (ROI) based approach using a receiver operating characteristic (ROC) curve analysis, maps of time to peak (TTP), Tmax, mean transit time (MTT) and cerebral blood flow (CBF) were analyzed in order to identify: (i) the best threshold for each PW map; (ii) the sensitivity and specificity for penumbral flow imaging (< 20 ml/100g/min on PET-CBF); (iii) the benefit of a simple scaling procedure. **Results:** In 20 acute stroke patients (time delay stroke to imaging <24h) comparative imaging was performed (median time from stroke: 8.2 hours; median time MRI to PET: 60 min). (i) The averaged best thresholds (median/IQR) were; rTTP 4.3 seconds (2.8-5.4); Tmax 5.4 seconds (4.1-6.9) s, MTT 5.2 seconds (3.5-6.4); CBF 21.5 ml/100g/min (19.7-31.7). (ii) The corresponding ratios of sensitivity/specificity (%) were: 91/83, 89/89, 88/79 and 88/87. (iii) The large variability of individual thresholds was well explained by the mean value of the hemispheric reference (HR) on PW images (linear regression analysis of the reference value vs individual best threshold: R2: TTP 0.94, Tmax 0.91, MTT 0.84, CBF 0.77) Thus, look-up tables were calculated that identified the individual best thresholds according to the individual HR value on PW images. **Conclusion:** For the detection of penumbral flow, TTP maps seem equivalent to deconvoluted CBF and Tmax maps, if validated thresholds are used. All PW images benefit from a simple MR based calibration correcting for global cerebral blood flow. We propose look up-tables that identify the individual best threshold for penumbral flow and do not require image recalculation. Such calibrated thresholds may improve mismatch detection in clinical imaging.

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W MP23

Extent of Hypoattenuation On CT Angiography Source Images In Basilar Artery Occlusion: Prognostic Accuracy Of Posterior Circulation ASPECTS And The Pons-midbrain Score In The Basilar Artery International Cooperation Study

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Background: The posterior circulation Acute Stroke Prognosis Early CT Score (pc-ASPECTS) and the combined Pons-midbrain score quantify the extent of early ischemic changes in the

posterior circulation. We compared the prognostic accuracy of both scores if applied to CT angiography (CTA) source images (CTA-SI) of patients in the Basilar Artery International Cooperation Study (BASICS). **Methods:** BASICS was a prospective, observational, multi-centre, registry of consecutive patients who presented with acute symptomatic basilar artery occlusion (BAO). Functional outcome was assessed at 1 month. We applied pc-ASPECTS and the combined Pons-midbrain score to CTA-SI by 3-reader-consensus. Readers were blinded to clinical data. We performed multivariable logistic regression analysis, adjusting for thrombolysis, baseline NIHSS score and age, and used the output to derive ROC curves to compare the ability of both scores to discriminate patients with favourable (modified Rankin Scale [mRS] scores 0-3) from patients with unfavourable (mRS scores 4-6) functional outcome. **Results:** We reviewed CTAs of 158 patients (64% men, mean age 65 $\pm$ 15 years, median NIHSS score 25 [0-38], median GCS score 7 [3-15], median onset-to-CTA time 234 minutes [11-7380]). At 1 month, 40 (25%) patients had a favourable outcome, 49 (31%) had an unfavourable outcome (mRS score 4-5) and 69 (44%) were deceased. Both techniques of assessing CTA-SI hypoattenuation in the posterior circulation showed equally good discriminative value in predicting final outcome (C-statistics; area under ROC curve 0.74 versus 0.75, respectively; p=0.37). Pc-ASPECTS dichotomized at $\geq$6 versus $<$6 was an independent predictor of favourable functional outcome (RR = 2.2; CI_{95} 1.1-4.7; p = 0.034). **Conclusion:** Compared to the combined Pons-midbrain score, the pc-ASPECTS score has similar prognostic accuracy to identify patients with a favourable functional outcome in BASICS. Dichotomized pc-ASPECTS ($\geq$6 versus $<$6) is an independent predictor of favourable functional outcome in this population.

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W MP24

Diffusion Tensor Imaging (DTI) Monitoring Of Motor Function Recovery After Middle Cerebral Artery Infarction: Searching For A DTI-Marker Of Neurorepair

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Background and Purpose: Magnetic resonance-diffusion tensor imaging (MR-DTI) may quantify the degeneration of nervous tracts caused by brain infarctions. However, whether DTI may monitor neurorepair processes after a cerebral infarction in humans remains largely unknown. We performed a longitudinal study to investigate the relationship between the temporal evolution of DTI parameters and motor function recovery after disabling middle cerebral artery (MCA) ischemic stroke. **Subjects and Methods:** We prospectively studied consecutive patients with a first-ever non-lacunar disabling MCA territory infarction. Patients must show a M1-MCA occlusion on admission and a complete recanalization before first MR-DTI was obtained. MCA infarction had to be severely disabling by first MR-DTI, with a score in NIHSS limb motor items (5a,5b,6a,6b) $\geq$ 4. DTI and neurological examinations were performed two weeks, one month and three months after stroke onset. Fractional Anisotropy (FA), Relative Anisotropy (RA), Mean Diffusivity (MD) and number of fibbers (NF) were determined on the affected and unaffected corticospinal tracts (CST) at each timepoint, and relative values of all parameters (diseased/healthy CST) were calculated. Motor recovery was assessed by the % decrease in NIHSS limb motor score from baseline to day 90. **Results:** We studied 10 MCA ischemic stroke patients (6 men, mean age 70.7, median first MRI NIHSS motor score 7). Affected CST showed significantly lower FA (p=0.001), RA (p=0.0001) and NF (p=0.043) at baseline compared with unaffected CST. Mean FA and RA of pathologic CST decreased progressively until 3rd month, whereas MD increased, and NF decreased between 1st and 2nd DTI and increased thereafter. Regarding neurological recovery, 5 (50%) patients gained at least 25% of lost motor function during follow-up. Among baseline DTI parameters, high rNF better discriminated those patients with later improvement in motor function. Increase in rRA over time correlated significantly with motor function recovery (r = 0.652, p = 0.04) and a clear trend was observed for rFA augment (r = 0.609, p = 0.06). Those patients with a better motor outcome had a higher increase in rFA (p = 0.03) and rRA (p = 0.03) during follow-up. **Conclusion:** Recovery of motor function was associated with an increase in relative RA and FA of CST during the first three months after MCA ischemic stroke. MR-DTI could be used to monitor endogenous and therapeutically modulated neurorepair after human stroke.

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W MP25

Worse Stroke Outcome In Atrial Fibrillation Links To More Severe Hypoperfusion

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Background: AF is associated with worse outcome following ischemic stroke, but the underlying mechanisms are uncertain. We aimed to elucidate the pathophysiological determinants of worse stroke outcome in patients with AF using pooled serial MRI data from the EPITHET-DEFUSE collaboration. **Methods:** EPITHET was a multinational phase II trial of 101 acute ischemic stroke patients randomized to IV tPA or placebo at 3-6 hours. DEFUSE was a prospective cohort of 74 acute ischemic stroke patients treated with IV tPA at 3-6 hours. Patients were assessed with clinical scores (NIHSS and mRS) and multimodal MRI before treatment, at days 3-5 and 3 months after stroke in EPITHET; before treatment, 3-6 hours after treatment and 1 month after stroke in DEFUSE. Post-processing of perfusion data was done with deconvolution algorithms to create maps of Tmax, defined as the time to peak of the impulse response. PWI volumes were defined using Tmax delays in 2-second increments from $>=$2 to $>=$12 seconds. The intensity of hypoperfusion was further characterized by the hypoperfusion intensity ratio (HIR), defined as the volume of severe hypoperfusion (Tmax$>=$8s) divided by the volume of tissue with any hypoperfusion (Tmax$>=$2s). DWI/PWI Mismatch was defined using Tmax$>=$6s PWI volume. Infarct growth was defined by the difference between final (day 3-5 EPITHET, day 30 DEFUSE) and acute infarct volumes. Hemorrhagic transformation was classified according to ECASS criteria. Comparisons of acute stroke severity, hypoperfusion volume, mismatch, arterial occlusion, infarct growth, outcome infarct size, hemorrhagic transformation and clinical outcome were made between patients with and without AF. **Results:** AF was present in 58 of 169 eligible patients. Six patients were excluded for poor data. At baseline, AF patients were older (median 78 vs 73 years, p=0.005), had more severe neurologic impairment (median NIHSS 15 vs 11, p=0.02) and greater volumes of more severe hypoperfusion (median Tmax$>=$8s PWI volume 56 vs 37mL, p=0.009; mean HIR 0.50$\pm$0.22 vs 0.38$\pm$0.22, p=0.001). There was no difference in the rate of arterial occlusion and mismatch volume, but AF patients exhibited greater infarct growth (median 25 vs 8mL, p=0.007). At outcome, AF patients had more severe neurologic impairment (median NIHSS 7 vs 4, p=0.03), greater disability (median mRS 4 vs 3, p=0.054), more frequent parenchymal hematoma (25 vs 10%, p=0.02) and larger infarcts (median volume 50 vs 23mL, p=0.01). AF was not predictive of functional outcome (OR1.00, CI 0.46-2.19 for mRS4-6) after adjusting for baseline differences in age, tPA use, blood glucose, stroke size and severity. **Conclusions:** The adverse effect of AF following ischemic stroke is linked to greater volumes of more severely hypoperfused tissue and infarct growth, leading to larger final infarct size and worse clinical outcome. This may reflect impaired cardiac output and collateral circulation in AF.

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W MP26

Cavitation in Symptomatic Lacunar Stroke: Revisiting Definition, Revisiting Rates

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Background: An apparent cavity, with cerebrospinal fluid-like signal, surrounded by a hyperintense rim has been proposed as characteristic of chronic lacunar infarction on the MRI fluid attenuated inversion recovery (FLAIR) sequence. A recent retrospective study suggested that most acute lacunar strokes do not develop a cavitated appearance, however. We determined the MRI characteristics of chronic lacunar infarction using data from 3 prospective studies of minor stroke with standardized MRI sequences and pre-specified follow up. **Methods:** Patients with acute lacunar infarction on diffusion-weighted imaging (DWI) were selected from 3 cohort studies of minor stroke presenting $<$24 hours. Follow up was performed at 30 days (VISION I study, n=20) or 90 days (VISION II and CATCH studies, n=25). One patient was excluded because there was no lesion at follow up. Evidence of cavitation on MRI was rated separately on FLAIR, T1 and T2 sequences by 2 independent study physicians; discrepant readings were resolved by consensus. A small number of MRI sequences were missing at follow up: T1-weighted, 3; T2, 4; FLAIR, none. **Results:** Median age of the 45 eligible patients was 67.4 (interquartile range 60.6-72.5), 28/45 were men (62%). There was good agreement on the presence of cavitation on FLAIR (kappa 0.78, 95% CI 0.60-0.96). FLAIR evidence of cavitation at follow up was seen in 20/25 (80%) scanned at 90 days but only 4/20 (25%) scanned at 30 days (p$<$0.001). All cavitated FLAIR lesions had a hyperintense surrounding rim (24/24, 100%). FLAIR cavitation was less frequent in brainstem or thalamus infarcts vs. the rest (6/19, 32%, vs. 18/26, 69%, p=0.02), including those scanned at 90 days (6/11, 55% vs. 14/14, 100%, p=0.009). Age, size of infarct, old chronic lacunes or microbleeds, white matter

lesions, and past medical history were not associated with FLAIR cavitation (data not shown). On the T1-weighted sequence, evidence of cavitation was seen in 22/23 at 90 days (96%) vs. 10/19 at 30 days (53%, p=0.002). On the T2-weighted sequence, evidence of cavitation was seen in 16/21 at 90 days (76%) vs. 4/20 at 30 days (53%) (p<0.001). Compared to FLAIR, the rate of cavitation on T1 was higher (p=0.001 by McNemar's test) while the rate of cavitation on T2 was the same (p=0.99). Overall, evidence of cavitation on any sequence (FLAIR, T1 or T2) was seen in 25/25 (100%) at 90 days and 11/20 (55%) at 30 days (p<0.001). **Conclusions:** Acute lacunar infarcts are still evolving at 30 days. In contrast to a prior study we found that most FLAIR lesions at 90 days had a central region of hypointensity consistent with cavitation, however there was still a 20% false negative rate. To increase sensitivity, MRI protocols for chronic lacunar lesions should include a T1-weighted sequence as well as a T2-weighted sequence such as FLAIR; reliance on FLAIR alone will underestimate the number of chronic lacunes particularly in the brainstem and thalamus.

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W MP27

Multiple Emboli On MRI In The Left Cerebral Hemisphere Indicates Aortic Arch Disease In Patients With Cryptogenic Strokes.

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Background: About one third of ischemic strokes remain cryptogenic, even after extensive work-up in the best stroke centres. Thromboembolic episodes caused by atherosclerotic plaques in the aortic arch are often overlooked and the aortic arch is not routinely screened. CT Angiography based arch to vertex protocol has been used in our centre as a primary investigation in management of ischemic strokes for the last few years. We analysed the topographical distribution of infarcts on MRI in patients labelled as cryptogenic strokes and correlated the findings with presence of aortic arch abnormalities on CTA. **Methods:** This is a retrospective case analysis of a CTA database at a comprehensive stroke centre (Foothills Medical Centre, Calgary Canada). 105 patients labeled as cryptogenic strokes after extensive workup in our centre from Jan 2008 to March 2010 and having Arch to vertex CT angiography (CTA)were included. Aortic arch abnormalities on CTA were analysed, on axial,sagittal views,post processing of these images were done to have the view of Aortic arch better.Abnormalities were divided into soft linear atheroma (thickness of aortic wall > 4 mm), protruding and complex looking plaques /thrombus. Calcification of Aorta was considered as stable plaque and not categorized as abnormality. Frequency of Diffusion weighted imaging (DWI) lesions on MRI categorized into 1, 2-3 and >=4 was the primary outcome variable. **Results:** Among 105 patients with cryptogenic strokes, 19 (18%) [11 protruding atheromas and 9 soft linear atheromas] had aortic arch abnormalities. Of these 105 patients, 72 patients with MRI as part of the imaging protocol were analysed.There were 49 males(68%) and mean age was 64.7yrs(SD14.2yrs). 48% (12/25) with >=2 DWI lesions had arch disease vs 13% (7/47) with a single DWI lesion (RR 3.2 95% CI 1.45 - 7.14; p=0.01). 27% (13/48) patients with left sided DWI lesions had arch disease when compared to 10.7 %(3/28) with right sided lesions (RR 2.52 95% CI 0.7 - 8.1; p=0.07). 3/4 patients with bilateral DWI lesions had aortic arch disease. The Breslow Day test of homogeneity of Odds ratio showed an interaction between frequency of DWI lesions >=4 and left hemispheric involvement in predicting arch of aorta abnormalities on CTA (p=0.01). **Conclusion:** Multiple lesions on DWI predominantly involving the left cerebral hemisphere in patients labeled as cryptogenic strokes should raise suspicion that aorta arch disease may be present. The aortic arch should therefore be screened in all patients with cryptogenic strokes.

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W MP28

Noninvasive Monitoring Of Cerebral Blood Flow Changes During Acetazolamide Challenge Using Diffuse Correlation Spectroscopy And Transcranial Doppler Ultrasound

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Background and Purpose: Compromised microvascular cerebral blood flow (CBF) and altered vasomotor reactivity (VMR) are critical to the assessment of the evolution of cerebral ischemia. A practical method for bedside monitoring of CBF changes would provide valuable information to guide stroke treatment. Diffuse correlation spectroscopy (DCS) is a relatively new optical technology for non-invasive continuous measurement of CBF. We compare micro- and macro-vascular VMR in response to acetazolamide challenge using DCS and transcranial Doppler ultrasound (TDC) in controls and in patients with carotid artery steno-occlusive lesions. **Methods:** Ten healthy subjects and 12 patients with hemodynamically significant carotid artery steno-occlusive lesions (>70%) were recruited. Bilateral TCD and DCS monitoring were performed simultaneously to measure mean flow velocity (MFV) in the middle cerebral arteries and CBF in the frontal lobes, respectively, before and after a bolus of acetazolamide (1 gr). VMR was calculated as the percentage of change in MFV (TCD-VMR) and CBF (DCS-VMR) after maximum acetazolamide stimulus compared to the baseline. **Results:** In healthy subjects (mean age 31.1±4.5 years, 80% men), there was an increase in CBF as determined by DCS [DCS-VMR: median 38.3% (IQR 22.8%-42.5%)] during the acetazolamide challenge, which was comparable to the MVF increase measured by TCD [TCD-VMR: median 31.9% (IQR 25.2%-40.6%), p=0.57]. Similarly, in patients with carotid steno-occlusive disease (mean age 67.4 ±7.8 years, 83.3% men, 50% symptomatic), CBF and MFV changes were in good agreement both in the affected sides [DCS-VMR: median 25% (IQR 16.4%-32.9%) versus TCD-VMR: median 15.8% (IQR -4.2%-31.4%), p=0.496] and normal sides [DCS-VMR: median 26.1% (IQR 17.7%-50.3%) versus TCD-VMR: median 29.4% (IQR 25.2%-40.7%), p=0.893]. Overall, DCS-VMR was significantly correlated with TCD-VMR (Spearmans correlation coefficient=0.36, p=0.029). **Conclusions:** DCS measurement of CBF changes was successfully obtained in healthy subjects and patients with carotid steno-occlusive disease. Assessment of VMR in the cerebral microcirculation by DCS yielded a satisfactory agreement with VMR measurement at the macrocirculatory level by TCD. DCS may represent a reliable useful tool for real-time non-invasive monitoring of local microvascular cerebral hemodynamics at the patient's bedside that can help the clinicians guide therapeutic strategies.

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W MP29

What Should be included in an Outpatient Diagnostic Evaluation of Transient Ischemic Attack?

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Objectives: Risk of stroke after TIA is significant and warrants emergent diagnostic evaluation. Outpatient TIA clinics are being established in the US in an effort to reduce cost. Most outpatient TIA clinics include brain and vessel imaging, EKG, blood work, and a transthoracic echocardiogram (TTE). Some stroke centers have chosen to stratify TIA patients' risk of stroke with the $ABCD^2$ score to determine if a patient is safe to be evaluated on an outpatient basis. The purpose of this study is to determine the most appropriate components of an outpatient TIA evaluation. **Methods:** Using a prospectively collected database, 1746 patients admitted to the University of Louisville Stroke Center January 1, 2003 to April 30, 2009 were diagnosed by vascular neurologists with TIA or acutte ischemic stroke (AIS). Cerebrovascular assessments of 415 patients with TIA were compared to 1331 patients with AIS. $ABCD^2$ scores were obtained retrospectively from the database on 324 of the 415 patients with TIA. Chi-Square analyses were used to assess the association of characteristics influencing TIA or AIS. Data are expressed as mean ± SD. $ABCD^2$ scores, were examined descriptively. All p-values were two-tailed. Statistical significance was set at $p < 0.01$ to reduce potential Type 1 errors. **Results:** No statistical differences were found in TIA versus AIS patients in history of HTN, DM, cigarette smoking, or prior stroke, LDL, HDL, or total cholesterol levels, use of warfarin and antihypertensives, or in abnormalities seen on TEE. Statistical differences were seen in history of carotid stenosis, history of atrial fibrillation, prior TIA, crp level, prior use of antiplatelets, and statins. TIA patients were less likely to have a history of atrial fibrillation, but were more likely to have a known history of carotid stenosis and prior TIA, had lower crp levels, and were more likely to take antiplatelets, and statin medications than patients with AIS. Of the 324 TIA patients with $ABCD^2$ scores, 130 (40.1%) scored 0-3 (low risk), 140 (43.2%) scored 4-5 (moderate risk), and 54 (16.7%) scored 6-7 (high risk). Of the patients in the low risk category, 14.6% had serious cardioembolic risks for stroke based on TEE: 6 had a mobile thrombus on TEE, 3 in the aortic arch, 5 had a low EF with blood flow stasis, 6 had a marked PFO with a shunt, 1 had a large valvular mobile fibrin strand, and 1 had a severely dilated left atrial appendage. **Conclusions:** We found no significant differences in TEE results between TIA and AIS patients. Due to visualization of the aortic arch and the left atrial appendage, TEE may be more sensitive for cardiogenic stroke risk evaluation than TTE. In this investigation the $ABCD^2$ scores in the low risk category did not predict serious cardioembolic risk seen on TEE. These results suggest that TEE should be included in outpatient TIA diagnostic evaluations. We should continue to treat TIA and AIS as the same condition.

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W MP30

Low Sensitivity and Specificity of Oxfordshire Community Stroke Project Classfication: A Prospective MRI Study

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Background: Stroke syndrome classification influences clinical patient management, particularly subsequent investigations. The Oxfordshire Community Stroke Project (OCSP) is the most commonly used clinical classification tool but its accuracy is unknown. We conducted a prospective study of OCSP versus MRI classification in stroke/TIA patients. **Methods:** Patients presenting with ischemic symptoms within 48 h of onset were included. Following CT-scan, OCSP classification; Total Anterior Circulation (TACI), Partial Anterior Circulation (PACI), Lacunar (LACI) and Posterior Circulation (POCI) was performed by 3 independent examiners. All patients underwent diffusion-weighted MRI (DWI). Enrolment was planned to continue until 100 patients with DWI lesions were included. MRI scans were classified into OCSP categories, based on DWI lesion location. DWI volumes were measured planimetrically. **Results:** Of 130 patients enrolled, 105 had stroke and 25 had TIA. Patients with stroke were more likely to have DWI lesions (90/105) than those with TIA (10/25; $\lambda 2 = 20.273$, P<0.001). Patients were clinically classified as TACI (12), PACI (62), LACI (38) and POCI (18). In the 100 patients with DWI lesions, correct classification rates were as follows: TACI (83.3%), PACI (83%), LACI (39%), POCI (86%). Clinical OCSP had the following sensitivity (SE), specificity (SP) and positive predictive value (PPV) in correctly predicting DWI lesion location; TACI (SE: 100%, SP:98%, PPV:83%), PACI (SE:73%, SP:78% PPV:83%), LACI (SE:47%, SP:83%, PPV:39%), POCI (SE:92%, SP:98%, PPV:86%). The positive likelihood ratio of clinical OCSP was (TACI: 50), (PACI: 3.318), (LACI: 2.76) and (POCI: 46). There was no significant difference in stroke severity between patients classified correctly (Median NIHSS= 4, IQR=7) and those who were classified incorrectly (Median NIHSS= 3,

IQR= 3) by OCSP. However patients classified correctly had a significantly larger mean infarct volume (32.20 ± 65.69 ml) compared to those incorrectly classified (3.8568 ± 4.30 ml), p= 0.008. The highest number of misclassifications occurred between LACI and PACI groups. Patients classified as PACI were more likely to have DWI lesions (52/62) than LACI patients (23/38; ë2= 6.848, p=0.009). Patients classified radiologically as LACI (1.082±0.8363ml) had significantly smaller infarct volumes than those classified clinically as LACI (3.537± 4.36ml, p=0.021). **Conclusions:** The OCSP clinical classification system does not permit accurate discrimination between lacunar and small volume cortical infarcts. Cortical infarcts are frequently misclassified as lacunar syndromes on the basis of clinical and CT findings alone. Differential patterns of investigation for stroke etiology should not be based on clinical classification alone.

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W MP31

Longitudinal Mortality Risk after Spontaneous Intracerebral Hemorrhage

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Background: Only limited data are currently available on predictors of mortality after spontaneous intracerebral hemorrhages (ICH). We studied potential risk factors for post-ICH mortality in a large longitudinal cohort study. **Subjects and Methods:** The international PROGRESS trial followed n=6105 patients with a prior history of any stroke or transient ischemic attack over a period of 4 years. Standard univariate and multivariate Cox proportional hazard models were used to determine the effect of patient age, sex, race/ethnicity, and vascular risk factors on the risk of death after spontaneous ICH. **Results:** During longitudinal follow-up, n=111 (2%) patients suffered spontaneous ICH. Among the latter, 50 died eventually. The effect of ICH on mortality was significantly higher in patients <60 years (HR 18.58, 95% CI 10.56 - 32.69), women (HR 9.94, 95% CI 5.72 - 17.27), in patients of Asian origin (HR 8.21, 95% CI 5.58 - 12.09), and in those with a prior history of hypertension. As compared to patients <60 years, the effect of age on mortality decreased significantly for patients aged 60-70 years (HR 5.85, 95% CI 3.77 - 9.10) and >70 years (3.03, 95% CI 1.76 - 5.20; test for trend P<0.0001). **Conclusion:** These findings suggest that younger age is a risk factor for ICH-related mortality. Further predictors include female sex, Asian origin, and a history of arterial hypertension.

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W MP32

Systolic BP Load Strongly Predicts Hematoma Growth And Mortality After Acute Intracerebral Hemorrhage

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Background: High blood pressure (BP) is considered an important therapeutic target after acute intracerebral hemorrhage (ICH), since it has been suggested to contribute to hematoma growth (HG) and rebleeding. However, the relationship between acute BP variability and the risk of HG is largely unknown. We aimed to determinate the impact of BP changes and course on HG and their interaction with the occurrence of CTA spot sign (SS) as a surrogate marker of active hemorrhage in patients with acute ICH. **Methods:** We prospectively studied 107 patients with acute (<6h) primary supratentorial ICH. Patients underwent baseline (<6h) and follow-up (24h) CT scans, and a CTA (<6h) for the blinded detection of SS. HG was defined as ICH enlargement >30% or >6mL at 24h. On admission, all patients underwent noninvasive BP monitoring at 15 minutes interval over first 24h with a validated oscillometric device. BP variability was calculated as the standard deviation of mean systolic (S), diastolic (D), mean (M) BP, and pulse pressure (PP) values. Maximum BP, minimum BP, maximum BP increase (maximum - baseline), and maximum BP drop (baseline - minimum) values were calculated. SBP and MBP loads were defined as the proportion of readings >180 and >130 mmHg, respectively, according to current guidelines. 90-day mortality was recorded. **Results:** HG patients (36.7%) showed lower GCS (p=0.018), higher NIHSS score (p=0.019), larger baseline ICH volume (p=0.009), and higher rate of CTA-SS (p=0.012). Although baseline BP variables were unrelated to HG, 24h-BP variables including BP variability, maximum BP increase and BP load were significantly associated with HG on univariate analysis (Table). SBP 180-load was correlated with the amount of HG (r=0.356, p=0.001), but not with baseline (p=0.422) and 24h (p=0.127) ICH volumes. In a logistic regression model, SBP 180-load >10.9% (OR 4.6, 95% CI 1.6-13.4, p=0.006), CTA-SS (OR 3.86, 95% CI 1.1-14.2, p=0.042), and GCS <11 (OR 6.6, 95% CI 1.1-42.1, p=0.047) predicted independently HG. The combination of CTA-SS and SBP 180-load >10.9% increased in 6-fold the risk of HG (20.5±21.9 vs. 3.4±8.5 mL, p=0.02). At three months, variables independently related to mortality were SBP 180-load >10.9% (OR 5.9, 95% CI 1.3-26.4, p=0.022), age >74 years (OR 14.4, 95% CI 2.6-80, p=0.002), and baseline ICH volume >17.7 mL (OR 22.3, 95% CI 4-123.8, P<0.001). **Conclusions:** In patients with acute ICH, only one-tenth of SBP readings above 180 mmHg are needed to increase in 5-fold the risk of HG. SBP 180-load >10.9% emerged as independent predictor of HG and 90-day mortality after acute ICH.

Table: 24h-BP variables significantly related to hematoma growth (HG) after acute ICH.

	HG (n=36)	No HG (n=62)	P-value
BP variability (mmHg)			
SBP	17.5 ±9.2	13.8 ±5.3	0.048
DBP	11.4 ±5.8	8.9 ±3.3	0.029
MBP	13.3 ±8.3	9.8 ±3.7	0.035
PP	13.5 ±6.2	10.9 ±3.3	0.039
Maximum BP increase (mmHg)			
SBP	23.1 ±20.9	13.8 ±15.3	0.04
DBP	20.3 ±13.3	14.6 ±12.2	0.049
MBP	17.2 ±13.6	11.3 ±11.3	0.039
PP	24.2 ±24.7	13.7 ±12.6	0.037
BP load			
SBP 180-load	37.8%	12.5%	<0.001
MBP 130-load	19.2%	7.2%	0.013

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W MP33

Poor Prognosis In Warfarin-associated Intracranial Hemorrhage Despite Prothrombin Complex Concentrate Therapy: The CanPro Registry

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Background: Anticoagulant-associated intracranial hemorrhage (AAICH) is associated with larger hematoma volumes, higher rates of hematoma expansion (HE) and worse outcome than spontaneous ICH. In 2008 prothrombin complex concentrate (PCC) was approved in Canada for reversal of anticoagulation. Given a lack of randomized control trial evidence of efficacy, and the potential for thrombotic complications, we launched a multi-centre registry to monitor the use of PCC in AAICH. We aimed to determine the natural history of AAICH treated with PCC. **Methods:** The Canadian Prothrombin Complex Concentrate Registry (CanPro) is a prospective registry of patients treated with PCC for AAICH. CanPro is based at 3 tertiary-care regional stroke centers in Calgary, AB, Edmonton, AB, and Ottawa, ON. Patients were identified by the Blood Bank following the release of PCC, and treatment indication was confirmed via medical records and imaging. A chart review abstracted clinical, imaging and laboratory data, and identified thrombotic events within 30 days of PCC therapy. Hematoma volumes were measured using computer-assisted planimetry and significant growth was defined as an increase of 12.5ml or 33%; HE was measured for parenchymal bleeds only. Clinical outcomes were mRS at discharge and in-hospital mortality. **Results:** Between October 2008 and June 2010, 105 patients received PCC for AAICH (53 intraparenchymal, 43 subdural, 1 epidural, and 8 subarachnoid hemorrhages). The median age was 77 (IQR 13), and 58.1% were male. Median baseline GCS was 14 (IQR 7). Median baseline INR was 2.6 (IQR 1.45) and median baseline ICH hematoma volume was 14.7ml (IQR 19.8). The median PCC dose administered was 1000U (Factor IX activity-equivalence, range 250-3000U), and median follow-up INR was 1.3 (IQR 0.2; median therapy-time to follow-up INR 50mins): 80.3% of patients had complete INR correction (<1.5) within 1 hour of PCC therapy, and 87% had complete correction within 10 hours. Significant HE occurred in 13.2% of patients with ICH (median follow-up CT 20 hours). Clinical outcomes for each hemorrhage type are shown in the table below. There were 5 confirmed thrombotic complications within 30 days of PCC therapy: three ischemic strokes (1 day, 5 days, and 3 weeks post-therapy, all had atrial fibrillation), one MI 7days post-therapy in a patient with recent pulmonary embolism, and one DVT 30 days post-therapy. **Discussion:** PCC therapy rapidly corrected INR in the majority of patients, yet mortality and morbidity rates remained high. Rapid INR correction is necessary but may not be sufficient to alter the poor prognosis in AAICH.

Intracranial hemorrhage type	n	In-hospital mortality	Discharge mRS in survivors, median (IQR)
Intracerebral	53	45.30%	3 (1.5)
Subdural	43	44.20%	3 (1)
Subarachnoid	8	25%	3 (1.75)

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W MP34

Silent Ischemic Lesions In Patients With Acute Symptomatic Spontaneous Intracerebral Hemorrhage: Relationship To Lobar Microbleeds And Clinically Probable Cerebral Amyloid Angiopathy

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Objectives: Cerebral amyloid angiopathy (CAA) is a common cause of spontaneous intracerebral hemorrhage (ICH) and cognitive impairment in the elderly. Neuropathological studies have shown small areas of infarction in CAA, but this has not been widely studied *in vivo*. We investigated the prevalence of silent ischemic lesions in patients with clinico-radiologically defined probable CAA (using the Boston criteria) compared to patients with non-CAA related spontaneous ICH, and to age-matched controls. **Methods:** Cases were ascertained from consecutive cohorts of patients with spontaneous ICH from 4 specialist stroke centres. MRIs were performed $\leq$ 3 months of symptomatic ICH. Age-matched controls were consecutive patients referred to the stroke service with a final non-stroke diagnosis. Ischemic lesions were assessed on diffusion-weighted imaging (DWI) sequences and apparent diffusion coefficient maps by a clinical neurologist trained in neuroimaging. Positive DWI lesions were reviewed by an experienced neuroradiologist and agreement was reached. The neurologist rated the white matter changes (WMC) and cerebral microbleeds (CMBs) using validated scales. We investigated the associations between DWI lesions, clinical and radiological characteristics. **Findings:** We included 104 patients with spontaneous ICH, of whom 39 fulfilled the Boston criteria for clinically-probable CAA; and 47 age-matched controls. The prevalence of silent DWI lesions was 9/39 (23%) in subjects with clinically probable CAA vs 6/75 (8%) in non CAA-related ICH (p=0.024); no controls had DWI lesions. Factors associated with DWI lesions were mean total WMC (OR 1.13, 95%CI 1.02-1.26, p=0.019) and presence of lobar CMBs (OR 10.75, 95%CI 1.36-84.96, p=0.024). In multivariate analysis, diagnosis of probable CAA (OR 3.52, 95%CI 1.11-11.18, p=0.033) and mean total WMC (OR 1.13, 95%CI 1.01-1.27, p=0.026) predicted positive DWI lesions. **Conclusions:** Clinically silent cerebral ischemia is common in patients with spontaneous ICH. The association of DWI lesions with lobar CMBs and a diagnosis of probable CAA suggest that CAA is a particular risk factor for ischemia. These findings have potential implications for the diagnosis and treatment of spontaneous ICH, and for CAA-related cognitive impairment.

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W MP35

Functional MRI Detection of Vessel Reactivity in CAA

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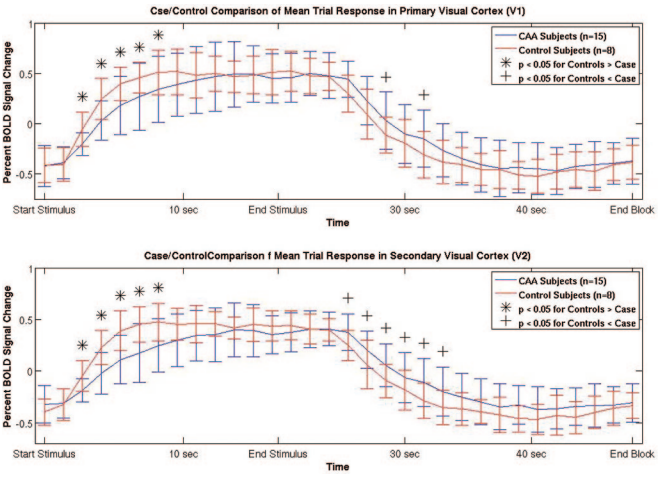
Background: Previous *in vitro*, ultrasound-based studies have demonstrated that â-amyloid deposition in cerebral amyloid angiopathy (CAA) results in loss of smooth muscle tissue and impaired response to vasodilatory stimuli. We sought to determine whether CAA-related abnormalities of cerebrovascular reactivity could be detected using functional magnetic resonance imaging (fMRI) to measure the evoked blood oxygenation level dependent (BOLD) response to visual stimuli. **Methods:** Following acquisition of T1-weighted anatomical MRI, 15 nondemented subjects diagnosed with probable CAA according to the Boston Criteria (13 male, 3 female, mean age 71.3 + 5.3) and 8 similar-aged volunteer control subjects (5M/3F, 78.1 + 5.0) were presented with a visual stimulus while we collected BOLD-weighted echo planar imaging data. The stimulus consisted of 16 trials of a flashing checkerboard displayed for 20 s followed by a gray screen for 28 s. Offline, FreeSurfer analysis software was used to generate surface models of the cortical gray matter, and predict primary and secondary visual cortical areas, V1 and V2. Co-registered BOLD data from voxels intersecting the gray matter surface model in V1 and V2 were extracted and averaged over the regions, and averaged over the 16 trials, resulting in a single mean trial response for each subject and each region. Cases and controls were compared based on measured time-to-peak-response after stimulus onset, time-to-return-to-baseline after stimulus end, and peak response amplitude. **Results:** CAA subjects exhibited prolonged time-to-peak-response and time-to-return-to-baseline in both V1 and V2 (Figure). Mean time-to-peak-response in V1 among CAA cases was 20.1$\pm$4.8 s compared to 14.3$\pm$4.2 s (p = 0.008) for controls; in V2, the values were 20.5$\pm$4.7 s and 13.0$\pm$5.1 s, respectively (p = 0.004). Mean time-to-return-to-baseline following stimulus end for CAA and control subjects was 11.4$\pm$2.4 s compared to 8.6$\pm$1.9 s in V1 (p = 0.004) and 11.6$\pm$2.9 s versus 8.6$\pm$1.7 s (p = 0.006) in V2. Peak response amplitude did not significantly differ between cases and controls. **Conclusions:** CAA subjects exhibited delayed peak BOLD response after stimulus onset and delayed post-stimulus return to baseline. Our findings support the possibility that the smooth muscle of the cerebrovasculature is damaged and stiffened by â-amyloid deposition, resulting in decreased reactivity to vasodilatory stimuli. These observations demonstrate the potential utility of BOLD fMRI for detecting the spatial distribution of reduced vascular reactivity in CAA.



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W MP36

The Surgical Trial in Lobar Intracerebral Haemorrhage (STICH II) - the First 300 Patients

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Background: To date there have been 14 trials of surgery for spontaneous intracerebral haemorrhage. The trials have included different populations and have had equivocal results but have narrowed down the population of patients that may be more likely to benefit from surgery to those with lobar intracerebral haemorrhages and no intraventricular haemorrhage. The STICH II trial began in the autumn of 2006 and is due to complete patient recruitment at the end of August 2011. **Methods:** This international multicentre pragmatic randomised parallel group trial is being undertaken to establish whether a policy of early surgery improves outcome compared to a policy of initial conservative treatment. Patients with spontaneous ICH should have a superficial lobar haematoma, be within 48 hours of the event, and have a best motor score of 5 or more and a best eye score of 2 or more on the GCS. The treating neurosurgeon should be in clinical equipoise over the risks and benefits of both treatments. The patients may be randomised by telephone or web. If the patient is randomised to surgery the haematoma should be evacuated within 12 hours of randomisation. The primary outcome will be based on extended Glasgow Outcome Scale at six months. **Results:** By mid April 2010, 300 patients had been randomised into STICH II. The patients came from 21 different countries and 57 centres from around the world, including 16 patients from 5 of the 9 registered USA sites. The patients had a median age of 64 years and a median GCS of 13; 56% were male. More than 50% were recruited within 24 hours of ictus. Their haematoma had a median volume of 36 ml and a median depth from the cortex surface of 1mm. Further results will be presented. **Conclusions:** This study is necessary to define the most appropriate treatment for patients with lobar ICH. As we approach our last year of recruitment it is essential to encourage all centres who are yet to recruit as well as our active recruiting centres to increase their efforts for one more year. For further information visit: http://research.ncl.ac.uk/stich/.

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W MP37

In-Hospital Administration of Statins Results in Immediate Benefit: A Short-term Outcome Study

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Background and Purpose: Pretreatment with statins has been shown to improve outcomes and prevent recurrence of ischemic strokes. Statins are thought to have both long term and immediate benefits. The immediate benefits have been hypothesized to involve pleiotropic mechanisms such as anti-inflammatory, neuroprotective, antithrombotic, direct vascular and plaque stabilizing effects. Our goal was to study the use of statins within 24 hours of stroke onset and determine if there is a positive impact on functional outcome by discharge. **Methods:** A retrospective review of a prospectively collected data of all patients with stroke admitted between 2005 and 2009 at a community teaching hospital was conducted. Demographics, stroke subtypes, cerebrovascular risk factors, treatment provided, and outcome were determined. Admission stroke severity was assessed using National Institute of Health Stroke Scale (NIHSS). Length of Stay (LOS) and modified Rankin Scale at discharge (DCmRS) as an outcome measure were also determined. The patients were divided into three groups: A, were not on statins at admission and during hospitalization; B, were not on statins at admission but were started on statins within 48-hours of admission; C, were admitted on a statin and kept

on statin during hospitalization. Measure of means and regression analysis was performed using SPSS (version 14.0) software. **Results:** Of the total 2598 patients, 1003 (Mean Age=72.3, SD +/-14.22; Male=440, 44%) suffered ischemic strokes and met the study criteria. The patient distributions in 3 groups were: A (n=140); B (n=134); and C (n=169). Mean LOS was 7.25 days (SD +/-5.93). Risk factors, (including 751 patients with hypertension, 356 with Diabetes mellitus, and 344 with dyslipidemia) and admission NIHSS were taken into account in the multivariate analysis. No significant difference was noted in the mean admission NIHSS between the groups. The mean DCmRS for group A, B, and C were 2.85, 2.23, and 2.19 respectively. We found significant differences in the mean discharge mRS of Groups A to B ($p=0.002$) and Groups A to C ($p<.001$). No significant results were found between Groups B and C. **Conclusion:** Our findings suggest that starting statins in the acute ischemic stroke setting has a significant positive impact on functional outcome by discharge. Larger controlled studies to determine the dose and timing of initiation of statins are warranted to look at the acute beneficial effect of statins.

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W MP38

Darbepoetin For Prophylactic Neuroprotection In High Risk Aortic Surgery: Results Of A Pilot Trial

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Introduction: Patients undergoing descending thoracic aortic repair are at high risk for spinal and cerebral infarction, and they receive lumbar CSF drains which allow for measurement of CSF markers of neurologic injury. Erythropoiesis medications have extensive preclinical data showing ischemic neuroprotective effects. Hypothesis: Prophylactic darbepoetin alfa (DARB) reduces ischemic neurologic injury in patients undergoing surgical aortic repair. **Methods:** We performed a prospective phase II single center adaptive dose-finding trial of prophylactic DARB that was prematurely ended due to publication of a study showing possible harm of erythropoietin in acute stroke. Enrollment was halted prior to any dose adjustments; 9 patients each received a single IV dose of 1 mg/kg DARB prior to the start of surgery. A prospective series of 9 untreated control patients was subsequently obtained as a comparison cohort. The primary clinical outcome was death or neurological impairment at discharge, defined as National Institutes of Health Stroke Scale (NIHSS) $\geq$ 5 or American Spinal Injury Association (ASIA) motor score $\leq$ 25. Secondary outcomes included changes in levels of CSF S100β and GFAP, ischemia noted on intraoperative SSEP/EEG, or postoperative spinal or cerebral infarction. **Results:** Among the 18 patients enrolled, the median age was 59 (interquartile range, IQR, 55 - 67), 72% were white, and 61% were male. There were no statistical differences between DARB and control patients with respect to demographics and known predictors of neurologic ischemia (age, prior cerebrovascular disease, and extent of aortic repair). Postoperatively, 3 patients (17%) had a cerebral infarction, 2 (11%) spinal infarction, and 1 (6%) both. Two patients (11%) died. At discharge, death or neurologic impairment occurred in 1/9 (11%) DARB patients and 3/9 (33%) controls ($P=0.58$). In patients with evidence of perioperative neurologic ischemia, there were greater median changes in CSF biomarkers from baseline to peak, compared to those without ischemia: S100β, 2301 (IQR 237 - 4371) pcg/ml vs 124 (68 - 250) pcg/ml ($P=0.04$); GFAP, 31780 (IQR -1478 - 77742) pcg/ml vs 311 (IQR -173 - 1089) pcg/ml ($P=0.34$). There were no statistical differences in median changes of CSF biomarkers comparing DARB patients to controls: S100β, 214 (IQR 118 - 235) pcg/ml vs 260 (IQR 68 - 1175) pcg/ml ($P = 0.69$); GFAP, 22 (IQR -490 - 1089) pcg/ml vs 576 (177 - 1403) pcg/ml ($P=0.45$). **Discussion:** This study of patients undergoing aortic repair found no significant effects of prophylactic DARB in reducing poor outcome or CSF markers of neurologic injury, although all point estimates favored treatment over control. Importantly, we have demonstrated that testing a prophylactic neuroprotectant medication in high risk surgical patients is feasible and that CSF markers of injury are dynamic and sensitive to perioperative neurologic ischemic events.

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W MP39

Modern-Day Profile of Young Adults with Ischemic Stroke

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Background: Data concerning stroke in young adults in the United States is limited to a handful of registries (e.g. Baltimore-Washington, Iowa), mostly established over a decade ago. We sought to characterize ischemic stroke in consecutive young adults admitted to our tertiary referral center equipped with modern diagnostic capabilities. **Methods:** We reviewed our Get with the Guidelines-Stroke database from 2005-2010 (n=2643 cases) to identify 215 consecutive inpatients, age 18-45 yrs. Additional clinical details were abstracted from the medical records by a trained stroke neurologist. **Results:** The mean age was 37.5$\pm$7; (age 35-45y in 67%), 51% males, 81% Caucasian. Median NIHSS score 3 (NIHSS$\leq$4 in 63%, 5-11 in 17%, 12-28 in 28%). Traditional risk factors included hypertension 20%, diabetes 11%, dyslipidemia 12%, family h/o stroke 11%, CAD 3%, and cardiac arrhythmia 1%. Other risk factors included illicit drugs 12%, OCP use 19%, migraine 14%, pregnancy 3%. Etiologic evaluation included hypercoagulable panel in 88%, toxicology screen 63%, cardiac echo 87%, CT 97%, MRI 98%, and DSA, CTA or MRA in 99%. PFO was documented in 97 patients (45%). Stroke etiology [with special consideration for PFO given its high rate of detection] was as follows: large artery atherosclerosis 2%, small vessel 7%, other defined 34%, undetermined 11%, cardio-embolic established in 18% (including PFO with ASA 5%), PFO with additional risk factors such as low protein S level in 12%, and isolated PFO in 17%. Defined causes (34%) included arterial dissection 14%, RCVS 7%, cerebral vasculitis 2%, hypercoagulable disorder 3%, Moya Moya syndrome 3%. In-hospital treatment included antiplatelets 62%, anticoagulants 35% and statins 32%. Discharge mRS score was 0-2 in 81%, 3-5 in 16%, and 6 (death) in 3%. Thrombolysis was administered in 13.5% (IV tPA 11%, IA lysis 5%). No patient developed symptomatic post-tPA brain hemorrhage. Comparisons by gender showed that women were younger than men (39 vs. 36 years, $p=0.03$) and had a higher frequency of migraine (22% vs. 7%, $p=0.003$), PFO (54% vs. 34%, $p=0.003$), protein S deficiency at admission (17% vs. 5%, $p=0.004$), and supratentorial infarcts (89% vs. 67%, $P<0.01$), but no significant difference in stroke etiology or discharge mRS. **Conclusion:** In our center, young stroke was common, most patients underwent extensive stroke diagnostic evaluation, and outcomes were generally very favorable. PFO was present in 33.5% of cases. These data reflect the modern-day profile of ischemic stroke in a population of predominantly Caucasian young adults in the Northeastern US.

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W MP40

Prediction of Malignant Middle Cerebral Artery Infarction by CCT and Perfusion CT

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Introduction: Surgical decompression improves outcome in patients with malignant middle cerebral artery (MCA) infarction when performed early. However, objective parameters that reliably predict a malignant course of MCA infarction have not been determined so far. We hypothesized that stroke volume and pre-stroke subarachnoid space (CSF), which indicates the intracranial volume reserve, are major determinants to develop a malignant MCA infarction. We here present a method which allows prediction of the course of large MCA infarction based on CT imaging at admission including perfusion CT. **Methods:** Patients with a proximal MCA occlusion and a reduced cerebral blood flow (CBV) involving at least 1/3 of the MCA territory were included. Patients were classified as having a malignant course of MCA infarction (clinical signs of herniation) or a non-malignant course. CCT at admission was used to determine the CSF-volume in the healthy hemisphere and the intracranial volume (IV). Brain parenchyma volume (BV) was defined as the difference of IV and CSF. CT perfusion with use of a 4D adaptive spiral allowed complete coverage of the MCA territory allowing segmentation of the total volume of significantly reduced cerebral blood flow (CBV), which indicates the infarct core. Normalized CSF volume (nCSF) was defined as CSF/IV and the normalized stroke volume (nSV) was defined as CBV/BV. We then calculated the ratio of nSV and nCSF. To determine which variables best predict a malignant course of MCA infarction a ROC analysis was conducted. **Results:** We included 29 patients (malignant n = 15, non-malignant n = 14). The ROC curve analysis is given in the table. The ratio of nSV and nCSF shows the lowest rate of false negative predictions (7.2%) in combination with a low rate of false positive predictions (6.6%). **Conclusions:** In this study a malignant course of MCA infarction was best predicted by the ratio of nCBV and nCSF. The suggested method therefore allows early identification of patients for surgical decompression. Since our method only requires CCT and perfusion CT it is particularly feasible in clinical practice.

TABLE Prediction of Malignant MCA Infarction

Predicting Factors	Sensitivity, %	Specificity, %	Positive Predictive Value, %	Negative Predictive Value, %
NIHSS, > 14.5	66.7	64.3	66.9	64.1
CBV volume, > 222.7	73.3	100.0	100.0	77.6
CSF volume, < 159.8	66.7	71.4	71.6	66.4
Intracranial volume, > 1407.9	53.3	64.3	61.8	56.0
Midline shift volume, > 13.2	86.7	92.9	92.8	86.6
Normalized stroke vol/normalized CSF, > 1483.6	93.3	92.9	93.4	92.8

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W MP41

Factors Related To Ischemic Lesion Growth In Thrombolysed and Non-Thrombolysed Stroke Patients

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Background: Stroke infarct evolution is known to be related to numerous factors such as age and 'mismatch' (MTT minus DWI) volume. Given possible interactions, we assessed the effects of factors previously shown to affect lesion growth, in cohorts of thrombolysed and non-thrombolysed patients. **Methods:** The full cohort included 274 consecutive ischemic stroke

patients admitted to Massachusetts General Hospital who received DWI/PWI <12 hours since onset and a follow-up MRI on day 5 or later. Patients without analyzable DWI and MTT lesion volumes were excluded and the remaining patients were divided as per their thrombolysis status 'Yes' (n=77) or 'No' (n=151). The effect of age, gender, time to MRI, MTT-DWI volume, admission NIHSS score, admission glucose level, and stroke subtype, on absolute lesion growth (LG) was analyzed using correlation and linear regression; P<0.05 was considered significant. **Results:** The *Non-Thrombolysis cohort* comprised 66% males; mean age 64±16; median aNIHSS 5; mean admission glucose 133±53; mean onset to MRI time 6.4 hours; mean mismatch volume 76±92 cc; stroke etiology 25% large artery, 46% cardio-embolic, 12% other, and 17% unknown-unclassified. On univariate analysis, there was a significant correlation between LG and age (p<0.01) and mismatch volume (p<0.001), a trend towards correlation with time to MRI (p=0.07). The *Thrombolysis cohort* comprised 60% males; mean age 68±14; median aNIHSS 11; mean admission glucose 126±28; mean onset to MRI time 5.3 hours; mean mismatch volume 83±76 cc; stroke etiology 25% large artery, 57% cardio-embolic, 12% other, and 6% unknown-unclassified. On univariate analysis there was a trend towards correlation between LG and age (0.08), and a significant correlation with time to MRI (p=0.01). On multivariate regression analysis in each cohort, only mismatch volume and onset to MRI time remained significant, respectively (Table). **Conclusion:** Age, gender, admission NIHSS, onset-to-MRI time, and mismatch volume are all factors that may influence lesion growth. Except for age, the effect of these factors on infarct evolution may be modified by thrombolysis.

Factor	Non Thrombolysis		Thrombolysis	
	Coefficient	P value	Coefficient	P value
Age	1.7	0.08	8.2	0.07
Male	-17.6	0.62	-208.8	0.09
Admission NIHSS	-5.5	0.08	8.9	0.36
Admission Glucose	0.3	0.36	-3.4	0.13
TOAST etiology	-8.2	0.49	-15.6	0.77
Onset-MRI Time	-1.7	0.76	-92.2	0.01
Mismatch volume	0.92	<0.001	0.4	0.6

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W MP42

Cbv Ratio On Perfusion Mri Revealing The Degree Of Collateral Circulation Predicts The Neurologic Deterioration In Acute Ischemic Stroke

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Collateral circulation is one of the important factors to determine the tissue fate after acute ischemic stroke. However, until now, it is not easy to evaluate its degree in emergency setting. Recently, several reports suggested that the usefulness of rCBV map on perfusion MRI to reveal the status of collateral circulation after AIS. We retrospectively recruited 111 consecutive patients with AIS involving anterior circulation. All patients were evaluated by MRI, including perfusion and diffusion images, and underwent digital subtraction angiography (DSA) for brain within 7 days. The collateral circulation was categorized into three groups, poor (0-1), intermediate (2-3), and good (4). We investigated whether rCBV ratio on perfusion MRI can reveal the status of collateral circulation and its ratio predict the early neurologic deterioration (END, within 7days) after AIS. Of the one-hundred eleven subjected patients, 15 were subjected to poor, 59 intermediate, and 37 good collateral circulation. Diffusion size (p<0.001), neurologic severity (p<0.001), stroke type (p<0.001) and its pattern (p<0.001) was significantly different according to the three groups. Regarding to the rCBV ratio on perfusion MRI, its value on poor collateral group was significantly lower than intermediate and good collateral circulation group. Among 111 patients, 27 patients (24%) had early neurologic deterioration (END) within 7 days of ischemic events. Diffusion size on MRI (p<0.001), neurologic deficit at baseline (p<0.001), poor collateral circulation on DSA (p<0.001), presence of diffusion-perfusion mismatch (DPM, p=0.028), and rCBV ratio on perfusion images (p<0.001) were significantly related with the END after acute ischemic stroke. In multiple logistic regression analysis for predicting the neurologic deterioration after AIS, the poor collateral circulation on DSA (OR=6.92, 95% CI= 1.59 to 30.20; p=0.01), the presence of diffusion perfusion mismatch (OR=3.45, 95% CI= 1.02 to 11.70; p=0.047), and low rCBV ratio on perfusion MRI (OR=6.34, 95% CI= 1.62 to 25.11; p=0.008) had an independent significance for that. This study demonstrated that rCBV ratio on perfusion MRI correlated with the extent of angiographic collateral circulation and had a predictable value for the neurologic deterioration after AIS. Therefore, rCBV ratio on perfusion images might be an important tool to estimate the prognosis the fate in AIS. Further studies will be needed to verify this notion in the future.

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W MP43

Superficial Temporal Artery- Middle Cerebral Artery Bypass in Patients with Severe Steno-occlusive Disease of Intracranial Carotid and Middle Cerebral Artery

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Background: International Cooperative Study of Extracranial / Intracranial arterial anastomosis (EC/IC bypass) in patients with symptomatic carotid occlusive disease did not demonstrate a reduction in risk of stroke recurrence. However, subsequent smaller studies found that superficial temporal artery-middle cerebral artery (STA-MCA) bypass could be beneficial in patients with impaired cerebral vasodilatory reserve (CVR). We evaluated CVR in patients with symptomatic & severe steno-occlusive disease of intracranial carotid (ICA) or MCA and selected patients who could benefit from STA-MCA bypass surgery. **Methods:** Patients with severe steno-occlusive disease of intracranial ICA or MCA were screened with transcranial Doppler (TCD) for their CVR by using breath-holding index (BHI). Breath-holding index (BHI) <0.69 constituted impaired CVR. Patients with impaired BHI were further evaluated with acetazolamide-challenged HMPAO-SPECT according to a standardized protocol. We excluded artery-to-artery embolization as the cause of neurological symptoms by extended TCD monitoring for spontaneous emboli. Patients with significantly impaired metabolic perfusion/CVR on SPECT imaging were offered STA-MCA bypass surgery. CVR was reevaluated with TCD and SPECT in all patients at 6 months and they were followed up for cerebral ischemic events. **Results:** 101 patients (73 males, mean age 56yrs; range 23-78yrs) with severe intracranial stenosis fulfilled our TCD criteria of inadequate CVR on TCD. 33 (33%) patients demonstrated intracranial steal phenomenon (reversed Robin Hood syndrome) with a median steal magnitude of 17% (inter-quartile range, IQR 10). Acetazolamide-challenged HMPAO-SPECT demonstrated impaired CVR in 59 (59%) patients and 34 of them underwent STA-MCA bypass surgery. There were no perioperative complications. TCD and acetazolamide-challenged HMPAO-SPECT repeated at 5±2months after surgery showed significant improvement in CVR in patients who underwent STA-MCA bypass surgery. All cases were followed up (mean 14months; range 3 to 32months) for stroke recurrence. During follow up 30 out of the 67 (45%) cases managed with best medical therapy developed subsequent cerebral ischemic events. In comparison, after STA-MCA bypass, only 4 of the 34 (11%) cases developed subsequent events (absolute risk reduction 34%, p=0.002). Significant benefit was noted in early morning headache and lethargy in the STA-MCA bypass patients (80% versus 12%; p<0.0001). **Conclusion:** Symptomatic severe intracranial steno-occlusive disease with impaired CVR carries a high risk of cerebral ischemic events. Significant reduction in stroke recurrence can be achieved by STA-MCA bypass in carefully selected patients.

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W MP44

Differences in Short-term Outcomes in Patients with Acute Lacunar Infarction Related to Small versus Large Artery Disease

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Background: Lacunar infarction was classically attributed to *small artery disease* (SAD), specifically lipohyalinosis of the small penetrating arteries. More recently, it has been proposed that in some patients lacunar infarction may be secondary to large artery atherosclerotic disease (LAD) of the parent artery. We wanted to determine the prevalence, risk factors and prognostic significance of LAD as a mechanism for lacunar infarction. **Methodology:** Consecutive patients admitted to the Toronto Western Hospital with an acute ischemic stroke between 2003 and 2008 were selected from the Registry of the Canadian Stroke Network database. Patients with an Oxfordshire Community Stroke Project of Total Anterior Circulation Stroke (TACS) or a Partial Anterior Circulation Stroke (PACS) and those without MR imaging or without vascular imaging were excluded. The final cohort for analysis included only patients with a single area of restricted diffusion ≤1.5 cm on MR imaging in the symptomatic penetrating artery territory. MR or CT angiography were used to determine whether there was narrowing (presumed plaque) in the relevant parent artery (e.g. middle cerebral artery for lenticulostriate territory infarcts) and as an indicator that the infarct was potentially on the basis of LAD. Vascular risk factors, clinical characteristics and outcomes (neurological worsening in hospital, modified Rankin (mRS) at discharge) were compared in patients with lacunar type infarcts with (LAD group) and without (SAD group) evidence of large artery atherosclerosis. **Results:** The final cohort consisted of 76 patients with confirmed lacunar infarction. Overall, 33% had underlying LAD. Large artery disease was present in 6/24 (25%) anterior circulation infarcts and 19/52 (37%) posterior circulation infarcts. There was no difference in age, gender, risk factors (hypertension, diabetes, cigarette smoking, hypercholesterolemia) and initial stroke severity between the two groups. Multivariate logistic regression analysis showed that LAD

group patients were less likely to have a good outcome (mRS ≤2 - OR 0.25; 95% CI 0.06 - 0.97) but paradoxically were less likely to have neurological worsening while in hospital (OR 0.13; 95% CI 0.03 - 0.67). **Conclusions:** These data suggest that one third of MR confirmed acute lacunar infarcts could be attributable to LAD. There were no significant differences in atherosclerotic risk factors between the groups. The LAD group had worse outcomes. The SAD group patients were more likely to have neurological worsening, although this may represent fluctuations in neurological deficits. These findings suggest that it is important to image the intracranial cerebral arteries in patients with lacunar infarction to determine the underlying etiological mechanism.

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W MP45

Prevalence and Outcome in Acute Ischemic Stroke Patients with MCA Stenosis: Results from the Taiwan Stroke Registry

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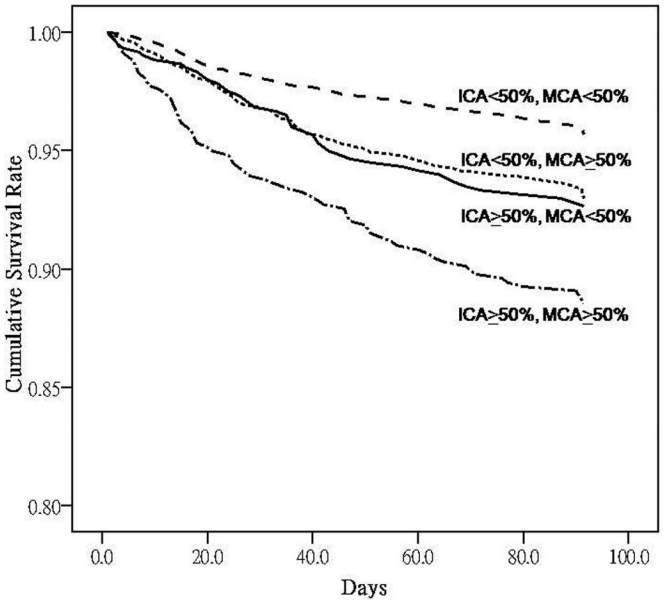
Background and Purpose: Asians have higher frequencies of intracranial artery stenosis. We investigated risk factors, outcomes, and survival in ischemic stroke patients with or without middle carotid artery (MCA) stenosis. **Methods:** Patients were consecutively registered in a prospective multicenter Stroke Registry in Taiwan (The Taiwan Stroke Registry, TSR) within 10 days of acute ischemic stroke or transient ischemic attacks. Patients were grouped according to the status of the stenosis (≥50% or <50%) in their MCA and extracranial internal carotid artery (ICA). A modified Rankin scale of 2 or above at 3 months was considered an unfavorable outcome. A survival analysis with Cox model was conducted to estimate the early stroke recurrence and mortality. **Results:** Among 11,118 patients, 10.6% had extracranial ICA stenosis and 28.4% had MCA stenosis. Patients with MCA stenosis had higher NIHSS on presentation than those without MCA stenosis (MCA and ICA stenosis, 9.6±8.0; only MCA stenosis, 7.7±7.0; only ICA stenosis, 7.1±6.8; no MCA and ICA stenosis, 5.4±5.5, P<0.0001). Patients with ICA stenosis were more likely to have ischemic heart disease, smoking habit, diabetes mellitus, and hypercholesterolemia; and those with MCA stenosis had a higher frequency of diabetes mellitus. Compared to patients without ICA or MCA stenosis, unfavorable outcome at 3 months poststroke were increased in patients with coexisting ICA and MCA stenosis (OR 1.98, 95% CI 1.54 to 2.53, P<0.0001) and with only MCA stenosis (OR 1.25, 95% CI 1.11 to 1.41, p=0.0002). **Conclusions:** MCA stenosis was more prevalent than extracranial ICA stenosis in ischemic stroke patients in Taiwan. Patients with MCA stenosis, alone or combined with extracranial ICA stenosis, had more severe neurological presentations and carried a higher risk for unfavorable outcome.



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W MP46

Middle Cerebral Artery Plaque in Patients with A Single Infarct in the Territory of Deep Penetrating Arteries: a High-resolution MRI Study

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Background and Purpose: Human microanatomy studies suggested most of the penetrating arteries of middle cerebral artery (MCA) arise from dorsal-superior surface of MCA trunk. An atheroma at the orifice of a penetrating artery may cause an infarct. In this study, using high-resolution magnetic resonance imaging (HR-MRI) in vivo, we aimed to investigate the incidence and the distribution of MCA plaques in patients with a single infarct in the territory of deep penetrating arteries. We attempted to analyze the clinical relevance of such plaque distribution in relation to the orifices of penetrating arteries. **Methods:** Using a 3-T MRI system, magnetic resonance angiography (MRA), HR-MRI, and routine cranial MRI (T1-, T2-weighted, FLAIR and diffusion-weighted imaging) were performed on 35 consecutive patients with a single infarct in the territory of deep penetrating arteries and without high grade (>50%) MCA stenosis. All the cross-sectional image slices of the MCA ipsilateral to the ischemic lesion were analyzed for the artery wall abnormalities. On HR-MRI, the normal MCA walls were defined as homogenous fine lines. Plaques were identified if there was markedly eccentric or focal wall-thickening with heterogeneous signals. Plaques were further categorized based on the involvement of superior, inferior, dorsal or ventral wall. The incidence and the distribution of MCA plaques, the maximum infarct area on axial FLAIR images, and the infarct patterns on HR-MRI images were studied. **Results:** Of the 35 patients, MRA indicated a normal or low-grade stenotic MCA (<30%) in all. Eccentric plaques were identified on HR-MRI in 10 (28.6%) patients, while normal walls were observed in 25 (71.4%) patients. MCA plaques located at the superior and/or dorsal wall in 6(17.1%) patients. The infarcts displayed inverted-trapezoid or wedge shape on HR-MRI images, irrespective of the presence of MCA plaques. In the patients with a MCA plaque involving dorsal or/and superior wall, the maximum infarct area on axial FLAIR images was 1.3±0.2 cm2 (range, 1.0 to 1.5 cm2). Comparatively, larger variance of the maximum infarct area was observed in the patients without MCA plaques on HR-MRI (1.5±1.3 cm2; range, 0.4 to 4.1 cm2). **Conclusions:** MCA plaques are not uncommonly identified on HR-MRI in patients with a "traditional lacunar infarct". The penetrating artery infarct with a MCA plaque involving dorsal or/and superior wall may be a unique subgroup of intracranial large artery disease.

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W MP47

Subclinical Extracranial Carotid And Peripheral Arterial Disease As Risk Factors For ASymptomatic Intracranial Atherosclerosis (ASIA) In The Barcelona-ASIA Study: The Relevance Of A Global Evaluation

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Background and Purpose: The prevalence of asymptomatic intracranial atherosclerosis (ASIA) in patients with subclinical carotid or peripheral arterial disease (PAD) is unknown. The aims of the Barcelona-ASIA study are (1) to determine the prevalence of ASIA in a moderate-high vascular risk population, (2) to study its prognostic impact on the risk of suffering future major ischemic events, and (3) to identify predictors of the development, progression and clinical expression of this condition. This study focuses on the frequency of intracranial involvement in patients with subclinical peripheral and extracranial carotid atherosclerotic disease in our cohort. **Methods:** Population-based study of a representative sample of 933 individuals (64% men, mean age 66.3 years) with a moderate-high vascular risk (assessed by REGICOR≥5, a Framingham function validated for Spanish population) and prior history of neither stroke nor ischemic heart disease. PAD was defined as an ankle-arm index (AAI) < 0.9 at baseline. All individuals underwent extracranial and transcranial Color-Coded Duplex performed by two unique investigators in a single laboratory to detect the presence of carotid plaques (CP: intima-media thickness ≥1.5), significant carotid stenosis (CS: ≥50% or occlusion) and ASIA (presence of intracranial stenosis by systolic peak and spectrum criteria). ASIA and carotid stenosis ≥70%/occlusions were also assessed by magnetic resonance angiography. **Results:** ASIA was detected in 78 subjects (8.4%), 27 with moderate-severe intracranial estenosis (2.9%). Impaired AAI at baseline was found in 7.2% of subjects (in 6.9% as the first manifestation of PAD), CP (≥1 plaque) in 50% of subjects and a CS in 3.1%. The prevalence of ASIA was significantly higher in patients with impaired AAI (25.4% vs 7.1%), CP (13.1% vs 3.7%) and CS (38% vs 7.5%) as compared to those without PAD or extracranial carotid atherosclerosis. Remarkably, the prevalence of ASIA was minimal (3%) when both AAI and carotid ultrasound were normal, but was as high as 30% when both examinations were pathological. Impaired AAI (OR, 3.6; 95% CI, 1.91-6.75), CP (OR, 3.27; 95% CI, 1.86-5.77) and CS (OR, 5.45; 95% CI, 2.37-12.54) were independently associated with ASIA after adjustment for the REGICOR score. **Conclusions:** Subclinical peripheral arterial disease and carotid atherosclerosis increase 3 to 5 fold the probability of ASIA. A complete intracranial arterial evaluation may be needed in these subjects.

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W MP48

Detection Of Intracranial Arterial Stenosis In The Anterior Circulation By Transcranial Doppler

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Background: Intracranial atherosclerosis is a common cause for stroke in Asian countries. Patients with >50% intracranial arterial stenosis can be detected by a simple, convenient and noninvasive method for intracranial stenosis by Transcranial Doppler (TCD). The accuracy of different mean flow velocity (MFV) thresholds for determining the degree of stenosis remains uncertain. **Methods:** Prospective, observational cross sectional study from Chennai, India of 2152 consecutive stroke patients in whom complete TCD evaluation were done using a Power M Mode portable TCD machine (Spencer Technologies, Seattle, USA) to detect the presence of intracranial arterial stenosis. Bitemporal, Orbital and transforaminal windows were insonated. TCD findings were correlated with magnetic resonance imaging (MRI), computed tomography(CT), and digital subtraction angiography(DSA). The demographics and standard risk factors for stroke were evaluated and carotid duplex imaging performed. Extracranial carotid stenosis was diagnosed if its peak systolic velocity was higher than 140 cm/s and the systolic ratio was more than 1.8. **Results:** Of 2152 consecutive patients, suboptimal or poor temporal widows were seen in 359 (16.68%), terminal internal carotid (TICA) artery stenosis in 321(14.91 %), middle cerebral artery (MCA) stenosis in 382(17.75 %), anterior cerebral artery (ACA) stenosis in 132(6.13 %) and posterior cerebral artery(PCA) stenosis in 148(6.95 %). For all vessels, with MFV > 100 cm/s, TCD had a sensitivity of 97 %, and a specificity of 92% (CI = 97%-99%). High grade extracranial Carotid stenosis of (>70%) were present in 231(10.73 %). **Conclusion:** TCD is a very sensitive and specific method for the diagnosis of more than 50% intracranial arterial stenosis. There is a good correlation between TCD findings and MRA/CTA. There is a high prevalence of intracranial atherosclerosis, when compared to carotid stenosis in India.

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W MP49

The Effect Of Intravenous Thrombolysis Using Recombinant Tissue Plasminogen Activator (rt-PA) For Acute Ischemic Stroke

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Background and Purpose: Stroke is the second cause of death and morbidity in china. Over four fifths of strokes are ischemic. We accessed the efficacy and safety of intravenous recombinant tissue plasminogen activator (rt-PA) to treat patients with acute ischemic stroke (AIS) 4.5 hours from stroke. **Methods:** 60 patients within 4.5 hours after stroke onset were randomized to rt-PA group or control group. National Institutes of Health Stroke Scale (NIHSS) before thrombolysis therapy and at 2h,24h,7d and 90d after thrombolysis were compared. Barthel index (BI) and modified Rankin score (mRs) before thrombolysis and at 7d and 90d after thrombolysis were also compared. The incidence of sICH (symptomatic intracerebral hemorrhage) was analysed. **Results:** We found statistically significant difference of NIHSS, BI and mRs at each time point between rt-PA group and control group ($p<0.05$). There was no significant difference in the incidence of sICH between two groups ($p>0.05$). **Conclusions:** Intravenous thrombolysis with rt-PA is efficient and safe in selected ischemic stroke patients. The efficacy of rt-PA is time dependent. We should shorten stroke-to-rt-PA times.

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W MP50

Is Multiple Sclerosis a Vascular Disease? Venous Stent-Angioplasty for Treatment of Multiple Sclerosis

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Introduction: Chronic cerebrospinal venous insufficiency has come to prominence recently in as a strong correlate in patients with multiple sclerosis (MS). Investigations have for the most part centered on non-invasive imaging protocols to document the presence, location and severity of these vascular hemodynamic anomalies in the principal extra cranial cerebral veins. Here we report a case study involving a patient undergoing endovascular therapy for such abnormalities. **Clinical:** The patient is a 38 years old female and was diagnosed with multiple sclerosis twelve years ago. She is currently on Copaxone and follows regularly with a neurologist. Her disease course has included several major exacerbations and multiple flare-ups, documented by serial MR imaging. This imaging was performed to assess for new lesions which could account for new symptomatology and is likely to be the most compatible with a secondarily progressive MS subtype. Gait instability and fatigue at increasingly shorter distances as well as increasing T2 lesion load on MR imaging prompted her to seek an alternative therapy. After undergoing interventional procedure improvement in her fatigue and walking distance were reported. Post-procedural neurological exam findings were subtle improvement in strength and gait. **Technique:** Initial catheter venography revealed a high-grade stenosis of the right internal jugular vein at its junction with the brachiocephalic vein. It was treated with angioplasty with significant improvemed emptying of the jugular vein. Follow-up venography after one month revealed a restenosis at the same location as well as a moderate stenosis at the origin of the left internal jugular vein. Both were treated with angioplasty with significant reduction of stenosis. Follow-up venography after two months revealed severe stenosis of the right internal jugular vein and a moderate to severe stenosis of the left internal jugular vein which were treated with angioplasty and stent placement with a good result. Further follow-up venography is pending. **Conclusion:** Catheter based angiography and venography in select patients with progressive and therapy-refractive MS may be a feasible and relatively safe option for consideration of endovascular therapy and would necessitate further investigation in the context of a clinical study.

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W MP51

Stroke Rehabilitation: Closing the Loop

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Background: Noninvasive brain computer interface (BCI) has potential advantages for restoration of motor function after stroke. There may be additional advantages for combining BCI with functional electrical stimulation (FES) and tongue stimulation (TS). In the preliminary phase of this study we investigate whether FES, in addition to TS, directed by electroencephalogram (EEG-BCI) output, can increase the extent of stroke recovery as indexed by behavioral measures and induce brain plasticity as measured by functional magnetic resonance imaging (fMRI). **Methods:** The proposed closed loop device consists of three components; 1) an EEG-BCI sensor system for detecting real-time volitional command signals from motor cortex, 2) a FES component for activating muscle contraction in the affected limb, and 3) a sensory stimulation module (i.e., TS unit) to provide sensory feedback and increase the general excitability of the afflicted sensory-motor system through latent intact neural pathways. Preliminary testing of the device will be performed on a stroke patient with upper extremity motor deficits. fMRI scans prior to the training on the BCI task will be collected from the patient while attempting or imagining motor tasks in the scanner. The same tasks will be used during training. The BCI-FES-TS intervention will consist of trials of either attempted finger movement contrasted with relax conditions or imagined finger movement and relax conditions. Brain signals from the affected hemisphere will be used to trigger FES for movement practice. The patient will undergo training on the closed loop device for a minimum period of three days, 30 minutes every day for three weeks. Following this training, the patient will be scanned again while performing motor tasks in the scanner. **Results:** We expect that the patient will show improvement in accuracy on the BCI task over time across the nine sessions. The training on the closed loop should show significant improvement in motor performance using the affected hand by the end of the training. **Conclusions:** In addition to serving as a guide valuable for placement of the EEG-BCI sensor system, fMRI can offer valuable insights into the reorganization changes occurring in the brain after a stroke. It is proposed that this closed loop rehabilitation device would be used during post-stroke rehabilitation procedures (i.e., physical therapy sessions) and would reduce the duration of rehabilitation and increase the level of recovery.

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W MP52

Selecting for Intra-arterial Thrombolysis Following Intravenous Thrombolytic Therapy for Acute Ischemic Stroke Using CT Perfusion

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Background and Purpose: Combined intravenous (IV) and intra-arterial (IA) thrombolytic therapy theoretically takes advantage of both modalities, but little is known about the efficacy and risks of this approach. The presence of mismatch, or salvageable tissue on CT perfusion (CTP) may help select for patients most likely to benefit. This study sought to evaluate the efficacy and safety of this approach. **Methods:** A retrospective chart review was conducted from January 1, 2008 to July 31, 2010. Patients presenting with acute ischemic stroke who had a CTP performed and received both IV and IA thrombolytic therapy with recombinant tissue plasminogen activator (r-tPA) were included in the analysis. **Results:** Twenty-two patients receiving combined IV and IA r-tPA therapy had a CTP performed; 21 patients had presence of mismatch, and one had a matched deficit. Ten patients had a CTP prior to IV r-tPA administration, and twelve prior to IA r-tPA administration. One patient on a continuous therapeutic heparin infusion received 0.45 mg/kg of IV r-tPA, while all others received 0.9 mg/kg. The mean dose of IA r-tPA was 20mg (range 6-52 mg). Among patients with matched deficits on CTP, median age was 63 (range 43-94). Eighteen (86%) patients had mechanical clot disruption or retrieval, or angioplasty performed in addition to IA r-tPA administration. Complete or partial revascularization of the target vessel was achieved in 20 (95%). Mean time to IV r-tPA and IA r-tPA administration was 163 minutes (range 55-865) and 432 minutes (range 184-1000), respectively. Twelve (57%) patients received IA r-tPA > 6 hours from symptom onset. Symptomatic intracerebral hemorrhage (ICH) occurred in 1 (4.7%) patient. Two patients died, one from ICH occurring 22 days after thrombolytic therapy, and one was made comfort measures after having progressive ischemic strokes from a cardioembolic source despite therapeutic anticoagulation. Median NIHSS prior to endovascular therapy was 17 (range 3-30); median NIHSS on discharge was 7 (range 0-45). Six (29%) patients had a discharge mRS of $\leq$ 2. Three (14%) patients were discharged home, and 13 (62%) were discharged to acute rehabilitation. **Conclusions:** Selection of patients for sequential IV and IA r-tPA administration for acute ischemic stroke based on presence of CTP mismatch appears to be safe, associated with a high recanalization rate, and good outcomes.

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W MP53

China Stroke Screening And Prevention Project

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According to Third National Survey on Causes of Death in China in 2008, the proportion of chronic non-communicable disease (NCD) death among total death increased from 76.5% in the early 1990s to 82.5% in 2008. Cerebrovascular death was the top cause of death among NCD deaths. Currently, over 7 million survival stroke patients exist in China and over 2 million new cases and 1.5 million new deaths each year on average. Most survived stroke patients live with severe disabilities and low quality of life. While hypertension control has been taken as the most important strategy for stroke prevention, the management of other risk factors are also given more and more attentions. However, carotid artery stenosis caused by atherosclerosis plaques does not get enough attention as the key risk factor of stroke. Carotid artery examination by echo has not included in routine physical examination for patients with high risk of stroke. Implementation of carotid endarterectomy (CEA), an effective preventive strategy for stroke, develops slowly in China and less than 1000 cases of CEA are performed each year even it is estimated that at least 500 000 patients need to receive CEA annually. In 2009, a project entitled "Screening and prevention of stroke in China" was initialed by Ministry of Health of the People's Republic of China. Aims of the project are to develop guidelines for the prevention of ischemic stroke, to strengthen the training of specialists on carotid artery screening and CEA , to screen the carotid artery stenosis among high risk population, and to establish one national stroke center in every large and medium cities in China within the next 5 years. Keywords: stroke, carotid endarterectomy, screening, prevention, carotid artery stenosis

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W MP54

Intravenous rt-PA Is Not Effective In Large Vessel Related Stroke

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Introduction: The NINDS trial suggests that intravenous rt-PA is effective for all ischemic stroke types including large vessel (ICA, MIMCA) stroke. We compared the outcomes of IV vs IA thrombolysis on hospital discharge outcomes. **Methods:** All patients with ischemicstroke after NCCT and CTA were treatedwith either IV or IA thrombolysis. Outcome: Discharge home or acute rehabilitation vs nursing home or death. **Results:** A Total of 88 patients between 2006-2009 were included in the analysis. 48 patients (20 large vessel, 28 distal branches) underwent IV and 40(large vessel) IA thrombolysis. Baseline NIHSS was higher in IA treatedpatient(17.33 vs 15.59, P<0.001). Of the 60 patientswith large vessel occlusion, IV thrombolysis resulted in no discharge home, 25% acuterehabilitation, 50% nursing home and 25% died. Of the IA group 20% were dischargedhome, 50% acuterehabilitation, 10% SNF and 10% died. Partial or complete recanalization predicted a good outcome(p=0.05,OR16.17), while baseline NIHSS(p=0.05,OR0.84), admission glucose((p=0.08,OR 0.97) andpost procedure bleeds(p=0.05, OR 0.153) predicted a poor outcome. Time to endovascular recanalization did not affect outcome. Of the 28 patients with distal occlusions, 15% , 25%, 18% and 3.6% respectively were discharged home, acute rehabilitation SNF or died respectively. **Conclusions:** Compared to IA, IV thrombolysis is not effective in large artery related stroke, but is effective for distal branch occlusion. Future studies should incorporate CTA in the imaging protocols to determine the most effective thrombolytic therapy modality.

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W MP55

Higher Diastolic Blood Pressure May Be Beneficial in Acute In-patient Stroke Rehabilitation

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Introduction and Hypothesis: Control of hypertension is a well established goal of primary stroke prevention but management of blood pressure (BP) after acute stroke is complicated by the effect BP changes may have on cerebral perfusion. While there seems to be convincing evidence that lowering BP improves outcome in patients with stroke in the long run, the impact of lowering BP in the short run is controversial. Some studies suggest that high systolic BP (SBP) in acute ischemic stroke is associated with death and dependency. Conversely, other studies show either no relationship between increased BP and outcome or a relationship between increased BP and better outcome. However, the impact of BP on stroke rehabilitation outcomes remains unknown. We assessed the hypothesis that BP affects rehabilitation outcomes. AIM: To explore the associations between mean SBP, mean DBP, minimum SBP, maximum SBP, minimum DBP, maximum DBP, mean arterial pressure (MAP) and rehabilitation outcomes as measured by the Functional Independence Measure (FIM) scores at admission and discharge from inpatient rehabilitation, in order to: 1. Evaluate the impact of BP levels on outcome, as measured by the Functional Independence Measure (FIM), in patients undergoing acute inpatient neuro-rehabilitation. 2. Determine the optimal range of BP for best FIM outcomes during stroke rehabilitation. Method: A prospective, observational study conducted in an acute inpatient rehabilitation setting between 2009 & 2010. Data on 214 neuro-rehabilitation patients, including 145 pure stroke patients, were reviewed for BP and FIM scores. Each patient had 3 BP recordings per 24 hour period - at 6am, 2pm and 10pm. Mean SBP and DBP were calculated for each patient, for their entire length of stay. Similarly, the means of their maximum daily and minimum daily SBP and DBP were extracted. Finally, each patient's mean arterial pressure during their rehabilitation stay was calculated. Linear regression and correlation were performed to seek an association between BP values the FIM change, i.e., change in FIM between admission and discharge. **Results:** for the entire neuro-rehabilitation population, only maximum DBP was statistically significantly associated with positive FIM changes, (p=0.053). Similar results were obtained when stroke patients were analyzed separately (p=0.043). Furthermore, BP were in the following ranges during inpatient rehabilitation: mean SBP 132, minimum 95 and maximum 181; mean DBP 72, minimum 50 and maximum 101; mean MAP 92, minimum 70 and maximum 120. We observed no adverse FIM consequences within these ranges. **Conclusion:** DBP may have an important bearing on functional gains in stroke and neuro-rehabilitation. Excessively low DBP should therefore be avoided. While it is difficult to state what the optimal BP should be for stroke rehabilitation, the above ranges were found to be safe in our patient population.

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W MP56

Central Post-stroke Pain And Musculoskeletal Pain: Their Relationship With Post-stroke Depression, Fatigue And Quality Of Life

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Background and Aims: Pain is a common and disabling sequela of stroke, and comprised largely of central post-stroke pain (CPSP) and musculoskeletal pain (MSP). The aim of our study was to investigate possible differences in factors related to CPSP and MSP in terms of post-stroke depression, fatigue, social support and patients' quality of life (QOL). **Methods:** Three hundred and twelve consecutive patients with acute stroke admitted at Asan Medical Center were prospectively followed up until 12 months post stroke. CPSP was defined as persistent paresthesia/pain (visual analogue scale $\geq$ 5) at the body part of sensory impairment. MSP was defined as nociceptive pain triggered or aggravated by joint movements. Patients with those painful symptoms before the stroke were excluded. PSD was assessed by Beck Depression Inventory, fatigue by fatigue severity scale, perceived social support by the ENRICHD Social Support Inventory, and QOL by Stroke Specific QOL by Williams. **Results:** At 12 months post-stroke, pain was present in 94 patients (30.1%); 43 (13.7%) had CPSP, 33 (10.6%) MSP and 18 (5.8%) had both. Logistic regression analysis showed that CPSP was associated with sensory dysfunction (OR 2.217, CI 1.005-4.940, p=0.049), motor dysfunction (OR 2.175, CI 1.021-4.634, p=0.044), depression (OR 2.266, CI 1.037-4.952, p=0.040), while MSP was associated with low level of education (OR 0.203, CI 0.066-0.628, p=0.006), motor dysfunction (OR 2.492, CI 1.096-5.665, p=0.029), and fatigue (OR 2.360, CI 1.153-4.832, p=0.019). CPSP and MSP are both significantly related to low QOL; the mean (standard deviation) score of QOL was 3.83 (0.82) in patients with CPSP vs. 4.40 (0.68) in those without (p<0.001), and 3.81 (0.81) in patients with MSP vs. 4.38 (0.69) in those without (p<0.001). **Conclusions:** CPSP is more closely related to depression while MSP is related to low level of education and fatigue. Both are significantly associated with decreased QOL in stroke patients.

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W MP57

Gender Does Not Predict Discharge Functional Independence Measure after Stroke

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Purpose/Hypothesis: Individuals who survive stroke comprise the largest group of adults with disability. Rehabilitation professionals provide therapeutic treatments with the goal of improving functional independence. There is some evidence that gender may be a predictor of stroke rehabilitation outcomes with females at the greater risk for poorer outcomes. However, results about the influence of gender on rehabilitation outcomes have been limited. The purpose of this retrospective study was to determine the role of gender in stroke rehabilitation outcomes in the United States. Subjects: For this retrospective analysis, 97,335 men and women with a diagnosis of stroke and admitted to an in-patient rehabilitation facility were identified in the Allied Health Research Institute (AHRI) database. **Methods:** Participant cases were excluded if there was any diagnosis or ICD 9 code that indicated a neurological diagnosis other than stroke, missing or incomplete data or individuals who resided in a nursing home or long-term care facility prior to stroke onset. Group differences (males, females) in demographic measures (age, length of stay and admit Functional Independence Measure (FIM) were tested with one-way ANOVA. To determine whether gender was a significant predictor of the FIM at discharge from inpatient rehabilitation, a stepwise regression analysis was used to determine which variables are significant predictors (age, gender, marital status, length of stay) of the discharge FIM score. **Results:** From our initial sample, 12,384 individuals (5,864 males and 6,520 females) met the inclusion/exclusion criteria for this study. For individuals in this data set, the mean age was 70.6 +/- 13.0 years, the length of stay was 12.5 +/- 7.6 days and the admission FIM was 72.8 +/- 18.2 out of a possible 126. We found significant differences between males and females for age (69.3 +/- 12.7 males; 71.9 +/- 13.2 females, p < 0.001), but not for length of stay (12.3 +/- 7.7 males; 12.6 +/- 7.4 females, p = 0.16) or for admission FIM (73.1 +/- 18.5 males; 72.5 +/- 18.0 females, p = 0.07). In the regression model, admit FIM score was the strongest predictor (R2= 0.634) of discharge FIM. When length of stay was added, the model improved slightly (R2 = 0.65). When controlling for age in the regression model, the admit FIM score remained a significant predictor (R2 = 0.634). Gender did not improve the model. **Conclusion:** For

our sample, gender was not a meaningful predictor of functional outcomes after stroke rehabilitation.

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W MP58

Predicting and Detecting Arm Motor Gains in a Trial of Robotic Therapy

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Introduction: Optimal patient selection and patient assessment can maximize the likelihood that a clinical trial of a restorative therapy will detect treatment-induced behavioral gains when present. The current analysis compared multiple arm motor assessments for ability to predict, and to detect, clinically meaningful behavioral gains from robotic therapy. **Methods:** Enrollees were combined across 3 studies that provided 23-24 hours of standardized arm motor robotic therapy, which consisted of repeated grasp-release affected hand movements. Entry criteria included age >18 yr, stroke >3 mo prior, >5 deg range of motion in affected index finger MCP, >25% prolongation to complete 9-hole pegboard (9HP), and no severe apraxia/sensory loss/aphasia/depression. Prior to and at end of therapy, patients were assessed on 8 different measures of arm motor status: Fugl-Meyer Arm Motor Scale (FM-total), Fugl-Meyer Arm Motor Scale-Hand Subsection (FM-Hand), Action Research Arm Test, Box/Blocks Test, time to complete 9HP, hand motor subscale of SIS-2, force of grasping, and force of pinching. Analyses used non-parametric statistics to (1) examine prediction of treatment gains; for each measure, baseline score was correlated with change in that score. (2) examine responsiveness of each scale, defined as percentage of subjects in whom the change in score exceeded 10% of that score's maximum value. **Results:** The 37 patients had a wide range of arm motor deficits at baseline, e.g., baseline FM scores ranged from 14-60 (38 +/- 15, mean +/- SD), with 38% having some aphasia and a wide range of generally moderate sensory deficits. Baseline scores were normally distributed for none of the 8 measures, instead showing tails at one or both ends. In terms of predictors, no single scale showed a significant and meaningful prediction across all subjects. However, among weaker patients (i.e., excluding patients in top quartile, as defined for each scale), FM-hand and FM-total ($r=0.5$, $P<0.02$ for both) were each significant predictors; among stronger patients (remove bottom quartile), Box/Blocks emerged as a significant predictor ($r=0.57$, $P<0.04$). In terms of responsiveness, SIS performed best (49% of subjects improved by 10% maximum score), followed by pinch and FM-hand. When analyzing only the 19 strongest or the 18 weakest patients, SIS remained the best performer. **Conclusions:** In a clinical trial setting, choice of test instrument is important for optimizing patient selection and for detecting treatment-induced gains when present. In the setting of arm motor therapy for chronic stroke, best prediction of treatment gains was achieved by using one test for weaker patients and a different test for stronger patients–no one test covered all. In terms of responsiveness, the self-rated SIS performed best. These results may be useful for guiding entry criteria and outcome measures in clinical trials of restorative agents.

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W MP59

Stroke Rehabilitation using a Portable Robot Improves Biomechanical and Clinical Outcome Measures

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Background: Spasticity, contracture and motor impairment are major sources of disability in stroke. Specifically, impaired ankle function is a frequent cause of limitation in ambulation. Previous studies reported positive improvements in ankle joint properties with intelligent feedback-controlled stretching intervention (Selles et al. APM&R 2005). There is a need for an effective and convenient rehabilitation program combining intelligent stretching and biofeedback active training to treat stroke survivors with impaired ankles and promote motor learning. The portable robotic rehabilitation device would make treatment at physical therapy clinics and patient homes easily accessible. Objective To investigate the biomechanical changes and clinical outcome in stroke survivors induced by controlled passive stretching and active movement training of the impaired ankle using a portable rehabilitation robot. **Methods:** Eight stroke survivors (mean age 50.4±8.9 years, stroke duration 44.2±19.2 months,6 left and 2right hemiplegic, 5 male, 3 female) participated in a passive and active movement training program (three times per week for six weeks), using a portable ankle rehabilitation robot. Each training session included passive stretching under intelligent control and biofeedback active movement training through motivating games with the robot providing assistance or resistance as needed. Biomechanical and clinical evaluations were done before and after the training and six weeks after the treatment (Table1). **Results:** The 8 subjects showed improvements in all the outcome measures (Table 1). Active dorsiflexion range and dorsiflexor muscle strength significantly improved ($p=0.001$ and 0.01, respectively) as well as the average MAS, STREAM, Berg Balance ($p=0.04$, 0.03, 0.04). These improvements except the MAS reduction were still observed six weeks after the study was completed (Table1). **Discussion:** The improvements in ROM, strength and spasticity reduction might contribute to the improved functional mobility seen in the improved STREAM score, 6-minute walk and Berg Balance Score. Frequent and convenient rehabilitation using the portable rehabilitation robot can benefit stroke survivors that have impaired ankles.

Table 1: Outcome Measures

	Outcome Measure	Before Training	After Training	Follow up (6-week post)
Biomechanical measures	Passive Dorsiflexion *	12.53±7.0deg	15.26±4.5deg	15.35±4.9deg
	Active Dorsiflexion *	-18.44±13.7deg	-5.83±11.9deg	-11.6±10.4deg
	Dorsiflexor Muscle Strength	3.26±3.1Nm	7.10±3.7Nm	7.10±4.1Nm
Clinical Evaluations	Modified Ashworth Scale (MAS)	3.38±0.7	2.38±1.5	3.17±1.3
	Stroke Rehabilitation Assessment of Movement (STREAM)	26.75±4.4	29.63±6.3	28.50±7.2
	6 Minute Walk	166.31±97.3m	182.05±97.9 m	203.2±98.5m
	Berg Balance Test	39.00±10.1	41.83±10.6	44.0±4.7

*reference from a 90 degree angle between the tibia and foot.

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W MP60

Structural Integrity Of The Contralateral Hemispheric White Matter Is Important For Recovery After Unilateral Ischemic Stroke

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Introduction: Experimental and human stroke studies suggest that preserved structural and functional integrity of the contralateral to the ischemic stroke hemisphere is strongly correlated with greater degree of subsequent recovery. Increasing fractional anisotropy (FA) values, measured by obtaining MRI diffusion tensor imaging studies, have been shown to correlate with integrity of the white matter. **Objectives:** To define the FA values in the region of the unaffected hemisphere that is homologous to the ischemic lesion (ROI-UN) at one month after stroke onset, and correlate these values with the clinical neurological scores in patients with ischemic stroke. **Main Hypothesis:** Elevated FA values in the ROI-UN at 1 month after stroke correlate with a greater NIHSS score improvement from baseline to outcome study (3 months). **Methods:** We prospectively studied ischemic stroke patients with clinical scores and MRI scans at baseline (1-3 days), 1 month an 3 months. The clinical neurological deficit was graded with NIHSS at each time point. The baseline scan was used for definition of lesion size. Subsequent scans were done in a 3T GE scanner. Multiparametric MRI protocol included: diffusion tensor imaging, T1WI, T2WI and DWI, which were acquired at each time point. The ischemic core was defined as the segment of the baseline ischemic lesion that remained abnormal in the subsequent MRI studies. The ROI-UN was defined after the ischemic core was outlined and flipped over onto the contralateral unaffected hemisphere. The FA values were defined in the infarct core and in the ROI-UN. Spearman's correlation coefficients were computed to assess the association between MR measurements at 1 and 3 months and the NIHSS score improvement from baseline to 3 months. The study was approved by the Institutional IRB. **Results:** We studied 20 patients, mean age 62 (±13) years. The mean baseline NIHSS score was 10.1 (±5.7). The mean 3-month NIHSS score was 4.6 (±5.3). There was strong correlation between the FA value in the ROI-UN and the NIHSS score improvement from baseline to 3 months ($r: 0.624$, $p=0.007$). There was however no significant correlation between the 1-month FA value in the ischemic core and the NIHSS score improvement from baseline to 3 months ($r:0.194$, $p=0.46$). **Conclusions:** Higher FA values in the unaffected hemisphere correlate with greater improvement in the NIHSS score from baseline to 3 months. These findings indicate that structural axonal integrity in the contralateral to the ischemic stroke hemisphere is one of the significant contributors to clinical recovery after ischemic stroke.

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W MP61

The Impact of Concurrent Review on Stroke Center Measures at The Miriam Hospital

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Background and Issues: Little research has been published about which interventions impact practice patterns such that quality measures have been impacted. Evidence is presented in support of concurrent review in stroke patient management by examining overall performance over time on quality indicators for The Miriam Hospital (TMH), a hospital certified as a primary stroke center by The Joint Commission (TJC) and a participating hospital of the American Heart Association and American Stroke Association (AHA/ASA) Get with the Guidelines program. TMH tracks a number of indices, one called a composite index. The defect-free measure is used to evaluate how well the hospital did in providing all appropriate interventions to every patient. The hospital's proportion of patients who received interventions they were eligible, is calculated. The data time period is January 2006 to December 2009. A concurrent review

process was implemented at TMH in June of 2008. **Purpose:** To evaluate the effectiveness of concurrent review on stroke center measures. **Method:** A dedicated quality improvement nurse coordinator launched the pilot June 2008. The design included: concurrent review plan, paper & electronic data collection tools, process for evaluating data, strategies to communicate with clinicians. The primary method for concurrent review is the daily examination of admitted patients using a combination of paper and electronic records. Information is transferred to a data collection tool to form a patient profile and to use to communicate with the responsible clinicians and nurses. This strategy was implemented beginning in June 2008. Data was reviewed regularly from the Outcome Science Database repository. Reports were generated and results were trended. Changes in composite scores over time were compared using a generalized estimating equation with a logit link function to fit a piecewise regression with an inflection point at the time TMH implemented concurrent review. **Results:** Composite scores for TMH overall showed significantly increasing trends in the composite scores for the time period January 2006 and April 2008 ($p<.0001$). TMH increased at a faster rate ($p=0.0013$) and these trends further increased significantly between May 2008 and August 2009 for TMH, following implementation of concurrent review ($p<.0001$). The difference between these increases was statistically significant ($p<.0001$). **Conclusions:** Concurrent review at TMH provides an advantage and improves stroke center measures over time.

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W MP62

Effects Of Elevating Head-of-bed On Blood Pressure And Carotid Blood Flow In Acute Ischemic Stroke Patients

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Background: It is recommended for acute ischemic stroke patients to elevate head-of-bed (HOB) over 30-degree to prevent aspiration. However, cardiovascular effects of elevating HOB is not well known. Purpose: To study the effect of 30-degree, 45-degree and 70-degree HOB elevation on blood pressure and carotid blood flow in acute ischemic stroke patients. **Methods:** This study used quasi-experimental design with repeated measures. Data were collected from the first week post stroke patients (n=24, mean age 70.3 y). Patients who could not understand the study procedure were not eligible to take part in this study. After resting 10 minutes in spine position, the patients kept elevated HOB for 10 minutes. During the measurements, automated sphygmomanometer cuff was placed on the non-paralyzed arm, and the ultrasound transducer was applied on the affected side of the carotid artery. Data were collected 10 minutes after the HOB elevation, and blood pressure was also measured immediately after the HOB elevation to check the orthostatic hypotension (OH). OH was defined as a decline in systolic/ diastolic blood pressure of >20 or >10 mmHg, respectively. **Results:** Of the subjects, 33.3% had systolic OH; the prevalence of OH at 30-degree, 45-degree and 70-degree elevation was 4.2%, 20.8%, 29.2%, respectively. Univariate analysis showed that OH was associated with diabetes mellitus ($p=0.07$) and stroke in the left hemisphere ($p=0.028$). Table 1 showed the results of repeated measures of analysis of variance to examine the change of the measurements from spine position to HOB elevation. The absolute change of systolic blood pressure increased with higher HOB elevation ($p=0.001$), and was significantly higher at 70-degree than at 30-degree by multiple comparison ($p<0.001$). Carotid blood flow at 30-degree and 45-degree elevation was lower than supine position, but there was no significant difference between 70-degree elevation and supine position. However, in the patients with OH, carotid blood flow at 70-degree elevation was significantly lower than supine position ($P=0.028$). **Conclusion:** The incidence of OH and the absolute change of systolic blood pressure increased in higher HOB elevation, and these results suggest that higher HOB elevation might cause larger cardiovascular effects in acute stroke patients. In the patients with OH, the recovery of carotid blood flow was not observed after 70-degree elevation, therefore, we should be more cautious in applying HOB elevation to these patients.

Table1. Alteration of blood pressure and carotid blood flow by elevating head of the bed

	0-degree	30-degree	45-degree	70-degree	*p* value
systolic blood pressure*	-	4.5± 3.7 §	7.5± 6.6	11.5± 7.7	0.001
diastolic blood pressure	-	5.3± 6.9	4.5± 3.0	6.4± 4.8	0.41
carotid blood flow					
total patients	359.7± 77.2	316.7± 76.1	317.4± 65.7	331.6± 95.0	0.098
patients with orthostatic hypotension	337.9± 60.4	282.1± 62.5	308.2± 34.4	266.7± 51.1	0.052

* Values were the absolute change from supine position.

§ Values are mean ± SD.

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W MP63

Stroke Laterality and Short Term Behavioral Outcomes in Pediatric Stroke

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Background and Purpose: Stroke affects approximately 2-13 per 100,000 children under age 18 every year and ranks among the top ten causes of death in children. Long-term motor and cognitive deficits that interfere with daily life and academic attainment affect 40-60% of survivors. Parents and caregivers ask what behavior changes to expect and whether or not their child with be "normal" after stroke. We noted that parents report behavioral changes in their children after stroke, such as short temper, irritability, easy frustration, or symptoms of depression. As a first step in assessing the etiology of these changes, we examined the relationship between hemispheric lateralization and the emotional/behavioral changes reported by parents. **Methods:** Over a two year period, we interviewed parents of 25 children, ages 2-18 who had suffered an acute arterial ischemic stroke. Utilizing the Pediatric Stroke Outcome Measure (PSOM), we asked parents about their child's behavior during a 3 month post stroke interview. This questionnaire asks direct questions regarding the presence or absence of emotional changes or depression. Strokes were categorized as involving the left, right, or bilateral hemispheres by MRI review. **Results:** Strokes were lateralized to the left hemisphere in 13, the right hemisphere in 8, with 4 bilateral. Parents noted emotional changes following stroke in 10 (40%), with parents reporting depression in 8 (32%). There was no significant difference in the hemispheric lateralization for children with emotional changes ($p=0.18$, Fischer's Exact Test). However, left hemisphere strokes were associated with depression ($p=0.046$) when excluding those with bilateral stroke. Interestingly, none of the children with right hemisphere stroke were noted to have symptoms of depression. This lateralization was more pronounced when the children with any left hemispheric stroke (including bilateral stroke) were included in the analysis ($p=0.026$). **Conclusions:** Emotional changes and symptoms of depression affect a large proportion of children after stroke. We found an association between parent reported depression and left hemispheric stroke. The etiology of this association is unclear but could be due to impaired language function. This study is limited by its small sample size and limited behavioral evaluation, but demonstrates the need for assessment of emotional changes and depression in pediatric stroke survivors and the need to educate parents about the potential emotional struggles as their children recover. These emotional changes could impede cognitive, language, and motor therapies and inhibit maximal recovery.

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W MP64

Assessing the Efficacy of Ask Me 3™/ Teach Back in Educating Patients Who Suffered a Stroke

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Assessing the Efficacy of Ask Me 3™/ Teach Back in Educating Patients Who Suffered a Stroke Introduction: According to the National Stroke Association a patient who has suffered a stroke has a twenty-five to forty percent increased likelihood of a subsequent stroke in the following five years. Critical elements to the full recovery and prevention of subsequent events in the stroke patient population include a well developed education program and an individualized understanding of the patient's health literacy. **Hypothesis:** Our project was based on the premise that the patient's understanding of their discharge education and the retention of that education would have a positive correlation when using the Ask Me 3™ and Teach Back methodology. **Methods:** Using a five point Likert scale, ninety eight surveys were obtained to get a baseline patient measure in three critical areas: understanding of their diagnosis, treatment plan, and the importance of following the treatment plan after discharge. Our Stroke Navigators, trained in health literacy and Ask Me 3™, used the Ask Me 3 and Teach Back method to measure patient comprehension in the same three areas for fifty patients. Two weeks post discharge, a second survey of the same fifty patients was completed to evaluate the Ask Me 3 and teach back methodology. **Results:** Using the Ask Me 3™ and Teach Back method patients improved their understanding of their diagnosis, their understanding of their treatment plan and the importance of understanding their treatment plan. These three critical areas improved at least seventeen percent post Ask Me 3™ and Teach Back. The followup phone call survey's completed by the Stroke Navigator two weeks post discharge showed adherence to the treatment plan including making their followup appointment and utilizing the Ask Me 3™ information at their post discharge Primary Care Physician visit. The survey also showed one hundred percent of the patients had their discharge medications filled after discharge. **Conclusions:** The application of Ask Me 3™ and Teach Back resulted in a significant improvement in the patients understanding of their diagnosis, treatment plan and importance of the treatment plan. The increase in the patient's understanding of the importance of the treatment plan is felt to be a result of the emphasis on the three major areas impacting the patient. Through a more focused understanding, the patient is empowered to maximize the quality of their life and reduce the likelihood of future strokes.

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W MP65

Validation of the TOR-BSST Swallow Screening Tool

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Background & Problem: Dysphagia is present in 42-67% of all stroke patients within the first 3 days of the event. Dysphagia places stroke patients at increased risk of developing pneumonia which may result in worsening disability. The Toronto Bedside Swallow Screening (TOR-BSST) tool was developed and validated in a Canadian stroke population and requires further validation in other populations. The purpose of this project was to validate the TOR-BSST tool in stroke patients in a US Primary Stroke Center. **Methods:** Stroke unit nurses attended one training session on the TOR-BSST taught by a certified Speech Language Pathologist with formal training in administration of the tool. Consecutive stroke patients admitted to a stroke unit were evaluated with both the TOR-BSST (by nursing) and formal speech therapy swallow evaluation. Results were blinded to each evaluator. Validation was

assessed by level of agreement via kappa scores of nurses' and speech therapy's diagnosis of dysphagia. A kappa of 0.0-0.2 was considered poor, 0.21-0.60 fair to moderate, 0.61-0.80 good, and 0.81-1.00 excellent. **Results:** The sample consisted of 67 patients (70% ischemic, 27% TIA, and 3% ICH). There was a good level of agreement for nursing and speech identification of dysphagia ($k=0.76$, $P<0.001$). There was disagreement between dysphagia diagnosis on the nursing TOR-BSST screen and speech therapy evaluation in 16% of cases ($n=11$). In the majority of cases of disagreement (82%, $n=9$) nurses did not identify dysphagia by the TOR-BSST tool when speech therapy did in the formal evaluation (as evidenced by recommending further studies or a modified diet, such as thickened liquids or pureed diet). In 18% of cases ($n=2$) nurses identified dysphagia by the screening tool when speech therapy did not. **Conclusion:** There was a good level of agreement for identification of dysphagia between TOR-BSST screening by nurses and swallow evaluation by speech therapy. This study indicates that the TOR-BSST is a valid dysphagia screening tool for stroke patients beyond the initial population it was validated in. On-going education and collaboration between speech therapy and nursing staff must be done to ensure proper administration of the TOR-BSST tool. Expansion of the use of the evidence-based TOR-BSST tool will aide in the early identification of patients at risk for aspiration to ensure rapid and appropriate use of prevention techniques, therapy, and resources.

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W MP66

Standardizing Neurological Assessment in an Adult Intensive Care Unit

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Background and Purpose: Subtle neurological changes in neurocritical care patients can indicate acute complications. The National Institutes of Health Stoke Scale (NIHSS) is a valid and reliable 11-item stroke assessment tool. The abbreviated NIHSS (aNIHSS) is a 5-item valid and reliable tool used for more frequent neurological assessments. The 2009 *American Heart Association Nursing and Interdisciplinary Care of the Ischemic Stroke Patient* scientific statement recommends an initial NIHSS assessment upon ICU admission, followed by aNIHSS assessment for more frequent monitoring. For ICUs that use non-standardized neurological assessment methods, these recommendations encourage evaluation of current practice. This quality improvement (QI) project was conducted at an academic medical center, in an adult medical/surgical ICU, where approximately 30% of patients are neurocritical care. The ICU electronic documentation lists neurological assessment items that nurses can select as needed (non-standardized neurological ICU assessment). There was no prior nursing exposure to the NIHSS or aNIHSS. The purpose of this QI project was to determine whether NIHSS and aNIHSS increased detection of neurological deficits in neurocritical care patients, compared with non-standardized neurological ICU assessment. **Methods:** Volunteer ICU nurses ($n=13$) obtained NIHSS certification via the NIHSS Computer Training-Online. Subsequently, selected neurocritical care patients were independently assessed, within 30-minutes, by two NIHSS-certified ICU nurses. In two separate groups, NIHSS ($n=10$ patients) and aNIHSS ($n=10$ patients), item and total scores were compared to the non-standardized neurological ICU assessment documentation. The non-standardized tool does not have a total score. Different patients were in each assessment group; the nurses conducting the assessments remained the same. **Results:** The nurses using the NIHSS identified 32 neurological deficits, compared with 14 in the non-standardized ICU documentation. The NIHSS mean score was 3.45 points (range 0-13). Of the10 total NIHSS scores per patient: 6/10 total scores were identical, 3/10 differed by 1 point, and 1/10 by 2 points. Nurses using the aNIHSS identified 23 deficits compared with 14 in the non-standardized ICU assessment documentation. The aNIHSS mean score was 3.9 points (range 0-12). Of the10 aNIHSS total scores: 8/10 total scores were identical, and 2/10 differed by 1 point. **Conclusions:** Both the NIHSS and the aNIHSS improved detection of neurological deficits in neurocritical care patients compared with non-standardized neurological ICU assessment. Results of this QI project were successfully used to recommend the adoption of the NIHSS and aNIHSS for standardized neurological assessment in the ICU, in accordance with recent AHA recommendations.

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W MP67

Do Demographic Disparities in Neuroimaging Utilization Exist in Stroke? The REGARDS Experience

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Introduction: Neuroimaging guides providers in the initial treatment and secondary prevention of stroke. The use of powerful tools such as CT, MRI and MRI with DWI has revolutionized stroke care, but there are few national data describing regional or racial differences in its use. **Methods:** The REasons for Geographic and Racial Differences in Stroke (REGARDS) cohort was recruited between 2003 and 2007 and is comprised of black and white Americans age 45 and older at baseline. One half of the cohort resides in the Southeastern United States (the "stroke belt"). Participants are surveyed every six months to ascertain incident strokes that are subsequently physician adjudicated based on medical record review. A symptom based approach using the World Health Organization definition of stroke was used to confirm events ($N=584$). During the adjudication process, information regarding the type and frequency of neuroimaging is collected. Confirmed ischemic stroke events ($n=518$) were examined for this analysis. Univariate comparison as well as logistic regression was used to examine the relationship between neuroimaging and race, and region, adjusting for sex, age, income, and year of stroke. **Results:** Of the 518 ischemic stroke events, we found that 168 (32.4%) were evaluated with CT alone, 331 (63.9%) with MRI and 19 (3.7%) with no imaging performed. There were no differences by region or race but those with lower income were less likely to receive an MRI ($p=0.05$) and there were trends for differences by sex and age (see table). There was also a temporal change with increased use of MRI over 2004 to 2009. Multivariable regression analysis found that the use of imaging was not associated with region, race, gender, income or age ($p>0.05$). **Conclusions:** In this national study, we found no racial or regional differences in neuroimgaing utilization for cases of ischemic stroke after adjusting for demographics and income status. This suggests that racial and/or regional disparities in ischemic stroke are not likely due to a detection bias from testing variation. We did find a consistent increase over time in the use of MRI, which has been reported elsewhere. Further research is needed to examine potential differences in neuroimaging by sex, age, and socioeconomic status.

		N	CT only (N=168)	MRI +/- CT (N=331)	No image (N=19)	p
Overall		518	32.40%	63.90%	3.70%	
Region	Belt	282	32.30%	65.30%	2.50%	0.28
	Non Belt	236	32.60%	62.30%	5.10%	
Race	Black	232	34.50%	62.50%	3.00%	0.56
	White	286	30.80%	65.00%	4.20%	
Gender	Female	238	31.90%	62.60%	5.50%	0.13
	Male	280	32.90%	65.00%	2.10%	
Income	$75K Above	42	16.70%	81.00%	2.40%	0.05
	less than $75K	411	35.00%	61.80%	3.20%	
Age	75 or older	172	37.80%	59.90%	2.30%	0.12
	75 or less	346	29.80%	65.90%	4.30%	
Year	2004	71	35.20%	53.30%	11.30%	0.016
	2005	85	38.80%	56.50%	4.70%	
	2006	110	30.00%	69.10%	0.90%	
	2007	88	34.10%	61.40%	4.60%	
	2008	94	30.90%	67.00%	2.10%	
	2009	59	23.70%	76.30%	0.00%	

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W MP68

How Does Access to Care in Urban versus Rural Centres Affect Treatment and Functional Outcomes of Acute Stroke Patients?

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Background: Stroke is a neurological emergency for which the early administration of specific treatment improves outcomes. However, high quality stroke care requires stroke-specific resources and expertise, which may not be equally available in all jurisdictions. We compared stroke care and outcomes in patients residing in rural versus urban areas in one Canadian province, Ontario, and in one U.S. state, North Carolina. **Methods:** We used data from two clinical databases, the Registry of the Canadian Stroke Network and the North Carolina Stroke Care Collaborative, to test the hypothesis that processes of care and outcomes would be better for patients in urban compared to rural areas. We included patients with acute stroke or transient ischemic attack seen at 153 Ontario acute care institutions between April 1, 2004 and March 31, 2005 and 45 participating North Carolina institutions from January 1, 2005 and December 31, 2006. Urban-rural differentiation was made through postal code of patient residence in Ontario, and by county of hospital location in North Carolina. We compared stroke care interventions and 7-day in-hospital mortality in patients with rural versus urban residence, with adjustment for age, gender, co-morbid medical conditions, stroke type and stroke severity. **Results:** The study sample included 4,902 patients from Ontario - 1,226 from rural areas and 3,676 from urban areas; and 11,148 patients from North Carolina - 2,120 rural and 9,028 urban. In both Ontario and North Carolina, patients seen in urban areas were more likely than those in rural areas to receive thrombolysis, stroke unit care, neuroimaging, rehabilitation assessments, and medications for secondary stroke and were less likely to be discharged to a rehabilitation facility. These urban-rural differences in stroke care were greater among patients in North Carolina than among those in Ontario. Adjusted 7-day in-hospital mortality rates were lower among patients in urban areas in North Carolina, but this difference did not reach statistical significance in Ontario. **Conclusions:** Compared to those seen in urban areas, patients seen in rural areas of both Ontario and North Carolina received less aggressive stroke care. Adjusted stroke case fatality rates were higher in rural than in urban areas in North Carolina but not in Ontario.

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W MP69

Neighborhood Socioeconomic Disadvantage and Mortality after Stroke: the Cardiovascular Health Study

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Background: Residence in a socioeconomically disadvantaged community is associated with cardiovascular and all-cause mortality, but the mechanisms are not well understood. We examined whether socioeconomic features of the residential neighborhood contribute to post stroke mortality and whether neighborhood influences are mediated by traditional behavioral and biologic risk factors. **Methods:** We used data from the Cardiovascular Health Study, a multicenter, population-based, longitudinal study of adults $\geq$65 years. The dependent variable was time to death after ischemic stroke. Residential neighborhood disadvantage was measured using neighborhood socioeconomic status (NSES), a composite of six census tract variables representing income, education, employment, and wealth. Multilevel Cox proportional hazard models were constructed to determine the association of NSES to mortality post stroke, after adjustment for demographic characteristics (age, race, gender, education, and income), stroke type (ischemic, hemorrhagic, and unknown), behavioral risk factors (smoking, physical activity, and alcohol use), and biologic risk factors (EKG abnormalities; subclinical cardiovascular disease; and diagnosed hypertension, diabetes, or hyperlipidemia). **Results:** Among the 3834 participants with no prior stroke at baseline (mean age 73.3 [SD=5.4] years; 62% female; 83% white; and 17% African American), 806 had a stroke over a mean 11.5 years of follow up (89% ischemic, 6% hemorrhagic, 5% unknown type), with 276 (34%) deaths at one year post stroke. In models adjusted for demographic characteristics and stroke type, mortality hazard at one year after stroke was significantly higher among residents of neighborhoods with the lowest NSES than those in the highest NSES neighborhoods (HR=1.69, 1.13, 2.51). With additional adjustment for behavioral and biologic risk factors, this risk persisted (HR=1.78, 1.18-2.68). **Conclusions:** Living in a socioeconomically disadvantaged neighborhood is associated with higher mortality hazard at one year following an index stroke, even after adjusting for individual SES. This association does not appear to be mediated by behavioral or biologic risk factors. Further work is needed to understand the structural and social characteristics of neighborhoods that may contribute to earlier mortality in the year after a stroke and the pathways through which these characteristics operate.

Table. Significant Multivariate Risk Factors for All Cause Mortality at One Year Post Stroke, Cardiovascular Health Study

	Model 1 (Adjusted for age, sex, race, income, education, stroke type[1])	Model 2 (Model 1 + behavioral risk factors[2] + biologic risk factors[3])
	HR (95% C.I)	HR (95% CI)
Neighborhood SES		
• Quartile 1 (Highest) - Reference	1.00	1.00
• Quartile 2	1.05 (0.73, 1.51)†	1.12 (0.77, 1.62)†
• Quartile 3	1.42 (0.99, 2.03)†	1.44 (0.99, 2.08)†
• Quartile 4 (Lowest)	1.69 (1.13, 2.51)*,†	1.78 (1.18, 2.68)*,†
Age (in 5 year intervals)	1.22 (1.09, 1.36)*	1.29 (1.14, 1.46)*
White (vs. African American)	1.50 (1.01, 2.21)*	1.57 (1.02, 2.40)*
Stroke Type		
• Ischemic - Reference	1.00	1.00
• Hemorrhagic	3.60 (2.66, 4.87)*	3.79 (2.75, 5.22)*
• Unknown	2.33 (1.55, 3.51)*	2.76 (1.82, 4.18)*
Total cholesterol / HDL-cholesterol	--	0.90 (0.81, 0.99)*

* $P<0.05$ compared to reference, †$P<0.05$ for test of trend
[1] Stroke type: Ischemic, hemorrhagic, or unknown;
[2] Behavioral Risk Factors: smoking, alcohol use, and diet
[3] Biologic Risk Factors: EKG abnormalities, subclinical cardiovascular disease, blood pressure, hypertension, diabetes, cholesterol ratio

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W MP70

Trends of Acute Ischemic Stroke Hospitalizations by Age and Gender in the United States: 1994-2007

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Background: There is limited information on population-based estimates of trends in acute ischemic stroke hospitalizations by age and gender. **Methods:** The study population consisted of 1994-2007 hospitalizations from the Nationwide Inpatient Sample of the Healthcare Cost and Utilization Project (HCUP). The acute ischemic stroke hospitalizations were identified with the primary diagnosis of ICD 9 CM codes. Seven consecutive 2-year time intervals were selected in this study. Six age groups were used: 0-4 years, 5-14 years, 15-34 years, 35-44 years, 45-64 years and 65 years and older. **Results:** During the period of our study, the prevalence of hospitalizations with a primary diagnosis of acute ischemic stroke decreased among female patients aged 0-4 years, both males and females for patients aged 45-64 years and 65 years and older (all p for linear trends $<$0.01). In contrast, the prevalence increased significantly for both males and females among patients aged 5-14, 15-34 and 35-44 years old ($p<0.01$, Table 1). The biggest increase (53%) from 9.8 per 10,000 hospitalizations in 1994-1995 to 14.8 per 10,000 hospitalizations in 2006-2007 was observed among males aged 15-34 years, followed by 47% (from 36.0 per 10,000 hospitalizations to 52.9 per 10,000 hospitalizations) and 36% (from 21.9 per 10,000 hospitalizations to 30.0 per 10,000 hospitalizations) increase among 35-44 years old males and females, respectively. Thirty-six percent, 31%, and 17% increases were observed in males aged 5-14 years, females aged 5-14 years, and females aged 15-34 years, respectively. **Conclusion:** The prevalence of acute ischemic stroke hospitalizations increased significantly from 1994-1995 to 2006-2007 among both males and females aged 5-44 years old; raising concern about this young population. Our results from national surveillance data punctuate the need to further investigate socio-demographic, clinical and health care factors associated with the recent increase in acute ischemic stroke hospitalizations among the younger population.

Table 1.Prevalence of Primary Ischemic Stroke Hospitalization by age and gender

	Rates per 10,000 hospitalizations (Standard error)	
	1994-1995	2006-2007
Age 0-4 years old		
Male	0.57 (0.09)	0.39 (0.07)
Female	0.78 (0.1)	0.38 (0.07) †
Age 5-14 years old		
Male	2.8 (0.5)	3.8 (1.0) †
Female	3.6 (0.6)	4.7 (0.8) †
Age 15-34 years old		
Male	9.8 (0.6)	14.8 (0.6) †
Female	3.6 (0.2)	4.2 (0.2) †
Age 35-44 years old		
Male	36.0 (0.9)	52.9 (1.4) †
Female	21.9 (0.7)	30.0 (0.8) †
Age 45-64 years old		
Male	194.7 (2.5)	172.0 (2.2) †
Female	145.5 (1.9)	126.3 (1.7) †
Age 65-130 years old		
Male	404.3 (3.3)	302.8 (3.0) †
Female	379.0 (2.8)	273.9 (2.5) †

†Statistically significant trend ($P<0.001$)

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W MP71

Are There Gender Based Differences In Acute Stroke Care In Michigan Hospitals?

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Background: Previous studies have reported less use of intravenous t-PA among women with ischemic stroke. **Objective:** Examine gender-based differences in acute ischemic stroke care from arrival to discharge. **Methods:** Chart review of patients with ischemic stroke from five JC (Joint Commission) certified centers and five noncertified hospitals in Michigan for year 2006 was performed. Sixty charts were chosen from each hospital with ICD codes: 434.1, 435, 436, 437, 437.1, and 437.9. They were analyzed for gender differences in the following: race, patient location at symptom onset, arrival by ambulance or self-transportation, evaluation by rapid response or stroke team, wake-up strokes, evaluation for thrombolytic therapy, tPA use, endovascular interventions, DVT prophylaxis, swallow evaluation, presence of atrial fibrillation, incidence of DVT, PE or pneumonia, discharge on antithrombotics, and cholesterol lowering agents, and discharge outcome status (good if discharged home or rehabilitation). Fischer's exact test was used to determine statistical significance. Multivariable logistic regression analysis was performed for good discharge outcome after adjusting for age. **Results:** 602 charts were analyzed, 302 from certified and 300 from noncertified centers. There were 282 men (148 from JC certified and 134 from noncertified centers) and 320 women (154 from certified and 166 from noncertified centers). More women arrived via ambulance (63.1% vs. 53.9%, p=0.025) while more men came by self- transportation (42.6% vs. 30%, p=0.0016). There was no overall difference by gender for evaluation for thrombolytics (25.5% vs. 23.1% p = 0.50) or intravenous t-PA administered (3.5% vs. 2.5%, p= 0.82). 33% were evaluated for thrombolytic therapy in JC certified centers compared to 15% in non-certified centers (p=0.0001). Most common reason for not getting thrombolysis was delay in arrival in both men and women. More men than women had mild/resolving symptoms (11% vs. 4.1%, p=0.0015), they had more interventional procedures done (8.1 % vs. 3.1%, p=0.0072) especially in JC certified hospitals compared to non certified ones (p=0.0004). More men than women were discharged on antithrombotics (88.2 % vs. 82.2 %, p=0.039). Men had better discharge outcomes (81.6% vs. 70.3%, p=0.001) but this was only marginally significant when adjusted for age (multivariable logistic regression, p= 0.053). **Conclusion:** Going to a JC certified center was a better predictor of consideration for thrombolytics than gender. Men had more aggressive acute stroke care in being considered for endovascular interventions and discharge on antithrombotics. More men had mild/resolving symptoms and a tendency towards better outcome on discharge. Further studies with greater sample size and the reasons need to be evaluated.

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W MP72

Factors Influencing The Door-to-needle Time: Women Are Treated Later With Thrombolysis In Acute Stroke

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Background: As part of a quality assurance program we analyzed the factors influencing the door-to-needle time in patients treated with intravenous thrombolytic therapy. The aim in our neurological emergency service which has more than 15 years experience with thrombolysis for stroke is to treat patients within 30 minutes after arrival. **Method:** Since 1998 all patients treated with thrombolytic therapy are collected in a prospective database. Since 2002 the door-to-needle time is collected. Thus this analysis was restricted to patients treated between 01.01.2002 and 15.05.2010. In addition patients treated later than 9 hours after symptom onset were excluded from the analysis. Univariate (Mann-Whitney U or Fisher's exact test) und multivariate (logistic regression) analyses were applied using door-to-needle time less 30 minutes as dependent and factors with a p-value variate analysis as independent variables. **Results:** The dataset consisted of 936 patients. Only 243 (26%) patients were treated within 30 minutes after arrival. In univariate statistics early treatment was associated with male gender (58.4% vs. 49.2%; p=0.0139), shorter time window (115 vs. 150 minutes; P<0.0001), lower age (72 vs. 74 years, p=0.0040), CT-based treatment (86% vs. 76%; p=0.0004), off-label treatment (34% vs. 54%, P<0.0001), previous stroke (12% vs. 19%, p=0.0130), oral anticoagulation (1.6% vs. 7.1%, p=0.0010) and treatment within usual working hours (62% vs. 53%; p=0.0355). From multivariate analysis male gender (OR 1.40; 95%CI 1.02-1.93), time window (OR 0.99, 95%CI 0.99-1.00), use of MRI (OR 0.57; 95%CI 0.36-0.90), previous stroke (OR 0.58, 95%CI 0.37-0.91), oral anticoagulation (OR 0.25; 95%CI 0.09-0.73) and treatment within usual working hours (OR 1.43; 95%CI 1.05-1.97) remained as significant factors influencing the door-to-needle time. **Discussion:** In our cohort male patients and those treated within usual working hours had a higher chance to be treated with thrombolytic therapy within 30 minutes after arrival in the emergency room. Although 33 patients received thrombolysis within 30 minutes when diagnosis was based on MRI, the use of MR was a negative predictor for fast treatment. In contrast, CTA did not delay treatment. This analysis gives us important information to improve our treatment processes. Figure

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W MP73

LPS Precondition Against Cerebral Ischemic Injury Is Modulated by Brain Maturity

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Background: LPS provided neuroprotection when administered prior to ischemic injury in adult brain. It is a known specific ligand to Toll-like receptor 4 (TLR4), one of the Toll-like receptors (TLRs) that recognize foreign pathogens. LPS mediated ischemic tolerance in the adult brain occurs by stimulation of TLR4 signalling pathways. Studies on LPS-induced preconditioning against ischemic injury in the immature brain are scarce. We aim to investigate the effect of brain maturity on the efficacy of LPS-induced preconditioning in the hypoxic-ischemic developing rat brain. **Methods:** Rat pups at postnatal day 3, 5, 7, 9 or 14 were randomly assigned to LPS treated group (0.1mg/kg) or untreated group. Forty eight hours after the injections, hypoxic-ischemic injury was induced by using the Rice-Vannucci model, the most commonly used model to study hypoxic-ischemic (HI) brain injury in the developing brain. Unilateral internal carotid artery ligation in rat pups followed by exposure to 8% hypoxia for approximately 65min will cause a reproducible unilateral infarct ipsilateral to the ligated artery involving caudate, putamen, hippocampus and cortex. Body temperature will be maintained at 37-37.5^{0}C during hypoxia using an incubator. Brains were removed 1 week after HI injury, fixed, embedded in paraffin and cut in 5im coronal sections. Brain sections were then stained with Hematoxylin and Eosin and infarct volumes were compared between the two groups using Nikon NIS-Element Basic Research Image analysis software system. TLR-4 expression was also compared among different age groups. **Results:** We found that LPS treated P7, P9 and P14 rat pups had significantly smaller infarct volume compared to the saline treated pups ($p = 0.006$, 0.03 and 0.01 respectively). This significant reduction in infarct volume was not observed in P3 and P5 rats ($p = 0.06$ and 0.35 respectively). TLR-4 expression was significantly higher in the P7 compared to P3 and P5 rat brains ($p < 0.01$). **Conclusions:** LPS-induced ischemic preconditioning is a plausible neuroprotective strategy for children with predictable high risk of ischemic injury such as patients undergoing cardiac or brain surgeries. However, the efficacy of this phenomenon is dependent on TLR-4 expression as determined by brain maturity.

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W MP74

Craniocervical Arterial Dissections in Children: Characteristics, Diagnosis, and Outcome

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Objective: To describe the presentation, imaging characteristics, management, and outcome of neuroimaging-confirmed craniocervical arterial dissection (CCAD) in children. **Methods:** A computerized search engine identified all cases of CCAD at Children's Hospital Boston in children under 18 years old from 1994 to 2010. Using neuroimaging diagnostic criteria, 44 cases were identified. **Results:** There was a male predominance (66%). Spontaneous occurrence was the most frequent etiology (n=19; 43%). History of antecedent trauma was common (n=17; 39% overall; of these, 35% were intracranial dissection (ICD), 53% were extra-cranial dissection (ECD), 12% both ICD and ECD). The most common presenting symptoms were hemiparesis (n=19; 43%), headache or neck pain (n=14; 32%) and aphasia (n=10; 23%). The most commonly used initial imaging modalities were MR- and catheter-angiography in 35(80%) and 5(11%) cases, respectively. Catheter angiography was the most commonly performed confirmatory test. Neuroimaging characteristics of CCAD included anterior circulation location in 28(64%) and left-sided location in 30(68%); 21(47%) were ICD, 18(41%) were ECD and 5 (11%) involved both intra- and extra-cranial vasculature. Most anterior circulation dissections, (n=22/28; 79%) involved ICD, while most posterior dissections (n=13/16; 81%) were extracranial. Neuroimaging evidence of cerebral ischemia at diagnosis appeared in 29(66%) cases. Of those with follow-up neuroimaging, 25(89%) had persistent arterial changes. Most patients were anticoagulated(n=25;56%); the majority (72%) involved ICD. No hemorrhage occurred following anticoagulation treatment. Average follow-up time was 3.3 years. Using Pediatric Stroke Outcome Measure (PSOM) criteria, 38% of children had a normal neurologic exam, while the remaining demonstrated mild- (22%), moderate- (22%) or severe (9%) motor impairment or persistent language dysfunction (9%). **Conclusions:** This large single-institution cohort of children with CCAD confirms prior findings and provides novel findings. We confirm a male predominance of CCAD, predilection for its occurrence in anterior circulation, and tendencies of ICD and ECD to occur in anterior and posterior circulations, respectively. Novel features found in the current cohort analysis include a high rate of spontaneous occurrence in over 40% of cases, the overall predominance of intracranial vascular location for dissection and neuroimaging signs of cerebral ischemia in only 2/3 of patients. Importantly, the majority of patients in the current cohort were anticoagulated and despite the intracranial location of dissection in 72% of this group, no consequent intracranial hemorrhage was observed. This cohort of pediatric CCAD demonstrated favorable clinical outcome.

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W MP75

Short-term Neurological Outcomes after Childhood Stroke: Results of a Population-based Cohort Study

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Background: Outcome data after childhood stroke have been limited to hospital series and stroke registries, and childhood hemorrhagic stroke outcome data are particularly limited. Previously reported high rates of deficits could reflect referral bias to tertiary care centers. Our objective was to determine neurologic outcomes at hospital discharge in children with stroke from a population-based cohort in Northern California. **Methods:** We performed a retrospective cohort study of children (29 days-19 years) enrolled in a Northern Californian integrated healthcare plan from 1/93- 12/03. Cases of symptomatic ischemic and hemorrhagic stroke were identified through electronic searches of in-patient, out-patient, and radiology databases, and confirmed through independent chart review. Data were abstracted by a medical records analyst and confirmed by a pediatric neurologist. Deficit at discharge was defined as documentation of any abnormal neurological finding at the time of discharge from the acute hospitalization. Analyses were stratified by ischemic versus hemorrhagic stroke. Dichotomous variables were compared using Fisher's exact test. Multivariate logistic regression models including age, gender and clinical symptoms at presentation were used to identify predictors of residual neurological deficits at discharge. **Results:** In a cohort of 2.3 million children, 124 ischemic and 132 hemorrhagic strokes were identified. Ischemic strokes presented most commonly with hemiparesis (64%), altered mental status (31%), headache (30%) and seizure (28%). Hemorrhagic strokes presented most commonly with headache (60%), followed by altered mental status (58%), hemiparesis (25%) and seizure (18%). Median length of stay was 5.5 days for ischemic and 7 days for hemorrhagic stroke (P=0.5). In hospital mortality was similar between ischemic (4%; 95% CI 0.05%, 7%) and hemorrhagic strokes (5%; 95% CI 1%, 8%). Neurological deficits at discharge were less frequent after hemorrhagic stroke, noted in 47% compared to 65% of ischemic strokes (OR 0.5, 95% CI 0.3, 0.8). On multivariate analysis, after adjusting for age and gender, hemiparesis (OR 6.5, 95% CI 2.0, 21) and altered mental status (OR 5.5, 95% CI 2.1, 14.3) at presentation were associated with neurological deficits at discharge after hemorrhagic stroke. The only predictor of deficits at discharge for ischemic stroke was presentation with hemiparesis (OR 5.4, 95% CI 1.9, 15.3). Neither seizure nor headache at stroke onset was predictive of neurological deficits at discharge. **Conclusions:** Even in a population-based cohort, children had high rates of neurological deficits at the time of hospital discharge after a pediatric stroke. Residual deficits at discharge were more frequent for ischemic than hemorrhagic stroke. Further studies are needed to determine long-term outcomes.

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W MP76

Pediatric Intracerebral Hemorrhage Score

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Objective: The ICH Score is the most commonly used clinical grading scale for outcome after adult intracerebral hemorrhage (ICH). We sought to create a similar scale in children to inform clinical care and assist in clinical research. **Methods:** We performed a prospective observational cohort study of all children full-term to 17 years-of-age with acute spontaneous ICH admitted to two tertiary pediatric medical centers from 2007-2009. Children were assessed at follow-up by a pediatric stroke neurologist with the King's Outcome Scale for Childhood Head Injury (KOSCHI) which ranges from 1 (death) to 5 (good recovery) at 3 and 12 months post-ICH. Exclusion: trauma; isolated subarachnoid hemorrhage, ICH due to brain tumor, hemorrhagic transformation of stroke, pre-existing neurological deficit, and death due to non-ICH causes. The Peds ICH score was created by identifying factors associated with poor outcome via univariable analysis (Fisher's exact test) and by including logical components of the adult ICH score. **Results:** We enrolled 46 children, median age 2.7 years (0-17); 26 had pure ICH, 10 had pure intraventricular hemorrhage (IVH), and 10 had both. Two children had a poor outcome, KOSCHI = 1 point, ($p=0.017$). ICH volume >2% of total brain volume= 1 point, ICH volume >4% = 2 points, ($p=0.027$), Hydrocephalus within 24 hours of ICH=1 point, ($p=0.037$), Herniation (uncal or tentorial) = 1 point ($p=0.02$), Infratentorial location = 1 point ($p=$NS), Total Peds ICH score range, 0-6. In 33 with favorable ICH score (<=2), 58% had a good outcome (KOSCHI of 5), 100% survived, and none had a KOSCHI of <4 (moderate disability). In 13 with less favorable ICH scores,(>=3) only 15% had good outcome (KOSCHI of 5), 15% died, and the remainder had disabilities. All 3 patients with an ICH Score of 0 survived with a good outcome. Of 2 patients with ICH Score of 6, 1 died and 1 infant with an open fontanel survived with moderate deficits. **Conclusion:** The Peds ICH score is a simple clinical grading scale that may ultimately be used for risk stratification, clinical care, and research. It mirrors the scale that is useful in adults, though some components differ. Differences are age, hydrocephalus rather than IVH, and herniation. IVH was not significant, but hydrocephalus was and may be a marker of substantial IVH. Validation in a large cohort is necessary.

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W MP77

Long-term Outcome of Pediatrc Hemorrhagic Stroke

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Objective: We investigated the neurological and quality of life outcomes of children with hemorrhagic stroke. We determined whether predictors of adult outcome, such as initial Glasgow Coma Scale (GCS) score, ventricular involvement, and lesion location apply to children. Earlier studies showed that hemorrhage-brain volume ratios of 2-4% predicted poorer outcome in children; we tested whether this relationship applied in our study group. **Participants and Methods:** We used ICD-9 searches of medical records and keyword searches of radiology records at the Nationwide Children's Hospital to identify potential participants. Charts and neuroimages were reviewed to verify the diagnosis of hemorrhagic stroke. Participants were included if the stroke occurred after the perinatal period through age 18 years from 2001 to 2009. Cases with trauma codes or hemorrhagic conversion were excluded. Clinical MRI brain scans were coded for hemorrhage location and ventricular involvement. Hemorrhage, brain, and ventricular volumes were determined by manual segmentation. Families of survivors were contacted using an IRB approved protocol and interviewed by phone. Parents completed the Recovery and Recurrence Questionnaire (RRQ), the King's Outcome Scale for Children (KOSCHI), and the Pediatric Quality of Life Scale (Peds-QOL). Children completed an age-appropriate version of the Peds-QOL. **Results:** We identified 59 children ages ranging 0-18 years at the time of hemorrhage. Associated diagnoses included vascular malformations, brain and systemic malignancies, congenital heart disease, and systemic illnesses. Overall, 20 (34%) died, 20 (34%) could not be contacted, and 19 (32%) provided outcome information. Median time to follow-up was 5.1 years with a range of 1.1 to 8.0 years. GCS, hemorrhage location, and ventricular hemorrhage did not predict outcomes. An increasing hemorrhage to brain ratio was significantly associated with an increasing RRQ score, a decreasing KOSCHI score, and a trend toward poorer Peds-QOL scores. A hemorrhage-brain ratio ≥4% was associated with poorer outcomes on the RRQ, KOSCHI, and Peds-QOL; however, deaths occurred throughout the entire range of hemorrhage-brain ratios. Diagnosis categories were significantly associated with poorer parental and patient Peds-QOL outcomes. **Conclusion:** In children, underlying diagnosis and the hemorrhage-brain ratio predict outcome better than GCS, ventricular involvement, or hemorrhage location. Although these last three factors have been proposed as predictors of outcome in adults, we did not observe that they did so in our sample of children. Our results support previous findings that a hemorrhage-brain ratio ≥4% is significantly associated with a poorer outcome. Hemorrhagic stroke in children behaves very differently from that in adults. The underlying cause is an important factor in the long-term quality of life.

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W MP78

Sources of Cost for Acute Pediatric Stroke Care

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Background and Purpose - Recent studies have examined the overall cost of pediatric stroke, but there is little data regarding the sources of these costs. If physicians are aware of these sources, they may be able to work towards more cost-effective care. **Methods:** We examined an administrative database from 24 children's hospitals in the US affiliated with the Child Health Corporation of America to characterize individual patient costs. We searched anonymized records of children older than age 1 month who had no associated trauma codes. Using ICD-9 code searches of the primary diagnosis position, we identified 1,813 discharges, corresponding to 1,667 patients who had a diagnosis of stroke from 2003 to 2009. Total costs were divided into seven categories that were then subdivided into individual costs. Categories were ranked to determine which contributed the most to total cost, and individual costs were subsequently ranked within their categories. We also analyzed costs based upon stroke type. Total costs were adjusted using the annual US Consumer Price Index to compare the rate of increase with inflation. **Results:** Median total cost was $19,548 (Interquartile Range $10,764-$40,721). Single admission occurred in 92.7% of the subjects, while 6.4% had two discharges. There were 703 patients (42%) with hemorrhagic strokes and 964 patients (58%) with ischemic strokes. The category "Other/nursing" contributed the most to total cost, followed by imaging, lab, pharmacy, clinical services, and supplies. Brain MRI and CT contributed the most to imaging costs. Inserting endotracheal tubes, continuous invasive mechanical ventilation, ventriculostomy, and brain procedures (diagnostic biopsies, excision of lesions, and brain incisions) were associated with high total cost (75th percentile or greater). Hemorrhagic strokes (median $24,843, IQR $11,739-S53,729) were more expensive than ischemic strokes (median $16,954, IQR $10,210-$30,663). Patients admitted multiple times had a median total cost of $39,451 (IQR $23,622-$77, 859). Total cost increased from 2003 to 2009 but the increase did not exceed the rate of inflation. **Conclusions:** This is the first detailed analysis of cost for acute pediatric stroke care in multiple US children's hospitals. Our findings support earlier reports that hemorrhage in children accounts for a higher proportion of stroke than with adults, and hemorrhagic stroke is more expensive than ischemic stroke. Inpatient nursing and imaging are the two largest sources of cost. These categories are potential targets for cost containment, yet they are crucial for effective diagnosis and treatment. Necessary yet prudent use of imaging and inpatient stays may be strategies for cost containment.

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W MP79

Diabetes Stimulates Brain Angiogenesis: *In Vitro* and *In Vivo* Evidence

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Background: Type II diabetes is associated with micro- and macrovascular complications which increases the risk of stroke and worsen outcomes. We have previously shown that ischemic brain injury results in greater hemorrhagic transformation (HT), a complication of acute ischemic stroke, in diabetic Goto-Kakizaki (GK) rats which also exhibits increased adaptive arteriogenesis characterized by increased tortuosity, collateral numbers, and diameter. These rats also exhibit increased cerebrovascular matrix metalloprotease (MMP) activity. Given that diabetes causes pathologic angiogenesis in the retina via an oxidative stress-dependent mechanism, the current study tested the hypothesis that peroxynitrite generation stimulates c-src and MMPs thereby enhancing the angiogenic response in diabetes. **Methods:** Angiogenesis was studied by evaluating the cerebral angioarchitecture by 3-dimensional reconstruction of the vasculature using Z-stacks images obtained by the confocal microscopy and measured stereological parameters like vascular volume, density and surface area in cortex and striatum.. Cell migration was measured using isolated brain microvascular endothelial cells from control and diabetic rats (10-12 weeks, 250-300g) as an indicator of *in vitro* angiogenic potential. **Results:** Angiogenic parameters were pronounced in the cerebral cortex compared to the striatum in diabetic rats compared to controls (Table). Brain microvascular endothelial cells from diabetic animals also expressed high levels of VEGF and MMP-2 had greater migratory response (% recovery of scratch distance) compared to control group (76 ± 6 vs 36 ± 5). Peroxynitrite decomposition catalyst FeTPPS 2.5μM, MMP inhibitor minocyline 50μg/ml and src kinase inhibitor PP2 1μM blocked migratory response in diabetic cells significantly (%31 ± 4**, 38 ± 4**, 42 ± 1*, respectively) without a significant effect on control cells. **Conclusions:** These results suggest that diabetes-induced oxidative stress enhances cerebral neovascularization via c-src and MMPs which may cause greater HT and complicate s stroke. N=4-10 * p≤ 0.05, ** p≤ 0.0005.

Angiogenic parameter	Control-Wistar		Diabetes-GK	
	Cortex	Striatum	Cortex	Striatum
% Vascular volume	0.5± 0.2	1.9 ± 0.3	9.6 ± 2.	5.8 ± 1.4
Surface area (μm²)	312600 ± 49320	287100 ± 67050	1026000 ± 165400	709100 ± 201400
% Vascular density	19.7 ± 4.0	12.3± 2.3	41.8 ± 7.9	21.0 ± 4.6
VEGF expression(OD)	0.7 ± 0.02		1.1 ± 0.06	
MMP2 activity(% standard)	215 ± 55		574± 55	

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W MP80

Type 2 Diabetes Blunts the Neurovascular Coupling and Cerebral Blood Flow: Relevance to Ischemic Injury

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Background: Diabetes increases the risk of stroke and is also associated with worse outcomes. We have reported greater hemorrhagic transformation (HT) and neurological deficit despite smaller infarcts in Goto-Kakizaki (GK) diabetic rats. GK rats also present with increased collateral numbers and lumen diameter of pial arteries. This study tested the hypothesis that diabetes-mediated cerebrovascular remodeling alters functional hyperemia and cerebral blood flow (CBF), which together result in poor outcomes when a focal ischemic injury is superimposed on diabetic vascular disease. **Methods:** Functional hyperemia was assessed by whisker stimulation induced changes in CBF measured by scanning laser Doppler in control Wistar and diabetic GK rats (n=7, each group). CBF was measured by magnetic resonance imaging (MRI) at baseline, during ischemia, acute reperfusion and at 24 h in both cortex and ischemic core regions of rats subjected to 3 h occlusion middle cerebral artery (MCAO) followed by 21 h reperfusion. Blood brain barrier (BBB) permeability changes were assessed at approximately 2 and 24 h after reperfusion using contrast-enhanced MRI. Localization of ischemia damaged areas was done by thresholding T2 values. Infarct size and HT were measured by TTC staining and ELISA, respectively. **Results:** Functional hyperemia was decreased in diabetes (21±5% vs 40±5 control, P<0.05) after whisker stimulation. Baseline MRI CBF values (ml/100 g/min) were significantly lower in the diabetes group (81.2±5.9 vs 143.9±24.6 control, P<0.05). Ischemic region CBF values decreased significantly during ischemia in both groups. Contralateral CBF became significantly elevated compared to baseline levels (89.3±6.3) in diabetes during ischemia (112.6±10.7) and early reperfusion (147.1±11.2), but not in controls. A similar pattern was observed when same measurements were repeated in the frontal cortex region (baseline 82.7±9.9 diabetes vs184±7.2 control). Acute BBB disruption was detected in the preoptic area and/or striatum in all rats by Gd-DTPA enhanced MRI and the average size of the BBB damaged area 24 h was significantly smaller in diabetes (122±96 vs 236±134 pixels control, P<0.05). Infarct size measured from TTC sections was also smaller (11.3±2.2 vs 35.9±6.9% control) but HT severity (12.7±3.2 vs 4.2±1.5 ng/mg tissue control) was greater in diabetes group (p<0.05). **Conclusion:** These results suggest that diabetes blunts baseline neurovascular coupling and CBF. Addition of an ischemic injury to this existing vascular pathology contributes to worsened outcomes in diabetic stroke despite smaller infarcts emphasizing the importance of vascular protection.

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W MP81

Sphingosylphosphorylcholine-rho-kinase-mediated Smooth Muscle Contraction In The Rat Basilar Artery Is Regulated By The Serum Total Cholesterol Or Vascular Tissue Cholesterol Level: A Mechanistic Role For Lipid Rafts

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Introduction: Rho-kinase (ROK)-mediated Ca^{2+} sensitization of vascular smooth muscle (VSM) plays a pivotal role in cerebral vasospasm (CV). We previously showed that sphingosylphosphorylcholine (SPC), a sphingolipid, induces ROK-mediated Ca^{2+} sensitization, which is regulated by serum total cholesterol (T-Cho). Here, we link this effect to the vascular tissue cholesterol level. **Methods:** Adult male Sprague-Dawley rats (400-500 g, n=45) received a control diet; a 1% cholesterol diet; or a 1% cholesterol diet+5% β-cyclodextrin (β-CD), which depletes VSM cholesterol, for 8 weeks. Changes in the basilar artery diameter were measured using cranial window preparations. Serum T-Cho was measured using an L-type Wako CHO-H kit. T-Cho and phosphatidylcholine (PC) levels in the internal carotid artery (ICA) were measured using Gas Chromatography and Thin Layer Chromatography. Human brain VSM cells (HBVSMCs) were stained with filipin III to visualize cholesterol and counterstained with rhodamine phalloidin to visualize F-actin. The filipin III intensity for each cell was measured using ImageJ. Statistical analysis was by Mann-Whitney U-test. Values are means±SD. **Results:** Serum T-Cho and T-Cho in the ICA were significantly higher in rats fed a cholesterol diet compared to controls (131.8±20.0 mg/dl, n=16 vs. 53.6±10.7 mg/dl, n=24, P<0.001; 0.82±0.24 mg/g, n=5 vs. 0.49±0.09 mg/g, n=5, p=0.028). SPC (100 ìmol/L)-induced contraction increased with the cholesterol diet and the extent correlated (r^2=0.75, n=40) with serum T-Cho levels. T-Cho in the ICA was reduced by â-CD (0.47±0.06 mg/g, n=5, p=0.016 vs. cholesterol diet) and the depletion of cholesterol inhibited the SPC-induced contraction. The mean % filipin III intensity of HBVSMCs treated with β-CD (5 mmol/L, 2 hr) also displayed a marked decrease (37.7±12.0%, n=35, P<0.001 vs. control cells). There were no significant differences in the PC content in the ICA among the three groups. **Conclusion:** Lipid rafts are cholesterol-enriched membrane microdomains that influence signal transduction. In this study, hypercholesterolemia increased VSM cholesterol (but not PC, a major component of nonraft membranes) and SPC-ROK-mediated VSM contraction. Depletion of VSM cholesterol (but not PC) by β-CD inhibited SPC-induced contraction. These results indicate that cholesterol potentiates SPC-ROK-mediated contractions of importance in CV and are compatible with a role for lipid rafts in this process.

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W MP82

Over-Expression Of Cyclin-Dependent Kinase 5 Stimulates Cell Migration But Not Cell Differentiation In Human Brain Microvascular Endothelial Cells

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Abnormal activation of neuronal and blood vessel cell death pathways are common features in acute stroke, whereas angiogenesis is a key requisite for brain tissue recovery. Spatial and temporal regulation of cytoskeletal dynamics critically modulates this process. A set of cell cycle kinases has been also implicated. Currently, their relationship to brain tissue recovery remains unclear. Our recent findings showed that the pharmacological inhibition of cyclin-dependent kinase 5 (Cdk5) with kinase inhibitor r-roscovitine and the deregulation of its activators p35/p25 with calpain inhibitor can affect angiogenesis in human brain microvascular endothelial cells (hCMEC/D3). Here, using in vivo cell imaging system (Chip-Man Technologies Ltd) we monitored for 24-72h the effects of stable GFP-Cdk5 over-expression (Cdk5ov) on hCMEC/D3 angiogenesis. Capillary branch chain formation (72h) and migration (24h) were studied in Matrigel and wounding healing assays, respectively. With the use of a hypoxia-chamber we mimicked the effects of stroke condition on cell migration. Protein levels were estimated by Western blot. Cdk5/p35 involvement in cytoskeletal organization was investigated by confocal microscope analysis, in spreading or moving untransfected cells (controls). Stable transfection efficiency was defined by GFP fluorescence and cdk5 protein levels in different cell passages. Our results show that over-expression of cdk5 reduced cell adhesion (p<0.01 vs controls or empty vector transfectants) but not spreading. This was associated with increased p35 and talin protein levels. Cell migration was increased in Cdk5ov transfectants and this was augmented further in hypoxic condition (p<0.05). Notably, Cdk5ov transfectants showed a greater formation of neocapillary branch structures but their appearance was more chaotic. Similar to the controls, cdk5 was distributed with actin fibres alongside the branch structures. Confocal analysis in untransfected cells, demonstrated a co-localization of p35 and activated pTyr(15)Cdk5 with actin fibres in all phases of cell motility. P35 and talin co-localized with activated Cdk5 and integrin beta-1 at the leading edge of moving cells, indicating their interplay in cytoskelatal dynamics during cell motility. Notably, pilot microarray analysis showed reduced expression of pro-angiogenic protein MEF2C and Notch ligand, Jagged-1 in mutated (D144N) Cdk5 transfectants. In conclusion our results suggest that a pathway operating through Cdk5 may critically modulate cell dynamics during hypoxia/brain injury associated condition. Cdk5 over-expression may positively contribute to preserve cell motility, but may require interplay with other pathways to promote microvascular cell differentiation.

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W MP83

White Matter Hyperintensity Burden Accumulation Is Accelerated In Inherited *vs.* Sporadic Disorders Of Small Cerebral Vasculature

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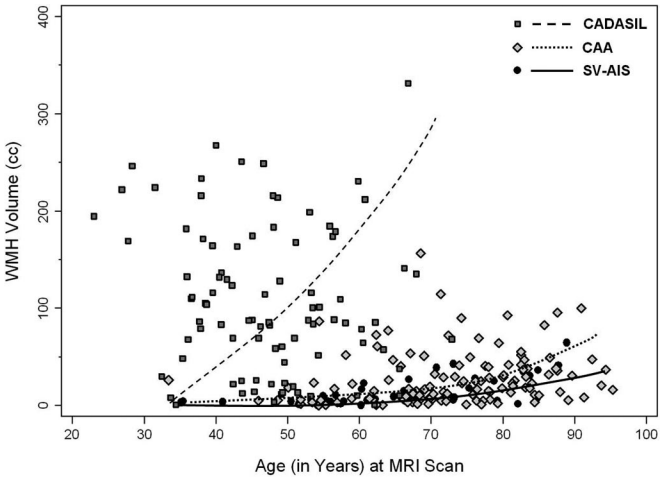
Background: White matter hyperintensities (WMH) are a common radiographic finding in disorders of cerebral small vessels such as cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) and cerebral amyloid angiopathy (CAA). However, limited data are available on WMH burden accumulation in cerebral microangiopathy syndromes, including those which can manifest as sporadic ischemic or hemorrhagic strokes. We sought to quantify and compare the burden of WMH in subjects with inherited (CADASIL) vs. predominantly sporadic (acute ischemic stroke [AIS] and intracerebral hemorrhage [ICH]) cerebral small vessels disease. **Methods:** We conducted a cross-sectional, multicenter study of prospectively enrolled cohorts of consecutive patients (1) admitted to the Emergency Department with a diagnosis of AIS or ICH, and (2) referred to our centers with a diagnosis of CADASIL. Among AIS patients, small vessel (SV) stroke subtype was assigned based on the TOAST criteria. ICH patients were diagnosed with CAA based on the Boston

criteria. Diagnosis of CADASIL was confirmed by skin biopsy and/or genetic testing for known mutations. Clinical evaluation by a vascular neurologist and brain MRI were performed. WMH volume (WMHV) was analyzed for using a validated semi-automated protocol. Multivariate linear and multinomial logistic regression analyses were used to asses the rate and determinants of WMH burden accumulation between the cohorts. **Results:** Subjects with CADASIL (n=90), CAA (n=122), and SV AIS (n=42) differed significantly by age (47.3±10.3; 72.2±11.6; 65.4±13.6 years, respectively [mean±SD]), systolic and diastolic blood pressure ($p<0.01$), as well as hypertension, diabetes, hyperlipidemia, and smoking status (all $P<0.01$). Median WMHV varied across the disease (CADASIL 88.8ml, IQR 51.7-169.3ml; CAA 17.8ml,7.3-38.3ml; SV AIS 7.1ml, 3.9-23.3ml)($p<0.0001$). In multivariate analyses, age, DBP, and hyperlipidemia were independently associated with greater WMH volume in patients with CADASIL, CAA, and SV AIS. The impact of age on WMHV burden was strongest among CADASIL subjects (WMHV/age slope: 88.7ml/10 years), followed by subjects with CAA (11.5ml/10 years), and SV AIS (6.3ml/10 years)(p for trend <0.001) (Figure). **Conclusions:** The burden of WMH differs significantly among subjects with genetic (CADASIL) or predominantly sporadic (CAA, SV AIS) disorders of cerebral small vasculature. Shared determinants of WMH burden suggest common biological processes leading to WMH accumulation in this subset of cerebrovascular disorders.



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W MP84

Improved Intraischemic Perfusion and Pial Arteriolar Dilation by Transfusion of Pegylated Hemoglobin in the Carbon Monoxide State

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Carbon monoxide (CO) releasing molecules enhance vasodilation, protect heart and kidney from ischemia, and reduce inflammation. Transfusion of chemically-modifed, cell-free hemoglobin (Hb) during middle cerebral artery occlusion (MCAO) can reduce infarct volume, but large amounts are typically required. We tested the concept that transfusion of Hb in the CO state would promote vasodilation during MCAO without requiring large amounts of Hb to be transfused. Transfusion of 10 ml/kg of a 4% solution of pegylated COHb (PEG-COHb) in isoflurane-anesthetized rats resulted in rapid release of CO and equilibration of CO with red cell-based Hb (2-3% COHb in whole blood and plasma) followed by pulmonary clearance over the next 2 h. Plasma [Hb] was ~0.5 g/dL. Induction of MCAO with the filament technique initially produced 37±8% (±SD) dilation of pial arterioles in the MCA border region that gradually subsided to 7±7% at 2 h in controls (n=9). Transfusion of 10 ml/kg at 20 min of MCAO with a 5% albumin solution attenuated but did not fully prevent the decline in diameter from the initial dilation of 37±8% to 25±13% at 2 h (n=7). Likewise, transfusion of PEG-Hb without CO attenuated but did not prevent the decline in diameter from the initial dilation of 37±11% to 22±8% at 2 h (n=7). However, with PEG-COHb transfusion the initial dilation of 41±11% was fully sustained at 40±13% (n=7) at 2 h MCAO (p=0.023, ANOVA). In time controls without ischemia, transfusion of albumin, PEG-Hb, or PEG-COHb produced no changes in arteriolar diameter over a 2-h period. In another experiment, transfusion was delayed until 90 min of MCAO, and laser-Doppler flow (LDF) was measured over the MCA border region. Transfusion of PEG-COHb (n=8) increased penumbral LDF from 58% to 80% (22% increase relative to pre-ischemic baseline), whereas transfusion of albumin (n=8) or PEG-Hb (n=8) produced relative increases of only 6% and 11%, respectively. We conclude that PEG-COHb can serve as a CO donor that effectively prevents time-dependent loss of pial arteriolar dilation during MCAO. Moreover, delayed transfusion of PEG-COHb improves blood flow in the penumbral region to levels above the threshold typically associated with eventual infarction.

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W MP85

Genome-wide Association Study of Brain Arteriovenous Malformation Patients

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Background: Brain arteriovenous malformations (BAVMs) are a tangle of abnormal vessels directly shunting blood from the arterial to venous circulation and are an important cause of intracranial hemorrhage in young adults. Several studies suggest that genetics may play a role in BAVM. We performed a genome-wide association study to investigate association of single-nucleotide polymorphisms (SNPs) with BAVM disease. **Methods:** A total of 371 self-reported Caucasian BAVM samples and 563 healthy Caucasian control samples were genotyped on the Affymetrix Genome-Wide Human SNP Array 6.0. Quality control assessment removed SNPs and samples with low genotyping call rates (<95%), SNPs out of Hardy-Weinberg equilibrium ($p<0.00001$), and SNPs with low minor allele frequency (<1%). A set of 94,559 loci with low pair-wise linkage disequilibrium ($r2<0.2$) were used to calculate principal components to identify and remove outliers (4 BAVMs and 6 controls) and adjust for residual population stratification. The final analytic dataset contained 334 BAVM samples and 504 controls; 708,750 SNPs were tested for association in PLINK v1.06 assuming an additive genetic model. Logistic regression analysis of SNPs was performed to adjust for the effects of age, sex, and the top 3 principal components. Genome-wide level of significance was set at $P<7x10-08$ using a Bonferroni adjustment. **Results:** Our genome-wide association study identified 109 SNPs associated with BAVM at $P<10-05$; 68 remained associated after adjustment for age, sex, and the top 3 principal components. Forty-five of these SNPs (2 exonic, 27 intronic, 16 intergenic) map within 20kb of 38 genes. One exonic SNP was associated with BAVM at a genome-wide level of significance ($p<7x10-08$). The minor allele of this SNP was present in 11% of cases and 2% of controls (OR=6.5, 95% CI=3.9-10.9, P=1.85x10-12). Adjustment for age, sex, and the top 3 principal components did not alter results (OR=6.5, 95% CI=3.8-11.2, P=1.7x10-11). The associated missense SNP maps to a gene on chromosome 6 encoding a protein that interacts with members of the mitogen-activated protein kinase (MAPK) signaling pathway. **Conclusions:** We performed a genome-wide association study examining Caucasian BAVM patients compared to Caucasian controls. We identified one coding SNP associated with BAVM at a genome-wide level of significance. These results require replication in additional samples and may lead to identification of novel genes for BAVM.

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W MP86

VEGF Induced More Severe Cerebrovascular Dysplasia in the Adult Mouse Brain with Regional Deletion of Alk1 Compared to Endoglin

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Background and Purpose: Endoglin (ENG) or activin receptor-like kinase 1 (ALK1) mutations cause hereditary hemorrhagic telangiectasia with high prevalence of brain arteriovenous malformations (bAVM). We demonstrated that vascular endothelial growth factor (VEGF) overexpression induced cerebrovascular dysplasia in adult Eng+/- and Alk1+/- mice. Eng+/- mice had 4-fold higher dysplasia than Alk1+/- mice. However, the phenotype was subtle. We hypothesized that VEGF stimulation with regional homozygous deletion of Alk1 or Eng induces severe dysplasia in the adult mouse brain, more akin to human bAVM. **Method:** $Alk1^{2f/2f}$ (exons 4-6 flanked by loxP sites), $Eng^{2f/2f}$ (exons 5-6 flanked by loxP sites) and wild type (WT) mice (8-10 weeks old) were injected with Ad-Cre ($2X10^7$ PFU, adenoviral vector expressing Cre recombinase) and AAV-VEGF ($2X10^9$ genome copies, adeno-associated viral vectors expressing VEGF) into the basal ganglia. At 8 weeks, blood vessels were visualized by microfil and lectin perfusion. Vascular density (capillaries in a 20X objective field) and dysplasia index (number of capillaries >15μm in diameter per 200 capillaries) were counted. **Results:** Gross vascular irregularities were seen in the $Alk1^{2f/2f}$ mouse brain injected with Ad-Cre and AAV-VEGF. The vessels were markedly enlarged with abnormal pattern; no gross irregularities were seen in similarly treated $Eng^{2f/2f}$ or WT mice. Dysplastic capillaries were seen in both $Alk1^{2f/2f}$ and $Eng^{2f/2f}$ mice, but not in WT mice. The dysplasia indexes were: 2.9±0.23 ($Alk1^{2f/2f}$), 1.47±0.80 ($Eng^{2f/2f}$) and 0.40±0.19 (WT). Injection of Ad-GFP and AAV-VEGF induced angiogenesis with normal structure. $Alk1^{2f/2f}$ mice showed a trend towards an increase (353±95) and $Eng^{2f/2f}$ mice showed a trend towards a decrease (194±31) in capillary densities compared to WT mice (248±72, P values =0.13 and 0.14). **Conclusions:** After VEGF stimulation and Ad-Cre-mediated regional gene deletion, the $Alk1^{2f/2f}$ mice had a greater dysplastic response with frank cerebrovascular malformations than $Eng^{2f/2f}$ mice. This is inexplicably opposite to what we observed in Alk1+/- or Eng+/- mice. Potential reasons for further study include: (1) Ad-Cre is more effective in $Alk1^{2f/2f}$ than $Eng^{2f/2f}$ mice; (2) preferential effects on certain cell types by somatic versus regional gene knockout; (3) potential dominant negative effect in Eng+/- mice.

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W MP87

Monomeric C-reactive Protein-Induced Angiogenesis Requires Gamma-Secretase Activity, Operates Through The PI3K/Akt Pathway And May Potentiate Notch-3 Function In Promotion Of Blood Vessel Stability

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Both monomeric C-reactive protein (mCRP) and Notch-3 receptor are induced in vascular areas of damaged tissue after ischemic stroke. We previously demonstrated pro-angiogenic effects of mCRP in cultured endothelial cells (EC) and a synergistic promotion with Notch-3/Fc chimera, an arterial/venous cell differentiator with a critical role in maintaining blood vessel stability. However, the molecular mechanisms implicated have not been investigated. Here, we highlighted the key proteins involved with an investigation of the signaling pathways. Angiogenesis assays were carried out using EC and smooth muscle cell (SMC); including proliferation, migration, tri-dimensional spheroids embedded in collagen gel and endothelial tube formation in Matrigel. The signaling pathways were investigated by a phospho-site microarray screening (KAM1.1) and by Western blotting. To highlight a common molecular mechanism involved, mCRP and Notch-3 effects were examined after treatment of the vascular cells with pharmacological inhibitors required for Notch-3 activation: DAPT (γ-secretase inhibitor) and LY294002 (phosphatidyl inositol (PI)-3 kinase/Akt inhibitor). Both mCRP and Notch-3/Fc induced EC and SMC proliferation, migration and differentiation in collagen gel and Matrigel. These effects were synergistically increased by the combination mCRP/Notch-3/Fc. Using microarray screening, we showed that the main phospho-protein expression induced by mCRP in EC was the insulin receptor substrate-1 (IRS-1), the major signaling molecule of insulin-like growth factor-1 receptor, which is a ã-secretase substrate. The treatment with the inhibitors showed that DAPT totally blocked Notch-3/Fc or mCRP/Notch-3/Fc-induced angiogenesis in vascular cells. A complete inhibition of mCRP-induced endothelial tube formation was only observed with DAPT. Treatment with LY294002 in combination with DAPT fully inhibited the pro-angiogenic effects of mCRP, Notch-3/Fc and mCRP/Notch-3/Fc on EC or SMC. In cultured EC, LY294002, DAPT and their combination fully inhibited mCRP-induced phospho-Akt expression whereas stimulated by Notch-3/Fc; phospho-Akt expression was only inhibited by DAPT. Phospho-Akt expression induced by the combination mCRP/Notch-3/Fc was only inhibited by LY294002/DAPT. However in co-culture EC/SMC, a notable decrease of mCRP/Notch-3/Fc-induced phospho-Akt expression was observed after treatment with both inhibitors and a total disappearance of phospho-Akt was obtained in the presence of LY294002/DAPT. Alongside to their common requirement of PI3K/Akt, for the first time we demonstrated the requirement of ã-secretase in mediation of mCRP pro-angiogenic activity. Thus, the combination of Notch-3 with mCRP amplifies angiogenesis and might both promote and stabilize the vessel formation whilst reducing the risk of hemorrhage following ischemic stroke.

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W MP88

Disrupted Arterial-venous Specification in the Adult Mouse Brain Following Alk1 Deletion and VEGF Stimulation

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Background and Purpose: Brain arteriovenous malformations (BAVM) can rupture and cause serious morbidity and mortality. Hereditary Hemorrhagic Telangectasia-2 patients with mutations in activin receptor-like kinase 1 (ALK1) have a high frequency of BAVM. The arterial marker, Jagged-1, is increased in human BAVM. Mutations of the venous marker, EphB4, can cause AVMs in the mouse embryo; genetic variation in EphB4 is associated with human BAVM hemorrhage. We recently developed a phenotype in the adult mouse brain that resembles human BAVM by regional conditional Alk1 deletion and vascular endothelial growth factor (VEGF) stimulation. We hypothesized that deletion of the Alk1 gene disrupts arterial-venous specification of VEGF-induced neovasculature in the adult mouse. **Methods:** Adult Alk1-floxed mice with loxP sites flanking Exons 4-6 were injected into the basal ganglia with $2X10^7$ PFU AdCre, an adenoviral vector expressing Cre recombinase, and $2X10^9$ genome copies of AAV-VEGF, an adeno-associated viral vector (AAV) expressing VEGF. The brain, intestine, and jugular vein were collected 8 weeks after injection. Vessels were characterized with lectin and immunohistochemical stains. **Results:** Irregular dysplastic vessels with enlarged lumens were detected in the brain of Alk1-floxed mice treated with Ad-Cre and AAV-VEGF. Only 52% of vessels at the injection site with lumens larger than 15 ìm were covered with smooth muscle. Jagged-1 staining was detected in the endothelial cells of 34% of the vessels, and EphB4 in 41% of the vessels, regardless of smooth muscle coverage. Interestingly, 22% of vessels expressed both Jagged-1 and EphB4, implicating an irregular phenotype. No abnormal vessels were detected in control vector injected brains, with 100% of vessels larger than 15 ìm covered with smooth muscle. In the intestine, basilar artery, and jugular vein, there was Jagged-1 and EphB4 positive staining on arteries and veins, respectively. These results implicate that deletion of Alk1 resulted in disruption of arterial-venous determination after VEGF stimulation. **Conclusions:** We observed a loss of distinct arterial-venous identity in the dysplastic vessels induced by VEGF stimulation in adult mouse brain with regional Alk1 deletion, suggesting that disruption of arterial-venous determination leads to the formation of dysplastic vessels that are prone to rupture.

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W MP89

The use of Onyx in Different Types of Intracranial Dural Arteriovenous Fistula

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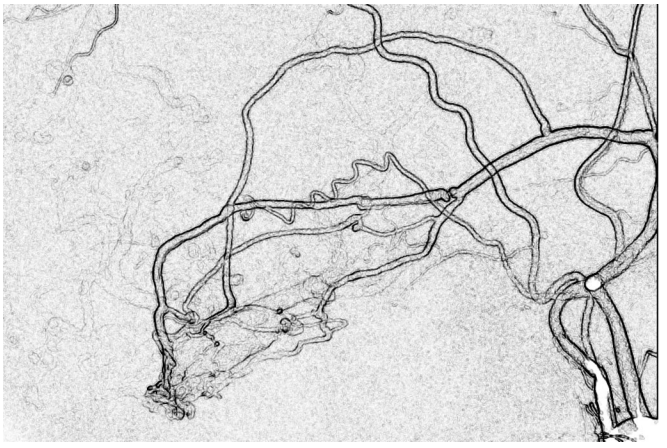
Purpose: Describe the treatment technique with injection of Onyx (ev3) by arterial approach of the different types of intracranial dural arteriovenous fistula (DAVF). **Methods:** Between January 2005 and January 2010 we treated at the Department of Interventional Neuroradiology, Hospital Lariboisière Paris, 44 DAVF in 42 patients. All patients were initially treated by arterial injection of Onyx. The average age was 56 years (27-86 years), 17 females and 28 males. The most frequent clinical presentation was pulsatile tinnitus (16), followed by intracranial hemorrhage (6) and headache (5). For the characterization of DAVF, we follow the classification of Hospital Lariboisière, Paris, France: 4 patients of Type I (direct drainage to the dural sinus and usual flow), 4 type IIa (with drainage to the sinus and sinus reflux), 11 type IIb (with drainage to the sinus and cortical vein reflux), 3 type IIa + IIb, 15 type III (direct drainage into the cortical vein), 5 type IV (drainage to the cortical vein associated with venous aneurysmal dilatation) and a type V (medullar venous drainage). **Results:** A total of 58 arterial pedicles were catheterized, in most cases (38) were catheterized the middle meningeal. The average time of injection was 30 min (15-60 min) and average amount was 2.5 cc (0.6 to 6.5 cc). Regarding the 20 fistulas with venous drainage to dural sinus dural (Type I and II) achieved the preservation of the venous sinus in 7 of them. Of the 44 embolized fistulas, eight had a second time of embolization, 1 a third time; in 4 cases complementary treatment was performed by intravenous embolization and placement of coils and / or surgery. Complications were observed in six patients. 4 for nerve injury: two with facial palsy and two with neuralgia. The other two patients had complications in relation to extension of venous thrombosis due to embolization. All cases showed partial or complete regression of the clinical post-complication. **Conclusion:** The treatment of DAVF by intracranial arterial injection of Onyx is safe and allows, in most cases, occlusion of the arterial venous shunt. In the case of DAVF with direct sinus drainage, the sinus preservation is possible.



Author Disclosures: T.G. Abud: None. J. St.-Maurice: None. D.G. Abud: None. A. Nguyen: None. Z. Szatmáry: None. M. Mazighi: None. A. Bisdorff: None. E. Enesi: None. L. Chiumarulo: None. D. Bresson: None. A. Aymard: None. E. Houdart: None.

W MP90

Neurointerventional Approach for Arteriovenous Malformations and Aneurysms in the Pediatric Population.

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Neuroendovascular interventions are now more common in children as an alternative for surgery in a diverse variety of vascular pathology, among these cerebral arteriovenous malformations (AVM) and aneurysms compromise children in approximately 12-18% and 1-5% respectively. Children with brain AVMs are prone to hemorrhages more frequently than adults with an associated high mortality. A retrospective review was performed in our institution regarding the efficacy of neuro-endovascular interventions in 53 patients under the age of 19 equally distributed by gender for ruptured and unruptured intracranial AVMs and aneurysms. Ninety seven AVM, 26 aneurysms and 5 AVF were encountered and 78 diagnostic angiograms, 42 embolizations (balloon assisted coil embolizations # 4, coil embolization #31 and embolization with onyx # 7) were performed. In 50 cases, follow up was completed and in 2 cases, recanalization was encountered for an AVM and one for an aneurysm. In both cases a second phase embolization was done. One asymptomatic complication occurred consisting in the rupture of an ultraflow microcatheter with extravasation of Onyx into the left vertebral artery treated with subsequent occlusion of the vertebral artery proximal to the embolic material. Advanced endovascular technologies implemented in neuroangiographic procedures in children seems to offer a feasible alternative to surgery for treatment of AVMs and aneurysms in the pediatric population.

Author Disclosures: A. Delgado: None.

Th MP1

Response to Intravenous Thrombolysis for Acute Ischemic Stroke in patients with Reduced Cardiac Ejection Fraction

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Background: Patients with cardiac ejection fraction (EF) ≤35% have higher stroke incidence with a reported 18% increased stroke risk with every 5% EF decline. A 58% increased risk of thromboembolic events has been found in women for every 10% decrease in EF. It is unclear, however, whether reduced EF affects the response to intravenous thrombolysis (IVT) for acute ischemic stroke (AIS). **Methods:** We identified patients from our prospective stroke registry who received IVT for AIS from 2004 to 2009. Demographics, baseline NIHSS, onset to needle times (OTNT), intra-arterial therapy (IAT), mortality, symptomatic ICH (sICH), and discharge mRS were collected. We compared discharge outcomes and mortality in patients with EF ≤35% (L-EF) versus those >35% (N-EF). **Results:** We identified 838 patients who received IVT with 159 and 679 patients in the L-EF and N-EF groups respectively. Patients in L-EF group were more likely to be African American (40.51% versus 26.60%, p=0.005) with higher baseline NIHSS (16 versus 12, P<0.0001). Other stroke risk factors, admission blood glucose, OTNT, and rate of IAT were similar in both groups. Coronary artery disease and atrial fibrillation were more common in the L-EF group (36.58% vs 23.71%, p=0.001 and 34.59% vs 24.89%, p=0.012 respectively). L-EF group had higher discharge mortality (24.53% vs 8.86%, P<0.0001) and lower incidence of good outcome (discharge mRS 0-2) (20.75% vs 33.68%, p=0.0016) with no difference in rates of sICH (9.43% vs 5.3%, p=0.06). On multivariate regression analysis, controlling for baseline NIHSS and IAT, L-EF remained independently associated with high discharge mortality (OR=2.123, 95%CI [1.28-3.51], p=0.0035). There were, however, no differences in good outcomes between the two groups. **Conclusions:** Patients with severely reduced EF compared with normal EF have higher mortality following IVT for AIS.

Table 1: Demographics, stroke characteristics and outcomes

	EF ≤ 35 (N=159)	EF > 35 (N=679)	p value
Caucasian	74 (46.84%)	383 (56.91%)	0.0053
African American	64 (40.51%)	179 (26.60%)	0.0053
CAD	58 (36.48%)	161 (23.71%)	0.001
A Fibrillation	55 (34.59%)	169 (24.89%)	0.013
Baseline NIHSS Median (range)	16 (1-40)	12 (1-40)	<0.0001
Onset to IV TPA (min) Median (range)	150 (35 – 267)	148 (10 – 270)	0.9030
IAT	28 (17.61%)	116 (17.08%)	0.8742
Discharge mRS 0-2	33 (20.75%)	228 (33.68%)	0.0016
Discharge mRS 0-3	59 (37.11%)	346 (51.11%)	0.0015
Death	39 (24.53 %)	60 (8.86%)	<0.0001
Symptomatic ICH	15 (9.43%)	36 (5.30%)	0.0636

Author Disclosures: V. Misra: None. N. Harun: None. M. Sline: None. A.D. Barreto: None. G.A. Lopez: None. N.R. Gonzales: None. J.C. Grotta: None. S.I. Savitz: None.

Th MP2

Safety And Outcome of IV Thrombolysis in Patients with Acute Stroke Treated In the 3-4.5 h Window Who Would Have Been Excluded From The ECASS III Trial

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Purpose of the study: To assess the safety of IV TPA in the 3 to 4.5 h window in patients who would have been excluded from the ECASS III trial. **Background:** More than 15 years ago, IV t-PA for acute stroke was shown to be safe and effective within 3 hours of symptom onset. The third European Cooperative Acute Stroke Study (ECASSIII) showed clear benefits of thrombolytic therapy in the 3 to 4.5 hour window; however certain patients were excluded from this trial, leaving uncertainty about whether they can be treated with IV t-PA. **Method:** We reviewed patients in our prospectively collected stroke registry who were treated with IV t-PA within 3 to 4.5 hrs of their symptoms. We separated the patients into those who would have met and would not have met ECASS III inclusion/exclusion criteria (older than 80 yo, NIHSS >22, prior stroke and DM, history of anticoagulation therapy). We collected mRS on discharge, and symptomatic intracerebral hemorrhage (sICH). We defined safety as incidence of sICH and mortality. We defined excellent outcome as mRS (0-1). **Results:** 85 patients were treated over the study period (2004- till 2010); 59 met the ECASIII criteria and 26 would have been excluded: 12 (46.15%) were >80 y old, 3 (11.55) had history of DM with prior stroke, 10 (38.4%) had recent history of anticoagulation, 8 (30.7%) had NIHSS >25, and 7 had 2 or more exclusion criteria, table 1: safety and the outcome after the adjustment of age and baseline NIHSS, Table 2: incidence of bleed and mortality in the group with exclusion criteria (some patients had 2 or more exclusion criteria). **Conclusion:** Thrombolytic therapy in 3-4.5 h window may be safe in patients with ECASS III exclusions, but there were trends suggesting that sICH and mortality were higher, particularly in certain subgroup (NIHSS >20 and history of anticoagulation). Prospective analysis of more patients is needed to answer this question.

table 1: safety and the outcome after the adjustment of age and baseline NIHSS,

	Met ECASS III criteria	Not met the criteria	P value
Age (Median)	62.5(66)	72.8 (76.5)	0.003
Male	29(49.2%)	12(46.2%)	0.82
Arrival Stroke Scale Median	12	20	0.003
Asymptomatic bleed	14 (24.4%)	7 (26.9%)	0.47
Symptomatic bleed	3 (5%)	3 (11.5%)	0.47
Mortality	6 (10.1%)	6 (23.1%)	0.21
Excellent outcome m RS (0-1)	12 (20.3%)	5 (19.2%)	0.27*
total	59	26	

Table 2: incidence of bleed and mortality in the group with exclusion criteria (some patients had 2 or more exclusion criteria).

	No bleeding	Asymptomatic bleed	Symptomatic bleed	Mortality
Age>80	7	4	1	1 (asymptomatic bleed) (8.3%)
NIHSS >25	4	3	1	4 (2 asymptomatic, 1 no bleed) (50%)
Anticoagulation	7	1	2	2(1 no bleed. 1 symptomatic) (28.5%)
DM & stroke	3	0	0	0
TOTAL	16 (61.5%)	7 (26.9%)	3 (11.5%)	6 died on our service (1 symptomatic, 3 asym, 2 no bleed) (23.07%) 1 DC to hospice

Author Disclosures: A.B. farrag: None. P. Sahota: None. J. Grotta: None. S. Savitz: None.

Th MP3

Negative CT in Witnessed Onset Acute Ischemic Stroke Patients is Not a Reliable Indicator for Early Stroke Onset

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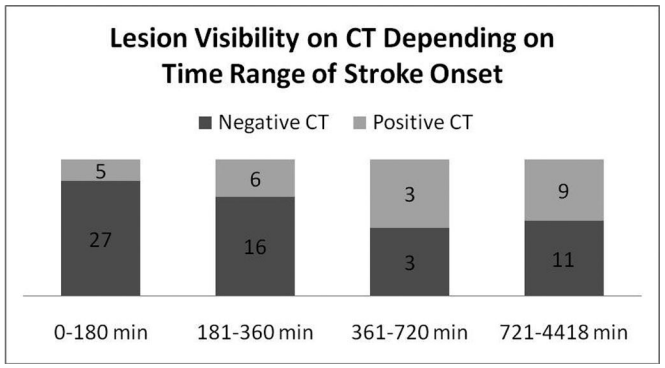
Purpose: Recent studies suggest negative FLAIR can identify patients within the thrombolytic time window. However, CT is more commonly used than MRI as a pretreatment screening tool with frank hypodensity suggesting later stroke onset. Therefore, negative CT and negative FLAIR of unknown stroke onset has been proposed to represent patients with early stroke onset. Our aim is to find whether confirmed stroke patients with negative CT can be correctly identified to be within the thrombolytic time window. **Methods:** For CT reads, 4 expert readers blinded to time of stroke onset scored pretreatment CT and MRI scans from Sep 2000-Feb 2002. Eighty patients were included based on acute ischemic stroke and last seen normal (LSN) time = time first seen with symptoms (FSS) ± 30minutes. For FLAIR MRI reads, patients having pre-treatment MRI within 24 hours from witnessed stroke onset were selected from Apr 2005- Sec 2008. Eighty five patients were included based on left hemisphere acute ischemic stroke with LSN time = FSS. Lacunar strokes and lesions with hemorrhagic transformation were excluded from both study sets. Two independent stroke neurologists blinded to time of MRI from LSN, scored FLAIR hyperintensity as present or not present corresponding to DWI-bright regions. The 3rd expert reader interpretation was used when there was a discrepancy between the first two readers. Logistic regression analysis was used to assess association between lesion visibility and time. **Results:** The sensitivity and specificity for negative CT to correctly identify early ischemic stroke onset < 6 hours is 80% and 46%, respectively. More than 40% of patients beyond 6 hours have a negative CT (Figure). Despite extended time range to 12 hours, negative CT specificity remained low at 45%. However, negative FLAIR specificity is 74% at 6 hours and 82% at 12 hours. The prevalence of lesion visibility increases with time on FLAIR (p=0.006), whereas CT lesion visibility is independent of stroke onset time (p=0.152). The average time for FLAIR to remain negative is 3.2h (SD=3.7h, Range 0.75-22.22; 95%CI 2.0-4.3) whereas average negative CT is at 8.9h (SD=14.5h, Range 0.60-69.9; 95%CI 5.0-12.8). **Conclusion:** Negative FLAIR is predictive of time but negative CT is independent of time and not a reliable indicator for estimating time range of early stroke onset. Because negative CT and negative FLAIR represent different time windows of stroke onset, it is not justified to combine them for the treatment of unwitnessed onset stroke patients. Negative FLAIR MRI is superior to negative CT in correctly identifying patients who are less than 6 hours of stroke onset.



Author Disclosures: S.S. Song: None. L.L. Latour: None. M. Luby: None. O. Wu: None. J.A. Chalela: None. J.A. Butman: None. A.M. Demchuk: None. M.D. Hill: None. N. Patronas: None. S. Warach: None.

Th MP4

Risk Factors for Symptomatic Intracranial Hemorrhage After Intravenous Thrombolysis for Acute Stroke

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Background: Recent studies have shown that chronic use of warfarin or antiplatelets prior to administration of IV tPA for acute stroke is associated with an increased risk of post-tPA symptomatic intracranial hemorrhage (SICH). Our study examines these risk factors for post-tPA SICH at our institution. **Methods:** With IRB approval, we reviewed 800 patient records from our thrombolytic database who received IV tPA at our institution between 2002 and 2010. We excluded patients who were treated outside the 4.5 hour time window, underwent intraarterial intervention, had IV tPA protocol violations, or were enrolled in experimental trials. SICH was defined as an increase in NIHSS score by $>$ 4 points or neurologic decline that is associated with ICH on imaging. Logistic regression analysis followed by multivariate analysis was carried out on several potential risk factors for post-tPA SICH: single antiplatelet use, dual antiplatelet therapy, warfarin use, statin use, and pre-treatment INR. We used the same statistical model to analyze other pre-treatment risk factors such as NIHSS score, blood pressure, and serum glucose, and also baseline risk factors such as hypertension and diabetes. **Results:** In total, 676 patient records that met inclusion criteria were analyzed. Antithrombotic use was as follows: ASA (193/29.2%), clopidogrel (32/4.84%), ASA + clopidogrel (39/5.9%), warfarin (65/9.83%). We noted a non-significant trend toward increased rate of SICH in aspirin-only users (OR = 2.81, 95% CI = 0.76-10.39, p = 0.122) and warfarin users (OR = 4.46, 95% CI = 0.87-22.76, p = 0.072), but not in clopidogrel-only users. Pre-treatment INR $>$ 1.2 and $<$ 1.8 was also not an independent predictor of SICH (p = 0.30). In multivariate analysis, chronic dual antiplatelet therapy was associated with increased risk of post-tPA SICH (OR = 11.95, 95% CI = 2.46-57.99, p = 0.002) in addition to pre-treatment systolic blood pressure (OR = 1.02, 95% CI = 1.01-1.04, p = 0.008), early CT changes (OR = 5.21, 95% CI = 1.08-25.17, p = 0.04), and history of diabetes (OR = 4.06, 95% CI = 1.46-11.30, p = 0.007). **Conclusions:** At our institution, we found that pre-treatment use of dual antiplatelet agents was an independent predictor of post-tPA SICH, which is consistent with the findings from prior SITS-ISTR studies. However, in contrast to prior studies, chronic use of warfarin and pre-treatment INR $>$ 1.2 were not associated with an increased risk of post-tPA SICH.

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Th MP5

Early Predictors and Therapeutic Strategies in Patients with Progressive-Type Lacunar Infarction: A Prospective, Multi-Centered, Observational Study

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Background: It has been reported that 25-40% of lacunar stroke patients show a progressive time course during the first several days of stroke and thus have poor functional outcome. We attempted to find 1) clinical and neuroimaging signs to predict neurological deterioration in the early phase, 2) whether to clarify the several antithrombotic drugs for preventing further progression and expecting a better functional outcome. **Methods:** We prospectively included 190 patients (mean age 67.9 yrs) admitted within 48 hrs after ischemic stroke between Jan 2007 and Dec 2009 in 7 stroke centers in Japan (Study for Treatment, Overt Signs and Pathophysiology of Branch Atheromatous Disease: STOP-BAD Group). Inclusion criteria were 1) 20-84 yrs of age, 2) pure motor hemiparesis, 3) acute ischemic lesion was identified only in the perforating artery territory on diffusion weighted MRI (DWI). Progressive-type stroke (PS) was defined as worsening by $>$ or = 1 point in the NIHSS for motor function within 7 days after onset. To identify predictors for PS, clinical characteristics including vascular risk factors, body temperature on admission, and initial DWI findings were evaluated. Antithrombotic agents of the first 7 days were recorded, such as heparin, argatroban hydrate, aspirin, cilostazol, clopidogrel sulfate, which were performed at each investigator's discretion. Functional outcome was assessed with the modified Rankin Scale (m-RS) at 3 months. **Results:** Fifty-two of 190 patients (27%) were classified into the PS group. In the PS group, 39 patients (75%) showed progression within the first 48 hrs after admission, while 13 patients (25%) deteriorated after 3 days of admission. Fluctuation of symptom before admission was more frequently observed in the PS group (28/52, 54%) than in the non-PS group (51/138, 37%) ($p<0.05$). Vascular risk factors, mean age, and laboratory tests were the same in two groups. Body temperature on admission was significantly higher in the PS group (36.9 degrees vs. 36.6 degrees, $P<0.05$). In the initial DWI, length and slice number of the lesion was larger in the PS group, while the width did not differ in the two groups. The unfavorable outcome (m-RS: 3-5) at 3 months was significantly higher in the PS group (31/52, 60%) than in the non-PS group (5/138, 4%) ($p<0.001$). In univariate analysis of each therapeutic agent, any treatment could not stop the progression. However, in a subanalysis of PS group, cilostazol (a phosphodiesterase 3 inhibitor) use within 7 days, especially in the early phase, were significantly correlated with good functional outcome (m-RS: 0-2) at 3 months (Day 1: $p=0.0043$, Day 2: $p=0.0145$, Day 7: $p=0.0411$). **Conclusion:** Fever on admission, initial DWI findings may allow us to predict PS. Early treatment using cilostazol, which protects the vessel endothelium in addition to antithrombotic function, resulted in good functional outcome in the chronic phase, even in the PS group.

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Th MP6

Outcomes Of t-PA Use In Octogenarians

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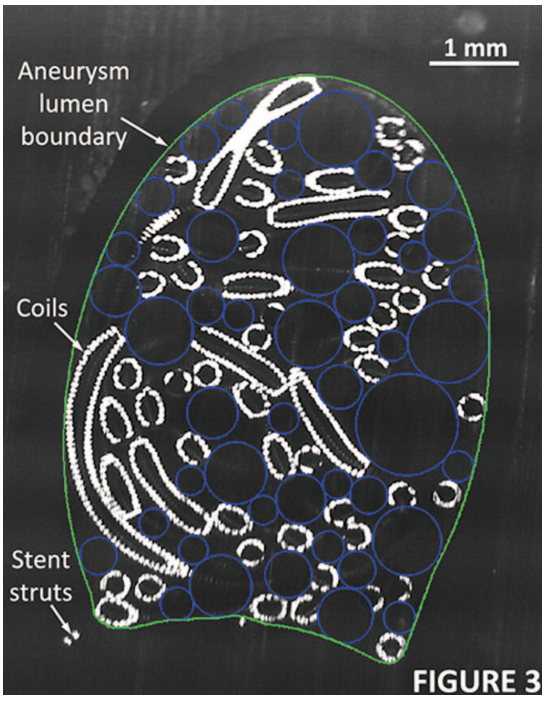
Introduction: Intravenous tissue plasminogen activator (IV t-PA) is used to treat acute ischemic stroke in adults regardless of age within 3 hours. The use of IV t-PA in the elderly remains controversial. We examined the clinical outcome and side effect profile after IV t-PA between patients $\geq$80 years and $<$80. **Methods:** All patients treated with IV t-PA within 3 hours after stroke onset were prospectively evaluated using the University of California San Diego Stroke Code database from 2004 to 2010. We compared frequency of good outcome (90-day Modified Rankin Score (mRS) 0 or 1), symptomatic intracerebral hemorrhage (sICH), new ischemic stroke, systemic hemorrhage, and allergic reaction between patients who are 80 years and older (Group 1) and those younger (Group 2) using multivariable logistic regression models. All comparisons are adjusted for admission NIHSS, pre-stroke mRS, diabetes, atrial fibrillation, gender, and treatment with rt-PA and presented as odds ratio between groups 1 and 2. **Results:** A total of 210 patients were treated with IV t-PA within 3 hours; 80 in group 1, and 130 in Group 2. The mean$\pm$SD age was 86$\pm$4.4 in group 1, 62$\pm$13.3 in group 2 (p = 0.01). The baseline NIHSS (mean$\pm$SD) was higher in group 1, 15.8$\pm$9.3 versus 10.9$\pm$7.7 ($p<0.0001$). More patients in group 1 had a pre-stroke mRS $>$1 (42.5% vs. 10.9%, $P<0.0001$), hypertension (78.8 vs. 63.1%, $p=0.02$) and atrial fibrillation (43.6 vs. 17.6%, $P<0.0001$). Smoking (26.3 vs. 34.6%, $p=0.22$) and diabetes (17.5 vs. 26.9%, $p=0.13$) were



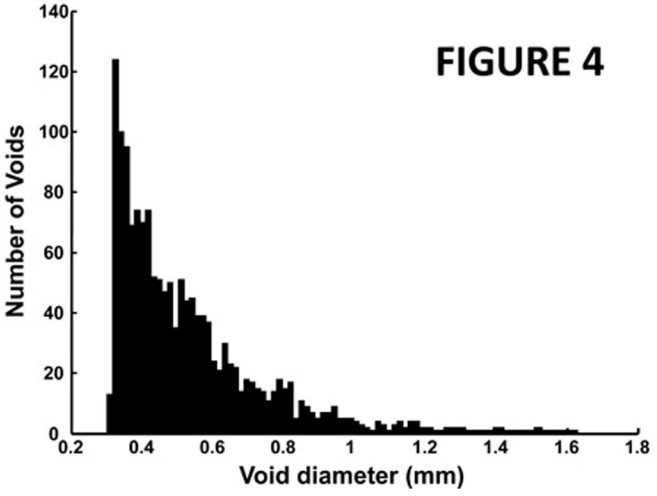


FIGURE 4

more common in group 2. In group 1, 13/80 (16.3%) had a mRS 0-1 at 90 days, group 2, 48/130 (36.9%). The adjusted odds ratio of age ≥80 affecting good clinical outcome after IV t-PA for stroke is 0.56(0.24 - 1.29) (p=0.17). Symptomatic ICH occurred in 3 (3.8%) in group 1, and 4 (3.1%) in group 2 (p = 0.81). Combined adverse events, including cerebral hemorrhage, major systemic hemorrhages, new ischemic stroke and allergic reaction occurred in 14 (17.5%) in group 1 and 14 (10.8%) in group 2 (p = 0.78). **Conclusions:** There was no significant difference in clinical outcome and safety profile between patients ≥80 years of age and those younger. These data suggest that there may be no reason to withhold IV t-PA from older patients with stroke within 3 hours of onset.

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Th MP7

Why There Are So Many Small Ruptured Intracranial Aneurysms?

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Introduction: Results from the International Study of Unruptured Intracranial Aneurysms (ISUIA) 2 have shown the prospective risk of rupture for small (largest diameter less than 7 mm) anterior circulation aneurysms are near zero. However, in practice, subarachnoid hemorrhage (SAH) from small intracranial aneurysms is commonly observed. This study uses simple mathematical model to calculate the expected SAH incidence based on ISUIA 2 results and compare it to the observed case series in one neurovascular center. **Methods:** Aneurysmal SAH cases were identified from a prospectively maintained neurosurgical database at a tertiary neurovascular center over 3 years. Aneurysm sizes and locations were recorded. Using literature reported unruptured intracranial aneurysm prevalence in population and ISUIA 2 results, expected cases of SAH from small aneurysm rupture in a North American metropolitan area were calculated. **Results:** According to 2009 US Census, our metro area has a population of 5.87 million. Two percent of the population likely harbors an intracranial aneurysm. Most of aneurysms are probably small (largest diameter less than 7 mm); assuming 90% of all aneurysms are small. Based on ISUIA 2 results, small intracranial aneurysms have an annual incidence of rupture of 0.05%. Therefore, 5.87M x 0.02 x 0.9 x 0.0005 = 52.8 SAH cases should be observed annually in our community. We are one of the four major neurovascular centers in the metro area. From 2007 to 2010, over 3 years, we have treated 136 cases of confirmed aneurysmal SAH. Among these, 114 SAH cases were the results of small aneurysm rupture (annual observed small aneurysm rupture volume 38 cases). It is very unlikely that we received referrals of more than one third of all SAH cases from our metro area. **Conclusions:** There is a large discrepancy between the expected risks of SAH from small intracranial aneurysms and the actual observed number in clinical practice. Further debate of the ISUIA results and study in the natural history of unruptured intracranial aneurysms are warranted.

Author Disclosures: Y. Zhang: None.

Th MP8

Hemodynamic-Morphologic Discriminants for Intracranial Aneurysm Rupture

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Background and Purpose: To identify significant morphologic and hemodynamic parameters that discriminate intracranial aneurysm (IA) rupture status using 3D angiography and computational fluid dynamics (CFD). **Methods:** 119 IAs (38 ruptured, 81 unruptured) were analyzed from 3D angiographic images and CFD. Six morphologic and seven hemodynamic parameters were evaluated for significance with respect to rupture. Receiver-operating characteristic (ROC) analysis identified area under the curve (AUC) and optimal thresholds separating ruptured from unruptured aneurysms for each parameter. Significant parameters were examined by multivariate logistic regression analysis in 3 predictive models–morphology only, hemodynamics only, and combined–to identify independent discriminants, and the AUC-ROC of the predicted probability of rupture status was compared among these models. **Results:** Morphologic parameters (*Size Ratio [SR], Undulation Index, Ellipticity Index,* and *Nonsphericity Index*) and hemodynamic parameters (*Average Wall Shear Stress [WSS], Maximum intra-aneurysmal WSS, Low WSS Area, Average Oscillatory Shear Index [OSI], Number of Vortices,* and *Relative Resident Time*) achieved statistical significance ($p<0.01$). Multivariate logistic regression analysis demonstrated *SR* to be the only independently significant factor in the morphology model (AUC=0.83, 95% confidence interval [CI] 0.75-0.91), whereas *WSS* and *OSI* were the only independently significant variables in the hemodynamics model (AUC=0.85, 95% CI 0.78-0.93). The combined model retained all three variables, *SR, WSS,* and *OSI* (AUC=0.89, 95% CI 0.82-0.96). **Conclusion:** All three models–morphological (based on *SR*), hemodynamic (based on *WSS* and *OSI*), and combined–discriminate IA rupture status with high AUC values. Hemodynamics is as important as morphology in discriminating aneurysm rupture status.

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Th MP9

In Vitro Quantification of the Size Distribution of Intrasaccular Voids Left after Endovascular Coiling of Cerebral Aneurysms

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Introduction: The endovascular treatment of aneurysms is currently quantified by a global coil packing density measure. The local distribution of coils in the aneurysm can provide further insight into the physical mechanisms leading to coil-compaction but such distributions are yet unknown. Here we quantify the local coil distribution by measuring the sizes of the aneurysmal voids left by the coil mass. **Methods:** Eight identical elastomer replicas of the rabbit elastase-induced aneurysm were embolized (Fig 1) by one interventional neurosurgeon; four models were coiled with balloon assistance and four with stent-support. The models were then embedded in epoxy blocks and the blocks sanded perpendicular to the aneurysm axis (height) at 100 micron intervals. A light-microscope image was acquired of the sanded surface at each interval (Fig 2). In each image, the space devoid of coils within the aneurysm lumen was optimally filled with circles of diameter not less than the coil diameter (Fig 3). The sizes of these circles over the entire sequence of images then represented the distribution of voids left by the coil mass. **Results:** The packing density of the stent-supported cases (mean ± std.dev = 40±7%) was significantly higher (t-test $P<0.05$) than the packing density of the balloon-assisted cases (31±2%). Figure 4 shows a histogram of the void sizes from one stent-support sample. **Conclusion:** Such quantifications of coil distribution can eventually be utilized in numerical simulations of intraneurysmal hemodynamics to estimate coil-compaction probabilities in the clinical setting.

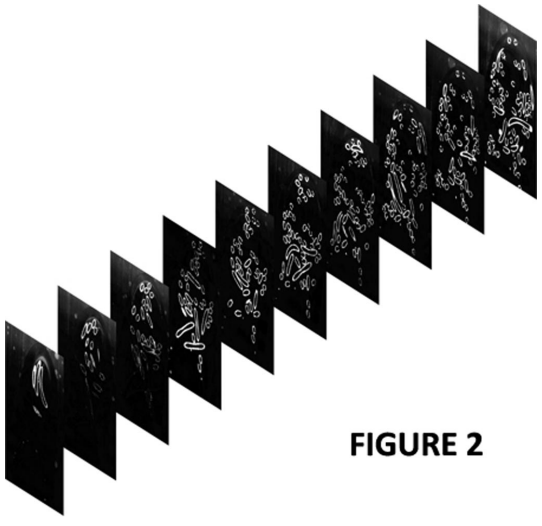
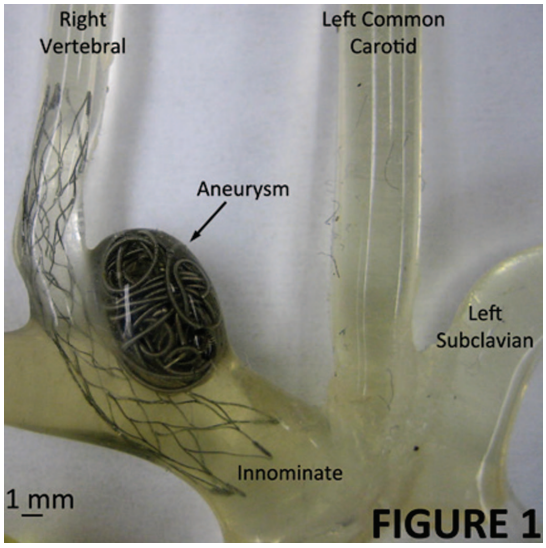


FIGURE 2



Author Disclosures: M.A. Aziz-Sultan: None. C. Sadasivan: None. J. Brownstein: None. B. Patel: None. E. Puig: None. K. Fernandez Prada: None. A. Rakian: None. H. Farhat: None. M.S. Elhammady: None. Q. Hao: None. A.L. Trager: None. H.H. Woo: None. D.J. Fiorella: None. B.B. Lieber: None.

Th MP10

Efficacy, Durability and Cost of Stent Assisted Coiling of Unruptured Intracranial Aneurysms Compared to Coiling and Clipping

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Introduction: Stent-assisted coiling (SAC) of intracranial aneurysms has emerged as a treatment alternative to clipping or coiling, particularly of large or wide necked aneurysms. Complication rates and procedure related mortality have been reported to be significantly higher in SAC compared to non-stent assisted repair. In this study, we aim to compare the efficacy, complications, discharge disposition, cost and length of stay (LOS) among patients with unruptured aneurysms who underwent either SAC, coiling or clipping. **Methods:** A retrospective study of patients with unruptured intracranial aneurysms treated at our institution between 2003-2010 was conducted. We compared patients who were treated with self-expanding stents followed by coiling, to patients who underwent coiling alone or clipping. Residual aneurysm after the first treatment and after delayed angiogram, recanalization, post-treatment aneurysm rupture, requirement for additional treatment, treatment complications, discharge disposition, cost and LOS were compared between groups using Chi-squared, Kruskall-Wallis and logistic regression analysis. **Results:** Of a total of 110 subjects, 42 underwent SAC, 33 coiling and 35 clipping. The groups were well matched for age, gender and aneurysm location, though the SAC group had significantly larger aneurysms (median 9 mm versus 6.8 and 7.7, $P=0.001$) with larger necks (6 mm versus 3 and 5, respectively, $P<0.001$). Compared to patients who were clipped, SAC patients had significantly more residual aneurysm after the 1st treatment (69% versus 18%, $P<0.0001$) in the neck and interstices, but this difference was smaller at follow-up angiography (50% versus 11% residual) and not significant after adjusting for aneurysm and neck size. There was no difference in recanalization, requirement for additional treatment, or aneurysm rupture between the groups after adjusting for aneurysm and neck size. Complications occurred in 2 SAC and 2 coiled patients and 1 clipped patient ($P=0.505$). On multivariate analysis, only aneurysm size was a significant predictor of residual aneurysm, recanalization, aneurysm rupture and the need for additional treatment. SAC and coiled patients were more likely to be discharged home or to acute rehab than clipped patients (100% versus 90%, $P=0.05$). Overall direct cost was higher for SAC patients than coiled or clipped patients (median $21,319 versus $11,974 versus $14,188, $P=0.006$) after adjusting for aneurysm and neck size. Hospital LOS was significantly shorter for SAC and coiled patients compared to clipped patients (median 1.5 days versus 1.5 versus 4, $P<0.0001$). **Conclusions:** SAC is an efficacious and safe alternative to coiling or clipping of unruptured aneurysms, though it is significantly more expensive.

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Th MP11

The Effect of Tissue Plasminogen Activator on Hemorrhage Rate in Ischemic Stroke Patients with Aneurysms, a Case Series Report

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Introduction: The use of tPA is contraindicated in certain conditions where the risk of bleeding supersedes the benefits of use. A contraindication that can be overlooked in the work-up of an ischemic stroke patient, and lead to a hemorrhagic event, is the presence of an intracranial aneurysm or arteriovenous malformation. We assessed the intracranial hemorrhage (ICH) rate in ischemic stroke patients who had aneurysms and were treated with intravenous (IV) tPA. **Methods:** We retrospectively identified all patients from 2008 through May 2010 at our institution who 1) were treated with IV tPA for ischemic stroke, 2) were treated as a part of our stroke alert protocol, and 3) who were found to have an aneurysm. Hemorrhagic events were categorized as symptomatic or asymptomatic by a board certified vascular neurologist. Baseline demographic and clinical data were also retrieved. **Results:** Seven patients had aneurysms, the mean age was 70 years, 71% were female, 57% were transferred from another facility, the mean initial NIHSS score was 11 and mean time from symptom onset to IV tPA administration was 91 minutes. The 7 patients were only screened for the presence of ICH prior to IV tPA administration using a non-contrast head CT; vessel studies were not conducted prior to IV tPA treatment. All aneurysms were found incidentally after the administration of IV tPA, and had a mean size of 3.6 mm. CT angiograms (CTAs) visualized aneurysms in 4 patients (57%) with a mean size of 5 mm. CTAs were unable to visualize aneurysms in 3 patients; these were visualized with conventional angiograms and had a mean size of 2 mm. Only 3 patients (43%) with aneurysms developed ICHs, all were asymptomatic. All 7 patients survived to hospital discharge. **Conclusions:** The majority of patients with intracranial aneurysms did not hemorrhage after the administration of IV tPA. Administration of IV tPA in ischemic stroke patients with aneurysms did not result in any in-hospital deaths. Moreover, this case series suggests that CTA may be lacking in its ability to visualize small aneurysms. In conclusion, we believe aneurysm as a contraindication for IV tPA use in ischemic stroke patients requires further study. Institutions with larger databases are encouraged to compare the hemorrhage rate following IV tPA administration in those with and without aneurysms because the benefits of tPA treatment may outweigh the risks of hemorrhage.

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Th MP12

In Vitro Evaluation of a Novel Hyper-Elastic Thin Film Nitinol Covered Stent for the Treatment of Intracranial Aneurysms

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Background and Purpose: Endovascular coiling has revolutionized the treatment of intracranial aneurysms. Coiling is not, however, a panacea and studies have found significant rates of recanalization, as well as difficulties treating wide-neck and fusiform morphologies. The purpose of this study was to examine the flow limiting capabilities and early thrombotic response to a novel Hyper-Elastic Thin Film Nitinol (HE-TFN) covered stent for the treatment of intracranial aneurysms. **Methods:** Two types of covered stents (device I and II) with different porosities (75% and 80%, respectively) were constructed. A laser particle image velocimetry (PIV) system was used to quantify intra-aneurysmal flow under steady and pulsatile conditions in a model sidewall aneurysm. Parameters measured include cross neck flow, intra-aneurysmal kinetic energy, and root mean square (RMS) velocity. Values were compared to those obtained without a device in place. To examine the early thrombotic response, an *in vitro* circulation model was constructed. The system consisted of a glass aneurysm model connected to a continuous loop of silicone tubing placed within a 37º waterbath. A peristaltic roller pump was used to propel fresh whole blood through the loop at a rate of 4 mL/sec. After 15 min., the devices were removed and analyzed with scanning electron microscopy (SEM). **Results:** PIV analysis under steady flow conditions (4 mL/sec) showed that device I reduced cross-neck flow by 54.1%, intra-aneurysmal kinetic energy by 98.4%, and intra-aneurysmal RMS velocity by 78.2% as compared to control. Device II reduced cross-neck flow by 23.5%, intra-aneurysmal kinetic energy by 85.9%, and intra-aneurysmal RMS velocity by 59.7%. A similar trend was observed at different flow rates and under pulsatile conditions. SEM of the devices following exposure to the circulation model showed accumulation of a dense fibrin network on the portion of HE-TFN covering the aneurysm's neck. The network was most dense at the corners of the pores, extending inwards towards the center and trapping both leukocytes and RBCs. **Conclusion:** The changes in intra-aneurysmal flow caused by, and the initial thrombotic response to, a novel HE-TFN covered stent for the treatment of intracranial aneurysms appear to be very favorable for aneurysm occlusion. PIV studies demonstrated dramatic reductions in cross-neck flow, kinetic energy, and RMS velocity. SEM analysis of the devices after exposure to blood showed a dense fibrinous network of blood products between the HE-TFN's pores, suggesting a possible mechanism for further flow reduction *in vivo* Although more extensive *in vivo* testing is needed, this device appears to represent a highly porous, flexible, and low profile novel flow diversion device.

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Th MP13

Neurovascular Unit Remodeling During Recovery Involves Matrix Metalloproteinases In Ischemic Rat Brain

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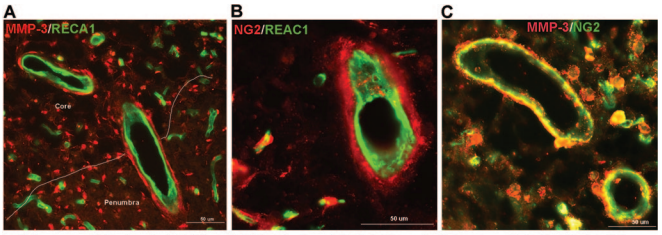
We previously reported that matrix metalloproteinases (MMPs) increase the permeability of the blood-brain barrier (BBB) by degrading tight junction proteins (TJPs) and treatment with MMP inhibitors prevents BBB disruption. However, MMPs may have a beneficial role during recovery after stroke. Stroke recovery is associated with angiogenesis and BBB remodeling though the mechanisms of neurovascular remodeling during recovery are uncertain. We hypothesized that

the protective role of MMP inhibition against BBB damage at an early stage may be beneficial and MMPs may play a crucial role in neurovascular remodeling during recovery after stroke. A 90 minute transient middle cerebral artery occlusion (MCAO) was induced in adult rats with reperfusion for 24 and 48 hrs, 7 days and 3 weeks. From 24 hrs to 7 days, we observed a significant loss of vessels in the ischemic hemispheres, and by 3 weeks there was a remarkable increase of vessels in the core and penumbra areas compared to 7 days. Double immunohistochemical staining with RECA-1, an endothelial cell marker, and NG2, a marker of immature pericytes, showed that these vessels are newly formed. Intravenous injection of Evans blue showed blood flow in ischemic regions, but new vessels showed leakage of dye into surrounding tissues. One dose of a broad-spectrum MMP inhibitor, BB1101 or GM6001, delivered immediately before MCAO, significantly increased the new vessel formation and reduced tissue loss in lesion areas at 3 weeks. TJPs claudin-5 and ZO-1 in endothelial cells and occludin and ZO-1 in astrocytes reappeared around the core lesion area that connected to new vessels at 3 weeks. Treatment with MMP inhibitors significantly enhanced the expression, phosphorlyation and integrity of TJPs as observed by western blot ($p<0.01$). An increase in MMP-2 and -3 was detected in the ischemic hemisphere at 3 weeks. MMP-2 co-localized with astrocytes expressing ZO-1 and occludin, while NG2-positive pericytes near newly formed vessels appeared to be the main source of MMP-3 (Figure). Expression of TGF-â receptors ALK1 and ALK5 was tested at 3 weeks. We found an increase of ALK1 expression and a decrease of ALK5 expression in lesion hemispheres, suggesting cellular proliferation and angiogenesis. Early inhibition of MMPs significantly promoted this process in lesion hemispheres. Our results suggest that although MMPs are known to be detrimental early, they improve new vessel formation and remodeling of injured tissues at later stages of the ischemic insult. Timing of MMP inhibitor action needs further study to determine optimal therapeutic window.



A. Immunohistochemical staining of MMP-3 (red) and RECA-1(green). **B**. Immunohistochemical staining of NG2 (red) and RECA-1 (green). **C**. Immunohistochemical staining of MMP-3 (red) and NG2 (green).

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Th MP14

Deficiency Of Metalloprotease ADAMTS13 Aggravates Brain Injury and Inflammation in a Murine Model of Experimental Stroke

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Background: Numerous epidemiological and clinical studies indicate that both excessive thrombosis and chronic inflammation contribute to the pathogenesis of ischemic stroke. ADAMTS13 is a plasma protease that cleaves ultra large von Willebrand factor (VWF) multimers (the most adhesive and thrombogenic form of VWF) in circulation and prevents excessive microvascular thrombosis in thrombotic thrombocytopenic purpura. Recently, it was demonstrated that deficiency of ADAMTS13 aggravates brain injury in mice (Zhao et. al., 2009, Blood). Since ADAMTS13 regulates both inflammation and thrombosis (Chauhan et. al., 2008, JEM), we tested the hypothesis that deficiency ADAMTS13 enhances the inflammatory response in an experimental model of ischemic stroke in mice. **Model and Method:** Transient focal cerebral ischemia was induced by 60 minutes of occlusion of the right middle cerebral artery with a 7.0 siliconized filament in Adamts13 -/- and wild-type (WT) mice (8-10 weeks in age). Mice were anesthetized with 1-1.5% isoflurane mixed with medical air. Body temperature was maintained at 37°C ± 1.0 using a heating pad. Laser Doppler flowmetry was used to confirm induction of ischemia and reperfusion. At 23 hours after MCAO, mice were sacrificed. Inflammatory response in stroke was evaluated by measuring myeloperoxidase (MPO) activity and immunohistochemical analysis of neutrophil at sites of ischemic brain injury in serial tissue sections. **Results:** In Adamts13-/- mice the infarct volume in the ischemic hemisphere was significantly increased by two-fold compared to WT mice. Regional cerebral blood flow between the groups was not different as assessed by laser Doppler flowmetry. The increase in infarct volume in Adamts13-/- mice correlated with an increase the inflammatory response in the ischemic region. There was a two-fold increase in myeloperoxidase (MPO) activity in Adamts13-/- mice (Mean ± SEM: 8.91 ± 1.60 U/mg protein, $n=7$, $P < 0.02$) compared to WT (Mean ± SEM: 3.59 ± 1.22 U/mg protein, $n=7$) mice. Enhanced MPO activity in the ischemic region of the Adamts13-/- mice also correlated with a significant two-fold increase in neutrophil influx as assessed by immunohistochemical analysis. **Conclusions:** Deficiency of ADAMTS13 in mice aggravates brain injury and inflammation. We propose that recombinant ADAMTS13 could potentially have near-term benefit for therapy for ischemic stroke, which remains a major public health issue worldwide.

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Th MP15

RNAi-mediated Knockdown of Injury-induced Prokineticin 2 And Its Effects On Neuron Death

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Objective: Prokineticins (PK1 and PK2) are secreted proteins that have been implicated in multiple biological functions including circadian rhythms, angiogenesis, neurogenesis and inflammation. Recently we have demonstrated that PK2 mRNA is induced in the ischemic striatum after middle cerebral artery occlusion, and exogenous central delivery of PK2 worsened infarct volume. Although intraperitoneal delivery of PK2 receptor antagonist reduced ischemic injury and improved behavioral outcome, it remains unclear whether this protection was directly due to blocking the effects of stroke-induced PK2 in the brain, or secondary to other peripheral effects of the antagonist. To address this, we have designed short hairpin RNA to directly knockdown the injury-induced PK2 in the striatum and examined its effects on neuron death in primary cultures and in focal ischemia. **Methods:** Short hairpin RNA (shRNA) candidates were designed and cloned into the pSilencer vector for screening. Candidates were screened for their ability to knock down recombinant PK2 fused to a ProLabel tag. The top candidate (OB2) and a negative control (Scr) were cloned into a lentiviral vector co-expressing GFP. For primary culture studies, striatal cultures were infected with lentivirus expressing OB2 or Scr. Cultures were then treated with glutamate for 5 hours, and RNA was extracted to examine PK2 using qPCR. For in vivo studies, lentiviral-mediated OB2 or Scr were stereotaxically delivered into the striatum of adult male Sprague Dawley rats. One week later, a permanent middle cerebral artery occlusion (dMCAO) was performed on these rats. Animals were sacrificed 24 hours later and brains were processed for Triphenyltetrazolium Chloride (TTC) staining to visualize infarct. Quantification of infarct volume was performed using Image J. **Results:** Screening of shRNA candidates indicated that shRNA targeting the middle region of the PK2 gene (147-178bp) resulted in the highest level of PK2 inhibition. In striatal mixed cultures, we showed that excitotoxic glutamate-induced PK2 mRNA expression, with the highest increase at 250-500μM glutamate. Short hairpin RNA against PK2 inhibited the glutamate-induced PK2 expression by ~60%. Furthermore, glutamate-induced PK2 expression remained upregulated in pure striatal neuronal cultures, suggesting that the excitotoxicity-induced PK2 expression occurred mainly in neurons. Using an invivo stroke model (dMCAO), lentiviral mediated knockdown of PK2 in the striatum resulted in reduced ischemic injury. **Conclusion:** Our data indicate that injury-induced PK2 is deleterious and PK2 contributes to the pathological mechanisms of stroke. Current studies examine the effects of RNAi PK2 on neuron death and inflammatory mediators after stroke. PK2 may be a potential novel target for the treatment of stroke.

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Th MP16

Let 7f microRNA As A Therapeutic Target Following Stroke In Female Rats

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Background: MicroRNAs (miRNAs) are small, non-coding RNA molecules of 18-25 nucleotides that control cellular function by inhibiting translation or by degrading mRNA. Cerebral miRNA profiles are significantly altered during pathological conditions such as stroke and identified neuroprotective miRNA may provide an attractive therapeutic target. Previous work from our lab indicated that older females sustain a larger infarct as compared to younger females, and that estrogen treatment to older females further increases cortical infarct volume (Selvamani and Sohrabji, 2008). Post-stroke infusions of IGF-1 (insulin-like growth factor-1) reverse estrogen-mediated toxicity (Selvamani and Sohrabji, 2010). Estrogen and IGF-1 interact to promote neuroprotection in several injury models and age-related loss of IGF-1 may promote greater ischemic-induced cell death in older animals. We therefore hypothesized that inhibiting miRNA that bind to the 3' UTR of the IGF-1 gene would exert neuroprotection. Of the several miRNA that bind to the IGF-1 3' UTR, we selected Let7f, because this miRNA is also known to regulate angiogenesis. **Results:** ICV infusions of Let 7f antagomirs 4h post stroke significantly reduced cortical and striatal infarct volume as compared to animals infused with scrambled oligos. Additionally animals treated with Let7f showed improved performance on the rotarod task. In silico analysis indicated approximately 18 target genes of Let7f that are routinely associated with neuronal survival and function. Quantitative PCR using gene-specific primers for these genes (normalized to cyclophilin expression) indicated that 11 genes, including Aquaporin-4 were upregulated by anti-Let7f infusions. Western blot analyses confirmed this upregulation of Aquaporin-4, which encodes a water channel and is associated with post stroke recovery. **Conclusions:** Collectively these data support the use of post-stroke treatment with anti-Let7f as a therapeutic strategy.

Author Disclosures: A. Selvamani: None. P. Sathyan: None. R. Miranda: None. F. Sohrabji: None.

Th MP17

Activation of Synaptic NMDA Receptors During Reperfusion Provides Protection against Oxygen and Glucose Deprivation

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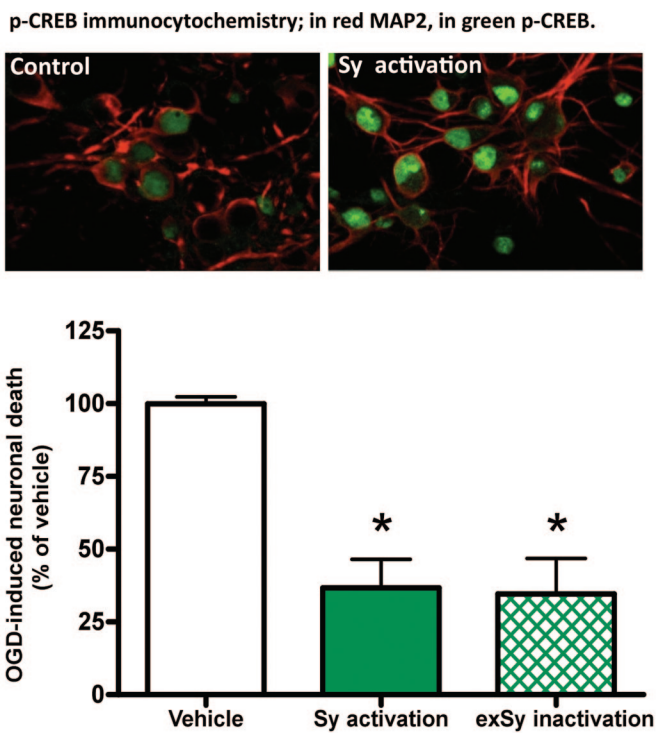
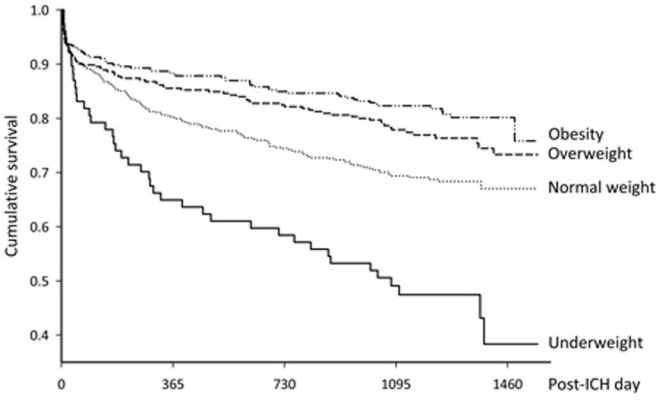
Background: Neurological deficit in stroke results from neuronal death triggered by excess glutamate acting at N-methyl-D-aspartate subtype of glutamate receptors (NMDAR). However,

several studies have demonstrated that only activation of extrasynaptic (exSy) NMDAR produce cell death, whereas activation of synaptic (Sy) NMDAR prior to oxygen and glucose deprivation (OGD) induces survival through activation of the c-AMP response element binding protein (CREB). **Objective:** Our aim was to investigate whether activation of Sy NMDAR at post-ischemia also prevents OGD-induced neuronal death. **Methods:** Experiments were performed in cortical neurons treated with NMDA, bicuculline or Ro25-6981 for 10 min, either in control or OGD/reperfusion conditions. Bicuculline selectively activates Sy NMDAR by inhibiting gabaergic neurotransmission, and Ro25-6981 selectively inhibits exSy NMDAR. OGD was performed by incubating neurons in glucose-free DMEM in a 2% O2 atmosphere for 90 min. After this OGD period, normoglycemia and normoxia were restored and treatments were added. Phospho CREB (pCREB)immunocytochemistry was performed in neurons 15 min after treatments and cell death was determined 24 hours later. **Results:** Selective activation of Sy NMDAR provoked a 4-fold increase in pCREB in neurons whereas joint activation of both Sy and exSy NMDAR by addition of NMDA abolished this effect. Treatment with NMDA in the presence of Ro25-6981 induced a 4-fold increase of pCREB. We found that 30% of the OGD-treated neurons died 24 h after reperfusion, and that this effect was dramatically reduced by a short selective activation of Sy NMDAR following reperfusion, either using treatment with bicuculline or with Ro25-6981. **Conclusion:** Selective activation of Sy NMDAR at reperfusion was able to protect neurons from OGD-induced neuronal death by providing a necessary survival signal. These results offer an explanatory mechanism of the paradoxical failure of NMDAR antagonists to provide clinical benefit in acute stroke patients.



Author Disclosures: V. Guirao: None. A. Davalos: None. T. Gasull: None.



Th MP18

Therapeutic Benefit of Combination Simvastatin and Human Umbilical Cord Blood Cells Treatment of Stroke: Neurogenesis, Vascular and White Matter Remodeling

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Background & Objective: The therapeutic efficacy of cell-based therapy after stroke can be enhanced by making the host brain tissue more receptive to the administered cells and thereby facilitate brain plasticity. We hypothesized that Simvastatin increases human umbilical cord blood cell (HUCBC) migration into the ischemic brain and promotes brain plasticity and neurological functional outcome after stroke. **Methods:** Wistar rats were subjected to transient middle cerebral artery occlusion (MCAo) and administered PBS, Simvastatin (0.5mg/kg, gavaged daily for 7 days), HUCBCs (1×10^6, one time tail vein injection), combination Simvastatin and HUCBCs starting 24h after MCAo. Rats were sacrificed 14 days after MCAo. A battery of neurological functional outcome (mNSS, Foot-fault and Adhesive removal) tests, neurogenesis, vascular and white matter changes were measured. Subventricular zone (SVZ) explant, primary mouse brain endothelial cell (MBEC) and primary cortical neuron (PCN) cultures in vitro were also employed. **Results:** Combination treatment additively improved neurological outcome and significantly decreased lesion volume compared to MCAo control ($p<0.05$, $n=8$/group). Combination treatment significantly increased the engrafted-HUCBC numbers in the ischemic brain compared with HUCBC-monotherapy, and the number of engrafted-HUCBCs were significantly correlated with functional outcome (mNSS, $r=0.751$). Combination treatment significantly increased SVZ cell proliferation and neuroblast migration, upregulated angiogenesis and arteriogenesis measured by the vascular/arteriole density, perimeter/diameter as well as endothelial cell and smooth muscle cell proliferation in the cerebral vessels compared to MCAo control and monotherapy groups. In addition, combination treatment significantly increased Synaptophysin expression and brain-derived neurotrophic factor (BDNF), and the density of axons and myelin in the white-matter bundles in the ischemic brain compared to MCAo control ($p<0.05$, $n=8$/group). In vitro data show that neuroblast proliferation and migration significantly increased in the SVZ explant derived from combination treatment animals compared with MCAo or monotherapy alone animals. In addition, the capillary-like tube formation in MBECs and the neurite outgrowth in PCN cultures significantly increased in BDNF (50ng/ml) and Simvastatin combination with HUCBC conditioned medium compared with non-treatment controls, TrkB inhibitor (K252 200nM) significantly attenuated combination treatment-induced tube formation and neurite outgrowth ($p<0.05$, $n=6$/group). **Conclusions:** Combination treatment enhances HUCBC migration into the ischemic brain, increases BNDF expression and amplifies endogenous neurogenesis, synaptogenesis, and vascular and white matter remodeling, and improves functional outcome after stroke.

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Th MP19

A Polymorphism In Raptor Is Associated With Moyamoya Disease In The East Asian Populations

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Background: The etiology of moyamoya disease (MMD) remains to be fully elucidated. Genetic approach is expected to provide critical information in understanding the disease. **Methods and Results:** Linkage analysis of 17 Japanese families with familial moyamoya disease showed a LOD score from 9.67 at chromosome 17q25.3. Fine mapping narrowed the linkage signal to a 2.1-Mb region containing 40 annotated genes. Three potential candidate genes, *CARD14, RAPTOR and AATK*, were directly sequenced in their promoter and coding regions. Only one novel polymorphism, V33 G>A located in the putative promoter region of *RAPTOR* gene, was common to all 4 unrelated sequenced probands. V33 was then shown to segregate in 34 pedigrees resulting in a two-point LOD score of 12.8 ($p = 1.23\text{x}10^{-7}$) with a penetrance of 77.4%. A case-control study was then conducted in the Japanese (82 cases vs 384 controls), Korean (41 case vs 223 controls), Chinese (23 cases vs 100 controls) and European (27 cases vs 164 controls) populations. In East Asian populations, the V33 A allele was significantly more frequent in cases than in controls (25.6% vs 1.0% in the Japanese, 32.9% vs 1.1% in the Korean and 4.3% vs 0% in the Chinese population), and then associated with an increased risk of MMD in East Asian population with an odds ratio of 52.5 (95%CI, 27.2-100..2; $p = 2.5 \text{ x } 10^{-49}$). The V33 was not polymorphic in the Caucasian population. The population-attributable risks associated with V33 were 48.9% in the Japanese, 65.9% in the Korean and 8.7% in the Chinese population. **Conclusions:** The V33 variant of *RAPTOR* gene confers susceptibility to MMD in the East Asian population.

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Th MP20

Antihypertensive treatment and stroke risk in a general population: The Akita Stroke Onset Registry

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Background: Although many interventional trials have demonstrated that blood pressure (BP) lowering can significantly reduce the risk of cardiovascular events, the relationship between the BP level and stroke risk has not been investigated in those with and without antihypertensive treatment. **Subjects and Methods:** We analyzed the mass health screening data based on 156,847 people by the Akita Prefectural Federation of Agricultural Cooperation for Health and Welfare from 1991 to 1998. Cerebrovascular events were identified from the data of the Akita Stroke Onset Registry (ASOR) in which stroke events were registered when the patients were admitted to the hospital in the acute stage and the clinical diagnosis was given based on the CT and/or MRI findings in Akita Prefecture. The first stroke episodes occurring within 3 years after the screening (between 1991 and 2000) were defined as "stroke events". Blood pressure level was classified into 6 categories: optimal, normal, normal-high, stage-1 hypertension (HT), stage-2 HT and stage-3 HT. The risk of a first stroke among 6 BP-based categories was analyzed using a multivariate logistic regression after the adjustment for possible confounding factors. 142,989 people were untreated, whereas 13,858 were on antihypertensive medication. **Results:** We identified 1323 (0.8%) first strokes, including 739 (55.9%) cerebral infarction, 361 (27.3%) cerebral hemorrhage and 223 (16.8%) subarachnoid hemorrhage. Among the untreated subjects, the relative risk of stroke linearly increased with the elevation of BP level. The stroke risk was more than two-fold (RR: 2.1; 95% CI: 1.6-2.7) even in the normal-high BP group as compared with the optimal BP group. Similar trend was observed among those on medication: stroke risk increased with the elevation of BP level, and was significantly higher even in the normal-high BP group than in the optimal BP (RR: 3.5; 95% CI: 1.0-4.2). **Conclusions:** Although the antihypertensive medication reduces stroke risk, even in those on antihypertensive medication, the stroke risk was higher in the 'normal" BP range. Healthcare providers should be aware of the hidden risk of stroke even when BP is within the normal range.

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Figure 1

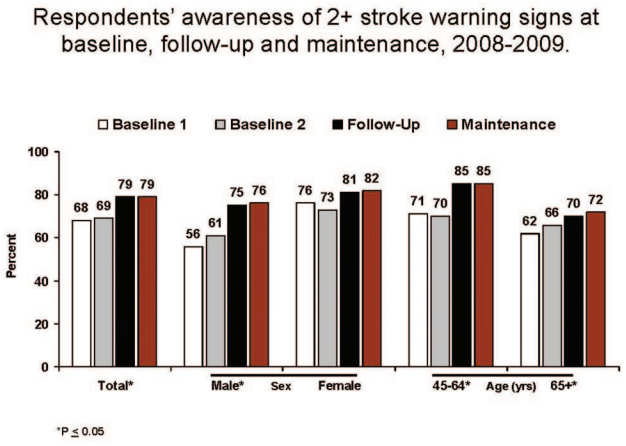
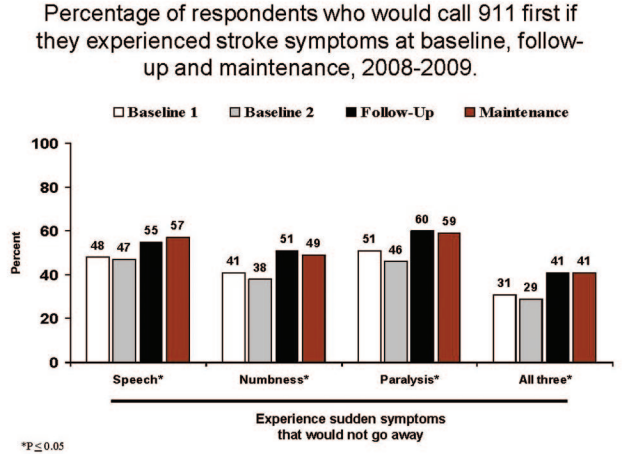
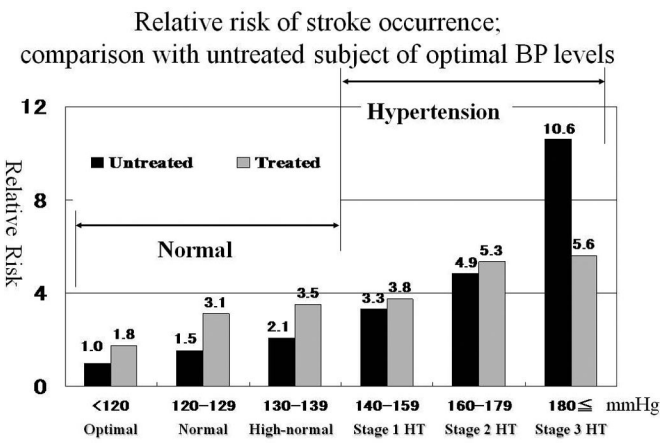


Figure 2





Th MP21

Paradoxical Longevity in Obese Patients with Intracerebral Hemorrhage

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Background: Obesity is a widely accepted risk factor for various cardiovascular diseases including stroke. However, the paradoxical phenomenon of relative longevity among obese patients with established diseases has recently been reported for various disease conditions. The authors sought to investigate whether the "obesity paradox" also applies to intracerebral hemorrhage (ICH) survivors. **Subjects and Methods:** A total of 1,604 ICH patients from 33 Korean centers with nationwide coverage were prospectively enrolled between October 2002 and March 2004. Baseline information, including body-mass index (BMI) was collected at admission, and mortality statuses were ascertained from the governmental mortality archive on December 2006. Obesity status was categorized according to the WHO criteria for Asian-Pacific region. Associations between obesity status and 30-day mortality or long-term risk of death were analyzed, by binary logistic regression and Cox proportional hazard models, as appropriate. **Results:** Among the 1,275 ICH patients included, 325 patients (25.5%) were classified as overweight (BMI, 23.0-24.9 Kg/m^2) and 345 (27.0%) were classified as obese (BMI, $\geq$25.0 Kg/m^2). Mean$\pm$SD of BMI was 23.30$\pm$3.21 Kg/m^2. The 30-day mortality rate was 7.5% and the long-term mortality rate was 27.5% after a mean follow-up of 33.60$\pm$15.53 months. Neither BMI nor obesity status were associated with 30-day mortality after ICH. However, BMI was found to be independently associated with a lower risk of long-term mortality (HR, 0.91; 95% CI, 0.87-0.95). As compared with patients of normal weight, underweighted subjects (BMI ^{2}) were found to have a higher risk of death (HR, 1.72; 95% CI, 1.17-2.52), and conversely, overweight (HR, 0.70; 95% CI, 0.50-0.98) or obese (HR, 0.62; 95% CI, 0.44-0.89) subjects were found to have a lower risk of post-ICH death. The survival curves from patients with each obesity status were portrayed in Figure, with $P<0.001$ for overall comparisons. **Conclusions:** In our study, obesity status was associated with a lower risk of long-term death but not with 30-day mortality after ICH. Thus, it may be considered that an obesity status in an ICH patient be treated as an indication of metabolic reservoir capacity and of an increased likelihood of survival.

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Th MP22

Thrombocytopenia and the Risk of In-hospital Mortality among Ischemic Stroke Patients

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Background: Thrombocytopenia has been associated with increased mortality in conditions such as acute coronary syndrome, liver disease, and chronic HIV infection. Some case series have indicated that mortality rates are higher among ischemic stroke patients with thrombocytopenia, however these studies were limited by small sample size and did not adequately adjust for important potential covariates. **Objective:** We sought to examine whether thrombocytopenia present upon admission was associated with in-hospital mortality among patients with ischemic stroke. **Methods:** We used data from a retrospective cohort of ischemic stroke patients who were admitted to one of five hospitals (1998-2003) within 48 hours of symptom onset excluding patients who received thrombolysis. Thrombocytopenia was defined as platelets less than 100,000/μL. The outcome was in-hospital mortality. Factors considered for risk adjustment included: conditions that can lead to thrombocytopenia (e.g., liver disease); conditions that increase risk of bleeding (e.g., hemophilia); medications taken prior to admission that have an effect on platelets (e.g., aspirin); and predictors of in-hospital mortality (e.g., retrospective NIH Stroke Scale (NIHSS) and Charlson comorbidity score). Chi-square tests were used for unadjusted analysis, and logistic regression with backward stepwise elimination was used to obtain the most parsimonious adjusted model of the association between thrombocytopenia and mortality. **Results:** Among 1233 ischemic stroke patients, the rate of thrombocytopenia was 2.3% (N=28), and overall 6.1% (N=75) died in the hospital. In

unadjusted analyses, thrombocytopenia at admission was associated with a higher mortality rate: 8/28 (28.6%) versus 67/1205 (5.6%), p=<0.0001). In multivariable analyses, only the NIHSS and Charlson comorbidity score remained in the model. After adjustment for these two variables, admission thrombocytopenia remained independently associated with in-hospital mortality with an adjusted odds ratio of 6.6 (95%CI: 2.3-18.6). There were 4 (14.3%) symptomatic intracranial hemorrhages among patients with thrombocytopenia compared with 18 (1.5%) among patients without thrombocytopenia (p=0.001). **Conclusion:** Although thrombocytopenia is relatively uncommon in this cohort, admission thrombocytopenia is a robust predictor of in-hospital mortality. Further characterization of thrombocytopenia in ischemic stroke patients is warranted.

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Th MP23

Stroke Messaging: Are We FAST Enough?

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Background: The FAST mnemonic (Face, Arm, Speech, Time to Call 911) has been widely used in stroke education programs, because it facilitates recall of specific stroke symptoms. However, FAST has been criticized because some stroke symptoms are not included in the message. One previous research study found that 11% of stroke patients presenting to an emergency department had symptoms that are not contained in FAST; whereas, almost 100% of these cases had symptoms found on the traditional list of 5 sudden stroke symptoms originally developed by the American Stroke Association (SUDDENS). However, this was a retrospective study that examined confirmed stroke cases. From a stroke education perspective, there is a need to assess whether or not there is a difference in the type of stroke symptoms recalled by individuals exposed to the FAST message versus the SUDDENS message. **Methods:** In this prospective study, participants were randomized to view a poster containing either the FAST mnemonic or the 5 SUDDENS. Stroke knowledge was tested before and after viewing each message using the previously validated Stroke Action Test (STAT). Ten of the 28 items in the STAT test contain the following symptoms that are not mentioned in the FAST message: dizziness, visual symptoms, headache, confusion, and leg symptoms. A correct answer on the STAT requires the participant to both recognize the stroke symptom and recommend immediate action (i.e. call 911). Differences in the proportion of respondents answering these 10 questions correctly after viewing one of the two posters were compared using the Chi-Square test (alpha = .05). **Results:** Overall, there were 181 participants (91 in the FAST group and 90 in the SUDDENS group). Prior to viewing the posters, there were no statistically significant differences in the proportion of respondents correctly answering 9 of these 10 questions. One question exhibiting a leg symptom was answered correctly by significantly more SUDDENS poster viewers, and was eliminated from further analysis. After viewing the posters, significantly (p < .05 for all comparisons) more SUDDENS poster viewers correctly answered STAT items exhibiting the following stroke symptoms: dizziness (50% of SUDDENS viewers vs. 27% of FAST viewers), vision symptoms (66% vs. 41%), dizziness and vision symptoms occurring together (66% versus 47%), and headache (58% vs. 24%). **Conclusions:** Compared to participants viewing a poster with the FAST mnemonic, significantly more participants viewing a poster containing the traditional list of 5 sudden stroke symptoms correctly recognized and recommended immediate treatment for symptoms of dizziness, visual problems, and severe headache, all of which are not included in the FAST message. In the race to discover messages that maximize stroke awareness, the FAST mnemonic may need to be modified to incorporate symptoms of headache, dizziness, and visual disturbances.

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Th MP24

Sustained Increases in Community Awareness of Stroke Signs and Symptoms and Use of 911 Using a Staged Media Campaign

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Background and Purpose: Awareness of stroke symptoms and the importance of rapid 911 activation is an important link in the chain of survival for stroke patients. Media campaigns to increase community awareness of stroke signs and symptoms and the importance of using 911 have shown short-term increases, but sustaining the increased levels of awareness has been a challenge. **Methods:** From October 2008 through October 2009, the Montana Stroke Initiative conducted a staged media campaign in a selected Montana county. Between October 2008 and May 2009, a 20-week high-intensity media campaign aired. The campaign included paid TV/radio ads, billboards, newspaper releases, and brochures. The high-intensity campaign was followed by a maintenance campaign which ran one week out of every three weeks (July-October 2009). The campaign was evaluated by 4 random digit dial telephone surveys (total of 1,600 people aged 45 and older). Two baseline telephone surveys, separated by 12 months, evaluated the variability of community responses without intervention. Surveys were also conducted after the high-intensity (June 2009) and maintenance campaigns (November 2009). **Results:** Between the 2 baseline surveys, there were no significant increases in awareness of stroke signs and symptoms or intent to call 911. After the high-intensity campaign, there were significant improvements in both awareness and intent to call 911, which were sustained after the maintenance phase. (Fig 1) Improvements were also noted in subgroups, including males, those aged 45-64 years and 65+ year olds. In addition, the percentage of respondents who would call 911 if they experienced numbness, speech difficulties, paralysis, or all 3 symptoms increased significantly from baseline. (Fig 2). **Conclusion:** Knowledge of stroke signs and symptoms and the intent to call 911 improved after a high-intensity media campaign, and the improvements remained after the maintenance phase. A staged media campaign was effective in increasing awareness and intent to call 911. Figure 1 Figure 2

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Th MP25

Brain Natriuretic Peptide Predicts Functional Outcome In Ischemic Stroke

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Background: Elevated plasma levels of brain natriuretic peptide (BNP) have been associated with cardioembolic (CE) stroke and higher post-stroke mortality. However, limited data are available on the value of BNP in determining functional outcome after stroke. We sought to determine whether plasma BNP levels were associated with long-term functional outcome in ischemic stroke patients. **Methods:** We conducted a cross-sectional study of the prospective cohort of consecutive patients aged ≥18 years admitted to our Stroke Unit through the Emergency Department between 2002 and 2005. All patients underwent clinical evaluation by a vascular neurologist, diagnostic neuroimaging, cardiac, and laboratory testing, including BNP collected during the index admission. Plasma BNP was measured using high-sensitivity immunoradiometric assay, and BNP level quintiles were used for analysis. Stroke subtypes were assigned using TOAST criteria. Outcomes were measured as 6-month modified Rankin Scale score ("good outcome" = 0-2 vs. "poor") as well as mortality. Multivariate logistic regression was used to assess the association between the plasma levels of BNP and functional outcome in this cohort. Predictive performance of BNP for functional outcome was assessed by comparing ROC curves. **Results:** Of 514 ischemic stroke patients, 187 (32.9%) had CE, 130 (22.9%) had large artery, 54 (9.5%) had small vessel, 143 (25.1%) had undetermined, and 55 (9.7%) had other stroke subtypes. Mean age was 67.9 ± 15 years; 46% were female. BNP levels were higher among the older subjects (p<0.0001) and women (p<0.0002). When adjusted for age and gender, elevated BNP levels were associated with lower ejection fraction (p<0.0001) and greater degree of left atrial dilatation (p<001). Furthermore, BNP was an independent predictor of atrial fibrillation (OR 2.0, 95%CI 1.6-2.5), and any CE mechanism (p<0.001). In multivariate analysis, elevated levels of BNP decreased the odds of good functional outcome (OR 0.2, 95%CI 0.1-0.6), as did female sex (OR 0.1, 95%CI 0.01-0.7) and coronary artery disease (OR 0.01, 95%CI 0.001-0.2). BNP was the only independent predictor of mortality in this cohort (OR 6.4, 95%CI 1.1-36.3). The addition of BNP to models predicting functional outcome and mortality after CE stroke significantly increased their predictive performance (AUC estimate increase from 0.85 to 0.91, P<0.013 and 0.84 to 0.94, P<0.03, respectively). **Conclusions:** In this large, cross-sectional study of patients with ischemic stroke, plasma BNP levels were strongly associated with CE stroke and long-term functional outcome. Elevated BNP levels independently predicted poor functional outcome and mortality at 6 months. Inclusion of BNP levels significantly improved prediction of mortality, especially in patients with CE stroke. Further studies are warranted to establish the utility of plasma BNP as a predictor of stroke outcome.

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Th MP27

Cerebral Blood Volume Gradient Maps Depict Vulnerability to Hemodynamic Failure and Infarct Growth in Acute Ischemic Stroke

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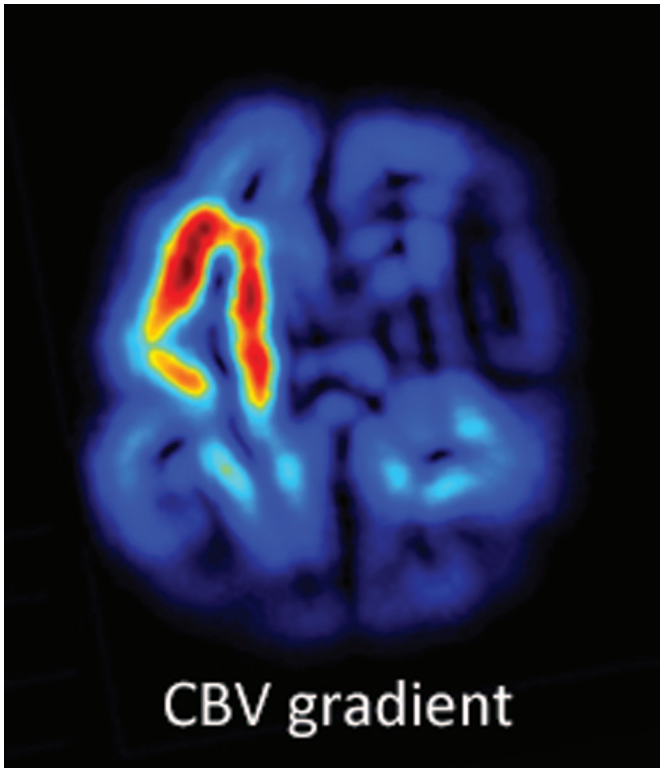
Background: Cerebral blood volume (CBV) is an essential measure of perfusion in acute ischemic stroke. The biphasic nature of CBV, with peripheral hyperemia and central collapse towards the ischemic core tends to underestimate ultimate infarction if only low CBV thresholds are used. Detection of focal changes within the ischemic territory superimposed on global differences in CBV may also be difficult to measure. We developed CBV gradient images that illustrate propensity for hemodynamic failure to distinguish benign hyperemia from penumbra surrounding the ischemic core. **Methods:** Consecutive stroke cases with acute middle cerebral artery occlusion (MCAO) and serial MRI at baseline and day 5 were analyzed. CBV gradient maps were constructed using values from nearby regional voxels to estimate the local slope of CBV measures. Various radii extending to neighboring voxels were utilized to maximize the tissue fate predictive power of the gradient maps. Following co-registration with day 5 images, a nonlinear statistical model was used to quantify the predictive capacity of the CBV gradient images for infarction and accuracy was compared with Tmax prediction of tissue fate. **Results:** 42 cases (mean age 66.7±18.5 years; 26 women, 16 men) of acute MCAO with serial MRI were analyzed. CBV gradient maps were able to demonstrate a concentric region of abnormality around the ischemic core.

Co-registered measures of the ischemic core with advanced hemodynamic collapse and uniformly low CBV were not apparent. Similarly, large areas of the surrounding territory with elevated CBV or hyperemia were not apparent on the CBV gradients maps. CBV gradient maps were able to accurately classify voxel outcome defined as infarction on day 5 fluid attenuation inversion recovery sequences, correctly predicting voxel-based hemodynamic failure. Voxel classification results revealed accuracies of 88.8±2.6% for CBV gradient maps compared with 90.2±2.4% using Tmax. Predictive capability was limited in a subset of cases with diffusely low CBV values. Cardioembolic stroke cases demonstrated more overt CBV gradient abnormalities compared with atherosclerotic etiologies. **Conclusions:** CBV gradient images can



depict zones around the ischemic core that are vulnerable to hemodynamic failure and infarct evolution. These novel parameter maps may be used in evaluating serial changes of superimposed focal and global perfusion associated with various hemodynamic interventions and collateral therapeutic strategies.

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Th MP28

Hyperacute Levels of High Sensitivity C-Reactive Protein are Associated with Mean Transit Time and Diffusion-Weighted Imaging Volumes and Improve Outcome Prediction in Acute Ischemic Stroke

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Objectives: Subacute levels of high sensitivity C-Reactive Protein (hsCRP), mean transit time (MTT) volumes, and diffusion-weighted imaging (DWI) volumes have been reported as predictors of ischemic stroke outcome. This is the first study to assess the correlation between hyperacute levels of hsCRP and neuroimaging characteristics of acute ischemic stroke (AIS). Using data from a prospective, hospital-based cohort of AIS patients, we sought to establish whether increased inflammation correlates with MRI evidence of ischemic injury and whether combining hsCRP, DWI, and/or MTT volume improves prognostication in AIS. **Methods:** We prospectively measured hsCRP on consecutive AIS patients (<9 hours from symptom onset) in a multicenter biomarker study. Subjects with acute MR imaging were included. We excluded patients with acute infection, active malignancy, or systemic inflammatory disorder. Volume of DWI (vDWI) and MTT (vMTT) were measured by analysts blinded to outcome using a validated semi-automated method. Pearson's correlation was used to quantify the association between continuous variables. Multivariate linear and logistic regression models were used to adjust for the effects of potential confounders. The outcome measure was the 90-day Barthel Index, treated as a continuous variable. **Results:** In these analyses we included 284 subjects, mean age 70.8 (s.d. 14.6), mean NIHSS 8.9 (s.d. 7.3), 44% female with hsCRP and a baseline DWI study. Perfusion imaging was performed in 105 subjects. The mean level of hsCRP was 8.7 mg/L (s.d. 16.0 mg/L). Mean vDWI and vMTT were 26.8 cm^3 (s.d. 53.6 cm^3) and 45.3 cm^3 (s.d. 51.6 cm^3), respectively. Levels of hsCRP correlated with vMTT ($r=0.24$, $p=0.02$) and vDWI ($r=0.18$, $p=0.003$). After adjustment for age and large vessel occlusion, hsCRP remained an independent predictor of vDWI ($p=0.007$) and vMTT ($p=0.01$). Levels of hsCRP correlated with the 90-day Barthel Index ($r=0.39$, $p=<0.0001$). Adding hsCRP to vDWI improved predictive performance of outcome, increasing the r^2 from 0.46 to 0.52 ($p=0.04$). **Conclusions:** Hyperacute levels of hsCRP independently predict MTT and DWI volumes. The addition of level of hsCRP augments the power of MRI evidence of acute ischemic injury by improving its ability to predict outcomes in patients with AIS.

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Th MP29

Discovery of a New Panel of Blood Biomarkers to Differentiate Acute Stroke from Stroke-Mimicking Conditions

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Background: At present, the absence of a widely available diagnostic test for acute cerebral ischemia remains a limitation for improving the management of stroke. The triaging stage is likely to have the highest rate of stroke mimicking conditions and being the best scenario for a quick, accurate diagnostic assay to send to reference hospitals all true strokes that might get therapeutically benefit. **Methods:** In front of stroke suspicion (<3h from symptoms onset) blood samples were obtained at the Emergency Department to test selected biomarkers and later on a complete diagnostic protocol allowed to decide the diagnosis of "true stroke" (stroke) or a "stroke mimicking condition" (mimic). Finally, 230 cases were studied [146 strokes, 61 mimics (seizures, tumours, migraine, hypoglycemia, syncope…) and 23 healthy controls]. From a screening in a large (>150 biomarkers) protein-antibody library, in a sub-group of cases (discovery cohort), we identified 23 biomarkers useful to differentiate stroke from mimics ($p<0.05$). Those key biomarkers were combined in arrays and tested for validation in the whole study population by Search Light technology (Thermo Fisher Scientific). **Results:** The most relevant identified biomarkers were: Interleukin-17, basic Neurothrophic Growth Factor, Insulin Growth Factor Binding Protein 3 and Tumor Necrosis Factor Receptor 1. In fact, the multivariate analysis identified IL-17 OR 114.7; BNGF OR 9.2; IGFBP-3 OR 34.5; TNFR1 OR 8.7; Hypertension OR 3.5; Atrial Fibrillation OR 26.7 and Dyslipidemia OR 8.1 (all $P<0.009$), as independent parameters to differentiate stroke from stroke-mimicking conditions. That allowed building up a model with great predictive value (AUC=0.93) adding significant information to both clinical data alone and biomarkers alone ($p<0.05$). Negative predictive value for stroke obtained by combinations of 3 biomarkers was 100% and some combinations of only 2 biomarkers had 100% positive predictive value. The test allowed correctly allocating 46.9% of the mimics and 98.6% of the strokes. **Conclusions:** Results of this extensive study identified biomarkers able to differentiate stroke from mimics that will permit rapid referral of stroke patients to hospitals were acute treatments are available. Multicenter studies using point-of-care techniques to evaluate such a stroke diagnostic test in daily-practice conditions is now required.

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Th MP30

Hyperacute Matrix Metalloproteinase-9 Levels Predicts Infarct Volume and Stroke Outcome

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Objectives: There are currently no validated acute stroke biomarkers to aid in risk stratification or selection of patients for acute therapeutic interventions. We previously reported a weak correlation between matrix metalloproteinase 9 (MMP-9) with NIHSS ($r=0.33$, $p=0.05$) and admission MRI ischemic infarct (DWI) volume ($r=0.35$, $p=0.05$) in a small sample of 52 hyperacute stroke subjects. We sought to replicate these findings in a larger sample in order to confirm and extend the validity of these relationships after adjustment for confounders. **Methods:** We prospectively measured MMP-9 on consecutive acute stroke patients (< 9 hours from symptom onset) in a multicenter acute ischemic stroke biomarker study. Clinical and demographic data including NIHSS scores at baseline, 48 hours, and discharge, stroke subtype, imaging, and 3 month mRS were collected. The outcome measure was the 90-day mRS, dichotomized as good (mRS 0-2) or poor (mRS 3-6). MMP-9 was analyzed using an ELISA assay. Patients with acute infection, active malignancy, or systemic inflammatory disorder were excluded. Pearson's correlation was used to quantify the association between continuous variables. Multivariate linear and logistic regression models were used to adjust for the effects

of potential confounding variables. **Results:** We included 282 subjects, mean age 69.9 (s.d. 15.3), 44% female in the analysis, of which 38% were treated with tPA. The mean NIHSS was 6.5 (s.d.7.0). In univariate analyses, baseline NIHSS ($r=0.23$, $P<0.0001$) and DWI volumes ($r=0.29$, $p=0.0047$) correlated with levels of MMP-9. Mean MMP-9 levels were higher in patients with poor outcome as compared to those with a good outcome (253.9 ng/mL vs. 195.2 ng/mL, $p=0.03$). MMP-9 levels were associated with HTN ($p=0.01$) and tPA administration ($p=0.01$). After adjustment for age and tPA use, MMP-9 remained an independent predictor of NIHSS ($p=0.03$), DWI volume ($p=0.0073$) and 3 month mRS ($p=0.04$). A 100 ng/mL increase in MMP-9 corresponded to a 20% increased risk of poor outcome. The logistic regression model yielded an AUC of 0.56. **Conclusions:** We have replicated and strengthened findings that levels of MMP-9 are independently correlated with stroke severity and infarct volume. These results provide further evidence that MMP-9 is a valuable surrogate marker of acute ischemic stroke injury and a predictor of outcome.

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Th MP31

Incorporating Smartphone Teleradiology Application into a Telestroke Network Environment

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Background: When implemented within a telestroke network, teleradiology systems are useful in supporting rapid imaging interpretation in time for thrombolysis decision making. Smartphone teleradiology application, Resolution MD Mobile (ResMD) affords vascular neurologists (VN) immediate site independent access to spoke hospital stroke alert patients' neuroimaging in the context of a telemedicine evaluation. Reliability studies have been conducted in a controlled environment, but not in a live hub & spoke telestroke network. The study objectives were to assess the level of computed tomography (CT) interpretation agreement between hub VN (Res MD) and spoke radiologist (picture archive and communication system, PACS) and a reference standard (PACS). Secondarily we sought to determine the proportion of times the hub VN selected ResMD as 1st choice CT viewing modality from amongst competing options. **Methods:** Prospective stroke alert patients at a single spoke hospital consented to receive an emergency telestroke consultation and participate in a registry. The VNs were proficient with available CT viewing technologies. Each CT head was evaluated in real time by the hub VN, spoke radiologist, and subsequently by a blinded telestroke adjudication committee. The VN recorded the preferred primary CT viewing modality. Diagnoses, time intervals, thrombolysis administration, and CT features were recorded on case report forms. Agreement (Kappa) over clinically important radiological features was calculated. **Results:** Sixty-five subjects were enrolled and underwent telemedicine consultation and review of CT head. Time interval results were expressed as mean and standard deviation (minutes): Stroke Alert (SA) activation to VN consultation 16 (9), to CT review 40 (12), and to tPA decision 45 (22). Hub VNs preferred to view the CT on iPhone ResMD in 80% of the consultations. The diagnoses were ischemic stroke (thrombolysis administered) 28%, ischemic stroke (thrombolysis not administered) 35%, intracranial hemorrhage 10%, transient ischemic attack 4%, not cerebrovascular related 13%, undetermined 10%. Agreement (Kappa and 95% CI) between hub VN ResMD and (1) spoke radiologist PACS and (2) reference standard PACS, respectively were: identification of ICH 1.0, 1.0, neoplasm 1.0, 1.0, contraindication to thrombolysis 1.0, 0.9, (0.7-1.0), early ischemic change 0.6, (0.3-1.0), 0.6, (0.3-0.9), hyperdense artery sign 0.4, (0.0-0.8), 0.4, (0.1-0.8). **Conclusions:** VNs preferred to interpret CTs of SA patients with the ResMD Mobile iPhone application in the context of an active hub & spoke telestroke network environment. The VN ResMD interpretations were in perfect agreement with radiologists and reference standard adjudication for contraindications to thrombolysis administration.

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Th MP32

The Addition of CT Imaging to the ABCD2 Score Improves the Ability to Identify Individuals at Medium and High Risk of Stroke

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Background: The ABCD2 score uses clinical criteria to stratify stroke risk after transient ischemic attack (TIA). The score has low specificity and a large proportion of individuals fall into the group in which guidelines recommend admission. The addition of brain imaging in the proposed ABCD2I score may reduce the number of unnecessary admissions. **Objectives:** 1) To validate the proposed ABCD2I score in TIA patients presenting to the emergency department (ED). 2) To evaluate the relative benefit of including only acute CT changes in the ABCD2I score. 3) To establish a low or high risk score with a similar risk to that proposed by the AHA guidelines. **Methods:** We prospectively identified and followed a cohort of patients receiving a final diagnosis of TIA in eight tertiary-care emergency departments and included all patients having a CT scan within 24 hrs. Primary outcome was stroke within 2, 7 and 90 days of index TIA. All CT scans were assessed by a neuroradiologist. The ABCD2I score (total 0 to 10) was calculated according to Giles et al. A modified ABCD2Ia score was calculated by assigning points only for evidence of acute infarction. An ABCD2 score of ≥ 4 or an ABCD2I or ABCD2Ia score of ≥ 5 separated low risk from medium-high risk patients. Discriminatory power was calculated from the area under the receiver operated characteristic curve (AUC) with 95% CIs. **Results:** 2046 patients met enrollment criteria and were included in the final analysis. The 90 day stroke rate was 3.4%. Ischemic changes were present in 565 (27.6%). The ABCD2Ia score had the greatest discriminatory power for stroke at 2, 7 and 90 days (Table). ABCD2, ABCD2I, and ABCD2Ia identified 61.4%, 50.4% and 38.7% of patients as medium-high risk with an associated 2 day stroke rate of 1.9% (1.3-2.5%), 2.0% (1.3-3.1%) and 2.5% (1.6-3.9%), respectively. ACBD2, ABCD2I, and ABCD2Ia patients defined as low risk had a 0.9% (0.4-1.9%), 1.0% (0.5-1.8%), and 0.9% (0.5-1.6%) rate of stroke at 2 days, respectively. **Conclusions:** The ABCD2Ia score allows separation of patients into those needing urgent evaluation with more specificity than the ABCD2 or ABCD2I scores. Defining patients with a score of ≥ 5 as medium-high risk would reduce hospital admissions while maintaining a low rate of the stroke in those not admitted.

Table. AUCs for prediction of stroke at 2, 7 and 90 days calculated for the ABCD2, ABCD2I, and ABCD2Ia scores.

	2 days	7 days	90 days
ABCD2	0.608 (0.514-0.703)	0.642 (0.562-0.722)	0.640 (0.576-0.703)
ABCD2I	0.601 (0.520-0.682)	0.634 (0.564-0.704)	0.654 (0.596-0.712)
ABCD2Ia	0.660 (0.571-0.748)	0.673 (0.598-0.749)	0.674 (0.612-0.735)

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Th MP33

Recruitment of Stroke Patients into Prehospital Research Before and After Implementation of a System-Wide Stroke Triage Policy

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Background: Currently over half of all Americans live in region where acute stroke is routed preferentially to pre-specified stroke centers. Regionalized systems of stroke care are a means to improve care and may impact prehospital stroke research. **Objective:** To determine how implementation of a county-wide stroke diversion system affected patient recruitment and emergency medical services transport times in an ongoing prehospital stroke study. **Methods:** The Field Administration of Stroke Therapy- Magnesium (FAST-MAG) clinical trial is a phase 3 NIH-funded study of magnesium sulfate or placebo initiated in the field throughout Los Angeles County within 2 hours of onset. FAST-MAG was ongoing and had recruited 876 subjects through 11/16/2009 when Los Angeles County implemented a county-wide stroke system of care. Patients suspected to have stroke using the Los Angeles Prehospital Stroke Screen with symptom onset 30 minutes. Since the implementation of this policy the number of PSCs has increased to 17. Monthly rates of enrollment were compared in the period prior to and following the date of implementation. The number of total enrollments, percentage of enrollments at PSC and field evaluation and transport times were compared. **Results:** FAST-MAG enrolled 1034 subjects as of June 25, 2010 for which data is available accounting for a period of 7 months and one week after the PSC diversion policy. There were 155 subject enrolled to 23 FM hospitals in the 31 weeks following regional stroke system implementation, compared to 134 patients brought to 41 FM hospitals in a similar period just prior to implementation. The monthly enrollment rates increased from 18.2 to 21.4, an 18% improvement. The percentage of subjects transported to PSCs increased from 21% in the period prior to implementation to 73% following PSC diversion ($p<0.0001$). The median prehospital evaluation and transport time increased by less than 3 minutes from 33.0 (SD 9.4) minutes before to 35.8 (SD 10.5) minutes after implementation of the PSC diversion. Mean transport time was not significantly different when comparing just patients taken to PSCs (33.8 ± 8.5 before and 35.8 ± 10.8 after implementation, $p=0.37$). **Conclusions:** Regionalized systems of stroke care can vastly increase the proportion of acute stroke patients cared for at stroke-capable hospitals and can improve recruitment of patients into prehospital stroke studies, with a small increase in prehospital evaluation and transport time. Implementation of a PSC system in Los Angeles County during the conduct of FAST-MAG provides a window into how regional policies can improve prehospital care and research yield.

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Th MP34

Use of Neuroimaging and Neurology Consultation to Evaluate Cerebrovascular Causes of Acute Dizziness in the Emergency Department (ED)

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Background: Dizziness is a common presenting complaint in the ED that may be caused by serious cerebrovascular diagnoses such as stroke or transient ischemic attack (TIA). However, both patients and clinicians have difficulty characterizing dizziness symptoms, and there is little consensus on the role of neuroimaging and neurology consultation in efficiently and adequately evaluating these patients for important cerebrovascular diagnoses. Therefore, we sought to better characterize the frequency and the diagnostic yield of neuroimaging and neurology consultation in ED patients with acute dizziness. **Methods:** We identified all adults presenting to the UCSF Medical Center ED between January 1, 2009 and December 31, 2009 with a primary triage complaint of *dizzy, dizziness*, *vertigo*, *spinning*, *imbalance,* or *disequilibrium* A neurologist was available on-site for ED consultations 24 hours a day and both MRI and CT imaging was also readily available. Demographics, focal neurologic examination findings, and the results of any neuroimaging studies or neurology consultations were collected using a standardized data abstraction tool. Final diagnoses were assigned from a pre-specified list of cerebrovascular diagnoses (ischemic stroke, hemorrhagic stroke, and TIA). We used logistic regression to assess associations between clinical factors, neuroimaging or neurology consultation in the ED, and cerebrovascular outcomes. **Results:** Among 369 patients (mean age 59 years, 56% female) who presented with dizziness to the ED, 135 (37%) had a head CT or brain MRI in the ED and 62 (17%) had a neurology consultation. Eight of the 34 (24%) MRI scans and 10 of the 111 (9%) CT scans had abnormal findings that were relevant to the patient's triage complaint. A focal finding on the ED clinician's neurologic examination was associated with neuroimaging from the ED (OR 4.4; CI 2.7-7.1) and with neurology consultation from the ED (OR 9.5; CI 5.2-17.5). In a multivariable analysis, neurology consultation (OR 15.9; CI 2.9-85) and a focal neurologic exam (OR 5.8; CI 1.1-30) remained independently associated with a final cerebrovascular diagnosis, whereas ED neuroimaging did not (OR 2.4, CI 0.4-13.4). Fifteen of the 135 patients (11%) who were imaged in the ED (OR 14.5; CI 3.3-65) and 15 of the 62 patients (24%) evaluated by a neurologist (OR 49; CI 11-220) were ultimately diagnosed with cerebrovascular disease. **Conclusions:** For patients presenting with dizziness to an academic center ED with an on-site neurology consultant, the use of neuroimaging studies and neurology consultation was substantial, particularly in patients with focal findings on neurological examination. Among those evaluated by neurologists, there was a high prevalence of cerebrovascular disease, which suggests that neurologists should have a high index of suspicion for stroke and TIA when asked to evaluate dizzy patients by their ED colleagues.

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Th MP35

Feasibility and Yield of a Brief Questionnaire to Help Identify Intracerebral Hemorrhage among Stroke Patients in the Field

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Background: Past clinical scales differentiating likely intracerebral hemorrhage (ICH) from likely ischemic stroke (IS) have been developed based on symptoms and signs elicited 6 to 24 hours after stroke onset. There is a need to identify features that distinguish ICH from IS in the first minutes - 2 hours after onset, to improve prehospital routing of patients (e.g. directing likely ICH patients to stroke centers with on site neurosurgery coverage), optimize prearrival notification of receiving hospitals, and permit field initiation of therapies tailored to likely stroke mechanism. **Objective:** To determine if a brief 3-question instrument can be administered in the field and whether responses may help differentiate ICH and IS in the first 1-2 hours after onset. **Methods:** The FAST-MAG Trial is a randomized placebo-control phase 3 study of magnesium sulfate vs. placebo initiated by paramedics in the field within 2 hours of stroke symptom onset. Physician-investigators elicit consent immediately from competent patients or on scene legally authorized representatives (LARs).Starting on 10/8/2008 investigators began to administer a 3-part stroke symptom questionnaire to all self-consenting patients: 1) do you have a headache (mild, moderate, severe), 2) do you have nausea, 3) have your symptoms worsened since onset. The questionnaire was administered to consecutive cases in parallel to paramedic field procedures. **Results:** From 10/8/2008 through 6/28/10 there were 391 subjects enrolled in FAST-MAG of whom 233 (60%) were competent and able to self consent. The questionnaire was successfully administered to 207 (89% of eligible). Among these 207 patients, average age was 70, 46% were female, median NIHSS on hospital arrival was 11, and time from last known well to field start of study drug was median 47 minutes. Of respondents, 99 (25%) had intracranial hemorrhage on the first imaging study after hospital arrival. Frequency of positive responses on the questionnaire among the 233 patients was 21% (n=43) for headache, 12% (24) for nausea, and 9% (18) for worsening of symptoms from onset. In univariate analyses the presence of headache (OR 8.6, 95% CI 4.1-18.2), nausea (OR 5.2, 2.1-12.7), and progression (OR 7.4, 2.5-22.1) were all significantly associated with hemorrhage on initial ED imaging. Having any positive responses on the screen was associated with ICH, while the number of positive responses and the intensity of symptoms (mild, moderate, severe) did not substantially increase predictive power. **Conclusions:** Self-reported headache, nausea, and early progression during the first 2 hours after stroke onset are powerful discriminators of likely ICH versus likely IS. A brief prehospital questionnaire is feasible to administer and identifies patients likely harboring ICH, potentially enabling enhanced neurosurgical response and tailored prehospital intervention.

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Th MP36

Improvement in Emergency Physician Stroke Thrombolysis Knowledge: The Increasing tPA Stroke Treatment through Interventional behavior Change Tactics (INSTINCT) Trial

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Background: Barriers to the implementation of widespread stroke thrombolysis exist on multiple levels including the patient, provider and health system. We hypothesized that a multi-faceted interactive educational intervention would improve emergency physician (EP) stroke thrombolysis knowledge. **Methods:** Randomly selected Michigan community hospitals (n=24) were selected and matched into pairs as part of a cluster randomized controlled trial. Within each pair, one hospital was selected to receive an educational intervention that included CME lectures, mock stroke codes, and targeted email messaging. All emergency physicians in practice at each site were identified by a local stroke champion. A previously pilot tested, 15 item baseline knowledge survey was administered before and after the intervention. The interval between surveys was about 18 months. The survey was calibrated such that approximately 50% of the answers would be correct in a sample of practicing EPs. The knowledge score was the percentage of correct responses. A generalized estimating equation (GEE) was used to evaluate for change in knowledge score, while accounting for clustering within hospitals alone, and a GEE model with additional adjustment for the covariates: Emergency Medicine (EM) board certification, EM residency training, physician gender, emergency department volume, and hospital teaching status. Secondary models were constructed for two sub-domains of knowledge: treatment eligibility and treatment performance. **Results:** At baseline 278 EPs were identified within the 24 hospitals, of which 199 (72%) returned baseline survey. At 18 months 163 (59%) EPs completed the follow up survey. At baseline, the overall performance was similar between intervention and control groups (56.6% vs. 55%.) Post-intervention there was a significant increase in overall knowledge score in the treatment group (68.9%) versus control (52.8%). While accounting for clustering within hospitals, this was a 14.5% (95% CI: 8.4-20.6%) adjusted mean increase in the treatment versus control sites. Inclusion of the additional co-variates did not significantly change this estimate. In addition, the intervention group improved relative to the control group within the eligibility (15.4%; 95% CI: 12.5-18.6%), and performance sub-domains (19.9% 95% CI: 13.8-26%). **Conclusions:** The INSTINCT trial intervention was associated with improved EP physician stroke treatment knowledge. The lack of improvement seen in the control group suggests this was not the result of a test-retest phenomenon. The improvement of EP knowledge may be associated with more accurate and efficient thrombolytic decision making and delivery.

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Th MP37

Effect Of Moderate And Excessive Alcohol Exposure On Female Versus Male Experimental Stroke Outcomes In Mice

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Stroke is a sexually dimorphic disease, with women being more protected from stroke relative to men. Heavy alcohol intake is a major stroke risk factor while moderate alcohol use (1 drink daily in women; 1-2 drinks daily in men) may offer neuroprotective benefits. However, little is known about the effects of varying levels of alcohol exposure on female outcomes as clinical and experimental research evaluating alcohol in stroke has focused mainly on males or did not stratify outcomes by sex. We evaluated the effects of acute moderate and excessive ethanol (EtOH) exposure on female vs. male mouse brain susceptibility to ischemic injury. We also explored the role of female sex steroids in the female response to EtOH exposure and experimental stroke. Female mice were ovariectomized (OVX) 7 to 8 days before EtOH exposure and experimental stroke to reduce endogenous levels of estrogen and progesterone. Intact and OVX females were given 0.2 g/kg (moderate dose, n=5-8/group) or 2 g/kg (excessive dose, n=7-8/group) EtOH i.p. while males were given 0.25 g/kg (moderate dose, n=8) or 2.5 g/kg (excessive dose, n=8) EtOH i.p. 1 h before 45 min of middle cerebral artery occlusion (MCAO). These EtOH doses mimic moderate or excessive alcohol in women and men based on blood

ethanol concentrations. Control female, OVX, and male mice (n=5-9/group) were given vehicle (saline, 0.015 mL/g) i.p. 1 h before MCAO. Brains were collected at 72 h reperfusion. Infarct volumes (% contralateral cortex) were determined by digital image analysis of 2 mm thick coronal brain slices stained with 2,3,5-triphenyltetrazolium chloride. In contrast to corresponding saline treated mice, acute moderate EtOH exposure (EtOH vs. saline) had no effect in females (40 ± 4% vs. 48 ± 4%) and OVX (58 ± 8% vs. 42 ± 9%) but decreased cortical infarct volumes in males (39 ± 4%* vs. 53 ± 2%) (*p ± 1%* vs. 48 ± 4%) and males (64 ± 3%* vs. 53 ± 2%) but were not significantly altered in OVX (49 ± 4% vs. 42 ± 9%) compared to corresponding saline treated mice (*pchemic injury in both sexes. However, the effect of excessive EtOH in female cortex is attenuated in OVX mice, suggesting female sex steroids may be involved. Further studies are needed to define the dose-response relationship and regional effects of EtOH in female ischemic brain and to assess the role of estrogen and/or progesterone in the female response to alcohol and stroke. Clinically, our observations suggest that excessive but not moderate alcohol consumption may alter stroke outcomes in women depending on hormonal status (pre- vs. post-menopause).

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Th MP38

Neonatal Testosterone Administration Provides Neuroprotection After Stroke In Adult Male Rats

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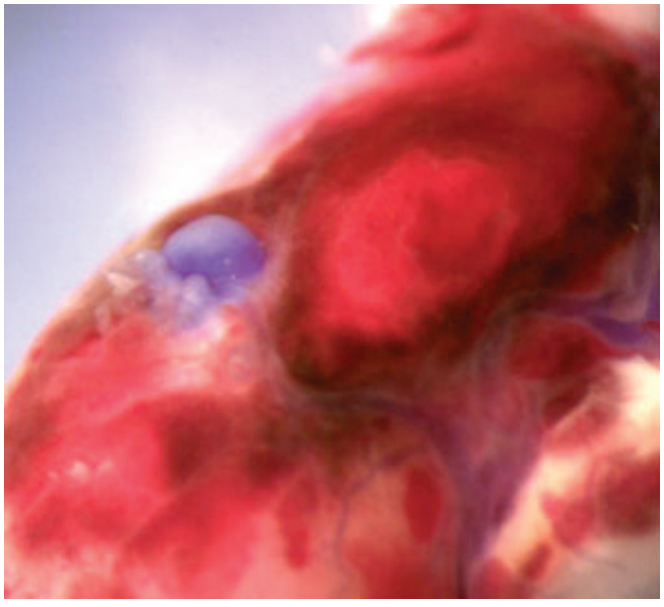
Introduction: Stroke incidence and outcome differ between men and women; likely due to a combination of chromosomal sex and gonadal hormones not fully understood. In clinical populations, male sex is correlated with higher stroke risk until advanced age. Low circulating testosterone levels are associated with increased vascular risk in adult males; however high testosterone levels are associated with increased risk of thromboembolic events in boys. Emerging data suggest that cell death pathways are sexually dimorphic. Caspase-mediated cell death predominates in female brain, whereas poly (ADP) ribose polymerase (PARP) mediated cell death pathways are preferentially activated in the male brain. In this study we investigated the effect of exogenous neonatal testosterone on adult stroke outcomes. We also evaluated the potential of neonatal hormones to reorganize sex-specific ischemic cell death pathways after



MCAO in adult rats. Hypothesis: We predicted that neonatal testosterone would enhance injury in adult rats of both sexes. **Methods:** Wistar rats were injected with 0.1mg testosterone proprionate in 0.05ml sesame oil or vehicle subcutaneously for 5 days following birth. On postnatal day 80, rats underwent 90 minute middle cerebral artery occlusion (MCAO) and were sacrificed 24 hours after stroke. Rats were perfused with PBS followed by 4% paraformaldehyde (for CV staining) or taken fresh and flash frozen (for Western). Western analysis was performed on subcellular fractions. Serum hormone levels were assessed by ELISA. **Results:** Infarct levels were significantly decreased in TP injected males compared with oil injected males in the striatum and hemisphere (36% vs. 79%, P<0.01, 15% vs. 33%, P<0.05, n=11). TP females had consistently lower infarct volumes than oil females. Serum testosterone levels were lower in TP males vs. oil males (p<0.01, n=10) and were low in both female groups. Estrogen levels were significantly increased in TP males compared to oil males and in tp females compared to oil females (p<0.05, n=10). TP male gonads were significantly larger than oil male gonads (p<0.01, n=7). An increase in cytosolic XIAP (X-linked inhibitor of apoptosis) cleavage was seen in TP males vs. oil males. **Conclusions:** Neonatal exogenous testosterone administration protected adult males from subsequent stroke. This was associated with lower adult testosterone levels, and higher adult estrogen levels. TP-treated males had increased activation of XIAP, a component of the cell death pathway conventionally seen in the female brain after stroke. Ongoing studies will examine the possibility that this effect is secondary to upregulation of aromatase.

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Th MP39

Gender-Independent Neuroprotection with Minocycline after Experimental Embolic Stroke

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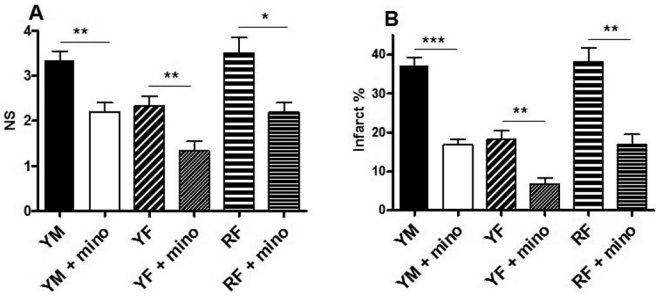
Ischemic stroke is the one of leading causes of death and disability among adults in the U.S. Growing evidence suggests that there is a gender difference in stroke pathophysiology and outcomes. Recent experimental models of stroke and clinical trials showed that minocycline provides neurovascular protection reducing acute cerebral injury. Minocycline has multiple mechanisms of action including inhibition of MMP-9 and poly ADP ribose -1. However, it is unclear whether minocycline is effective in females. We tested minocycline in both genders using a novel embolic stroke model that closely mimics thromboembolic stroke in humans. **Methods:** Acute ischemic stroke was initiated by injection of an autologous fibrin-rich clot to the right middle cerebral artery (MCA) in wild type C57BL/BJ mice. Six groups of animals were used: *a*) young adult males (21±2 weeks old); *b*) young adult females (21±2 weeks old); and *c*) retired females (64±4 weeks old) with or without minocycline (6 mg/kg) given intravenously at stroke onset. At 24 hours after embolization, the neurological status of animals and their brains were analyzed. The infarct size of MCA territory was estimated by TTC as percentage of the contralateral hemisphere. The insertion of the clot into the distal internal carotid artery led to consistent reduction of CBF to about 21±4% of baseline. This highly reproducible reduction persisted for two hours (28±5% of baseline) and then we observed a slow spontaneous CBF restoration (~50-65%) at 24 hours after stroke onset. **Results:** The model resulted in highly reproducible infarct in young males (37.0±2.3, n=6), young females (18.3±2.3, n=6) and retired females (38.1±3.6, n=6). As expected, young females were significantly more resistant to cerebral ischemic injury that was abolished by age in retired females. Overall neurologic deficits score was consistent with infarct volume for all groups and estimated as 3.3±0.2, 2.3±0.2 and 3.5±0.3 by Bederson Scale. Minocycline significantly reduced neurologic score (2.2±0.2, n=5, P<0.01) and infarct volume (16.8±1.5, P<0.001) in young males. Moreover, in our embolic model minocycline was neuroprotective for both females groups. The treatment with minocycline at stroke onset improved female behavioral deficits and significantly reduced infarct size (62-55% reduction). **Conclusion:** In a thromboembolic stroke model minocycline is an effective neuroprotector in both genders. *Figure: Neurological score (A) and infarct volume (B). * P<0.05; ** P<0.01; *** P<0.001.*



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Th MP40

Nicotinamide Adenine Dinucleotide (NAD): Another molecule contributing to sex differences?

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Introduction: Energy failure is a major component of cerebral ischemia. During stroke, the DNA repair enzyme, Poly ADP-Ribose Polymerase-1 (PARP) is activated. This leads to increasing levels of Poly ADP-Ribose (PAR) polymers, AIF translocation, NAD depletion, energy failure, and cell death. Sex differences exist in this pathway, as PARP deletion or inhibition are neuroprotective in males, but exacerbate injury in females. We hypothesized that NAD levels may differ between the sexes, which could contribute to the differential sensitivity of females

to the loss of PARP. **Methods:** Transient 90-minute middle cerebral artery occlusion was performed on male, gonadally intact (GI) female, and ovariectomized (OVX) female wild-type (WT) and PARP-/- SV-129 mice. Core infarct tissue was obtained 60 minutes into ischemia or 30 minutes after reperfusion and NAD levels were measured (n=4 stroke and 2 sham/group: significance $P<0.05$). Nicotinamide was administered 20 minutes prior to ischemia (500mg/kg i.p.), and TTC staining was performed 24 hours after stroke (n=10/group WT, n=6/group PARP KO: significance $P<0.05$). **Results:** Sham operated WT mice had significantly higher NAD levels than PARP KO mice at both time points (73.9μM$\pm$0.28: WT vs. 24.5μM$\pm$0.02: KO male: 93.9μM$\pm$4.5: WT vs. 31.0μM$\pm$1.5: KO female, 81.1μM$\pm$2.4: WT vs. 28.6μM$\pm$2.6: KO OVX). Sixty minutes into ischemia NAD levels were significantly decreased in WT males (73.9μM$\pm$0.28; sham vs. 47.8μM$\pm$1.48: stroke), while NAD levels were preserved in PARP knockout males (24.5μM$\pm$0.02: sham vs. 24.7μM$\pm$0.3: stroke). Intra-ischemic NAD levels were unchanged in WT GI or OVX females, but were strikingly decreased in PARP KO females (31.0μM$\pm$1.5: sham vs. 19.1μM$\pm$2.2: stroke). Intra-ischemic NAD levels in PARP KO males were preserved (24.5μM$\pm$0.02: sham vs. 24.7μM$\pm$0.3: stroke) compared to WT males (73.9μM$\pm$0.28: sham vs. 47.7μM$\pm$1.5: stroke). Nicotinamide treatment protected WT males (46.4%$\pm$5.6% vs. 30.8%$\pm$5.2), but had no effect in GI or OVX females. Nicotinamide protected both PARP KO males (25.5%$\pm$6.7 vs. 8.9%$\pm$3.9) and PARP KO GI females (52.7%$\pm$5.4 vs. 21.5%$\pm$4.8), while no effect was seen in PARP KO OVX females. **Discussion:** Male and female WT mice have similar baseline levels of NAD. Stroke induced NAD loss is significantly more robust in the male brain. NAD loss is ameliorated in PARP KO males, but exacerbated in PARP KO females. Nicotinamide treatment protected both WT and PARP KO males. PARP KO females have significantly larger infarcts than WT females, but nicotinamide treatment reversed the detrimental effects of PARP deletion. These data suggests that ischemic cell death is triggered by the loss of NAD in males, and nicotinamide may have therapeutic potential for male stroke patients.

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Th MP41

Protective Role of Estrogen against the Formation of Intracranial Aneurysms in Mice

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Introduction: We recently established a novel mouse model of intracranial aneurysm that utilizes elastase-induced disruption of elastic lamina and pharmacologically-induced hypertension. Using this model, we demonstrated critical roles of inflammatory cells and matrix metalloproteinases in intracranial aneurysm formation. Epidemiological studies suggest that estrogen has protective effects against the formation and rupture of intracranial aneurysms. These protective effects are considered to be through estrogen's anti-inflammatory effects. We hypothesized that estrogen would reduce the incidence of intracranial aneurysms in this newly-established model. **Methods:** Three groups of female mice (10-weeks-old) were studied. In the first group, we induced menopause by bilateral ovariectomy in each mouse (n=8). Mice in the second group received estrogen replacement therapy via implantation of a 17â-estradiol pellet (0.25mg estradiol, 60-day release) immediately after bilateral ovariectomy (n=8). The third group of mice received a sham ovariectomy (n=10). Two weeks later, mice were subjected to a single stereotaxic injection of elastase (10 milli-units) into the cerebrospinal fluid in the right basal cistern, and four weeks of continuous infusion of angiotensin II (750ng/kg/min) to induce intracranial aneurysms. Four weeks after aneurysm induction, mice were sacrificed. **Results:** The incidence of intracranial aneurysm was significantly higher in ovariectomized mice (75%) than in mice in the sham group (30%). There was a trend that the treatment with 17â-estradiol reduced the incidence of intracranial aneurysms from 75% to 37.5%. There was no difference in systolic blood pressure among the three groups. Histologically, intracranial aneurysms observed in this model closely resembled human intracranial aneurysms. Intracranial aneurysms had a vascular wall with thin and thick segments. Macrophage and leukocyte infiltration was observed in aneurysmal wall. **Conclusion:** The findings suggested that estrogen has protective roles against the formation of intracranial aneurysms in female mice. This model can be used to study molecular mechanisms that lead to aneurysm formation and growth. Results may provide new insights into the roles of estrogen in the pathophysiology of intracranial aneurysms, and in the mechanisms for the gender difference. Intracranial aneurysm at the right middle cerebral artery and subarachnoid hemorrhage around the aneurysm in ovariectomized mouse.

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Th MP42

Up-regulation Of Estrogen Receptor Alpha With Down-regulation Of The Brain Renin-angiotensin System By Olmesartan Contributes To Neuroprotection Against Cerebral Infarction In Estrogen-deficient Rats

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Background: Estrogen is neuroprotective against cerebral ischemia. Its effects are thought to be mediated by estrogen receptors (ERs), however, their role after ischemia is unclear. Although angiotensin II type 1 receptor (AT1R) blockers are protective against cerebral ischemia, there are few studies in female rats. We focused on the role of ERs and the inhibition of the brain renin-angiotensin system (RAS) as mechanisms underlying neuroprotection after ischemia. **Methods:** Female Wistar rats, 13 weeks old, were subjected to oophorectomy (OVX^+) and middle cerebral artery occlusion (MCAO). They were compared with non-OVX (OVX^-) MCAO rats and OVX^+ rats treated with 0.3- or 3.0 mg/kg olmesartan for 2 weeks before MCAO. **Results:** Independent of blood pressure, the cortical infarct volume was larger in OVX^+- than OVX^- rats; it was smaller in olmesartan-pretreated OVX^+ rats. The up-regulation of ERá but not ERâ was associated with neuroprotection in the cortical peri-infarct area. ERá expression was correlated with the increased mRNA level of angiotensin-converting enzyme 2 (ACE 2), Bcl-2, and Bcl-xL and a decrease in angiotensin II and cleaved caspase-3. Interestingly, these effects were augmented by olmesartan and abolished by the ER inhibitor, suggesting that the transactivation of neuroprotective genes and the reduction of brain angiotensin II via ACE2 are ERá dependent. The effects of olmesartan may augment neuroprotection together with AT1R blockade. **Conclusion:** Our study provides the new insight that the activation of ERá independent of estrogen contributes at least partly to limit cerebral ischemic damage.

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Th MP43

Speed Of ultra-early Hematoma Growth As A Powerful Predictor Of Clinical Deterioration And Long-term Outcome In Patients With Acute Intracranial Hemorrhage

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Background: Initial hematoma volume is one of the most powerful predictors of mortality after acute intracerebral hemorrhage (ICH). However, its impact on clinical course and outcome may vary widely depending on the time from symptom onset to baseline imaging (OIT). The speed of ultra-early hematoma growth (SuHG) may refine the predictive accuracy of initial hematoma volume and identify patients at risk of further ICH growth. We sought to explore the impact of SuHG on further ICH growth at 24h, clinical course and outcome in patients with acute ICH. **Methods:** We prospectively studied consecutive patients with acute primary supratentorial ICH evaluated <6 hours and with a known time from symptoms onset. Patients underwent baseline (<6h) and follow-up (24h) CT scans, and a CTA (<6h) for the blinded detection of spot sign (SS). ICH volumes were measured on baseline and 24h CT scans. SuHG was defined as the relation between baseline ICH volume/OIT. Hematoma growth (HG) was defined as ICH enlargement >30% or >6mL at 24h. Early neurological deterioration (END) was defined as increase ≥4 points in the NIHSS score or death at 24 hours. The mRS score was used to assess clinical outcome at 3 months. **Results:** A total of 123 acute primary supratentorial ICH were included in this study. Mean OIT was 165.2$\pm$84.6 min. Mean baseline ICH volume was 28.8$\pm$34 cc. Mean SuHG was 18.8$\pm$54.5 cc/h. SuHG was correlated with Glasgow Coma Scale ($r=-0.525$; $P<0.001$) and NIHSS ($r=0.493$; $P<0.001$) scores. CTA SS was seen in 19% of patients. SuHG was 3.5-fold faster in SS positive (33.2$\pm$43.2 cc/h) compared to SS negative (9.4$\pm$17.2 cc/h) patients ($p=0.001$). On 24h CT scan, HG was seen in 33.3% of patients. SuHG was significantly faster in patients who experienced further HG compared to those who did not (15$\pm$21.2 vs. 7.4$\pm$8.3 cc/h, $p=0.049$). SuHG markedly improved the accuracy of initial ICH volume and CTA SS in the prediction of END (Table). A ROC curve identified a cut-off point value of SuHG of 9.2 cc/h (sensitivity 92.6%, specificity 80.9%) that independently predicted HG at 24h (OR 4.4, 95% CI 1.6 to 12.5, $p=0.005$), END (OR 27.5, 95% CI 5.5 to 136, $P<0.001$), and poor long-term outcome (OR 6.3, 95% CI 1.3 to 30.1, $p=0.021$) after adjusting for baseline NIHSS score, initial ICH volume and CTA SS. **Conclusions:** The speed of ultra-early hematoma growth represents a novel approach for improving the prediction of further HG, END and long-term outcome in patients with acute ICH. SuHG >9.2 cc/h emerged as the most powerful independent predictor of HG at 24h, END and long-term outcome.

Table: Predictive values of speed of ultra-early hematoma growth, initial ICH volume and CTA spot sign for early neurological deterioration.

	SuHG>9.2 cc/h	Initial ICH volume >16.5 cc	CTA spot sign
Sensitivity	92.6%	85.2%	87.9%
Specificity	80.9%	69.1%	50%
PPV	58.1%	44.2%	46.7%
NPV	97.4%	94.2%	89.2%

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Th MP44

Volumetric Analysis of the CT Angiography Spot Sign Enables Calculation of the Rate of On-Going Hemorrhage in Patients with Primary Intracerebral Hemorrhage

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Purpose: To determine whether volumetric analysis of the CT angiography (CTA) spot sign, a potent predictor of hematoma expansion and poor outcome in patients with primary

intracerebral hemorrhage (ICH), can be used to calculate the rate of on-going hemorrhage. **Methods:** We retrospectively identified all primary ICH patients with spot signs who underwent both first-pass and delayed CTA acquisitions at our institution over a 10-year period. We then recorded the time interval between the 2 CTA acquisitions (T, in minutes) and utilized computer-assisted volumetric analysis to determine the volume of extravasated contrast material within the hematoma in each acquisition (Vspot1 for first-pass and Vspot2 for delayed, in mL). The rate of on-going hemorrhage was calculated as follows: (Vspot2-Vspot1)/T (in mL/min). If Vspot1>Vspot2, the rate of on-going hemorrhage was designated as 0 mL/min. Medical records were reviewed for baseline clinical characteristics, in-hospital mortality and poor outcome among survivors (defined as a modified Rankin scale ≥4 at 3-month follow-up). Baseline and follow-up ICH volumes were calculated with computer-assisted volumetric analysis. **Results:** Sixty-nine patients were included in our study, with a mean age of 71.9 years (median 76 years, range 26-92 years). 42 patients were male (60.9%) and 27 female (39.1%). Mean initial ICH volume was 56.3mL (median 52.5mL, range 2-169.9mL). Mean time interval between first-pass and delayed CTA acquisitions was 2.24 minutes (median 1.87 minutes, range 0.13-9.58 minutes). 37 patients had a follow-up non-contrast CT examination performed (53.6%, mean time to follow-up 9.1 h, median 7.5 h, range 2.5-42.8 h). Mean volume of extravasated contrast material in the first-pass CTA was 0.16mL (median 0.04mL, range 0-2.32mL), and mean volume of extravasated contrast material in the delayed CTA was 1.15mL (median 0.35mL, range 0-11.6mL). The mean calculated rate of on-going hemorrhage was 0.48mL/min (median 0.13mL/min, range 0-3.53mL/min). Table 1 summarizes the risk of hematoma expansion and poor outcome for 3 patient groups with different rates of on-going hemorrhage. In multivariate logistic regression analysis, the rate of on-going hemorrhage was an independent predictor of hematoma expansion (OR 19.9, 95% CI 2.4-169.2, p-value 0.006) and in-hospital mortality (OR 3.6, 95%CI 1.1-12.2, p-value 0.036). **Conclusion:** Volumetric analysis of the CTA spot sign in primary ICH enables calculation of the rate of on-going hemorrhage, which, in turn, predicts the risk of hematoma expansion, in-hospital mortality and poor outcome among survivors.

Table 1. Risk of Hematoma Expansion, In-Hospital Mortality and Poor Outcome Among Survivors According to Rate of On-Going Hemorrhage in Primary ICH

Rate of Hemorrhage, mL/min	Risk of Expansion,* %	In-Hospital Mortality, %	Poor Outcome,† %	Mean 3-month mRS in Survivors
0 to 0.03 n=23	30.8	43.5	38.5	2.5
0.04 to 0.22 n=23	66.7	69.6	57.1	3.1
0.34 to 3.53 n=23	100	73.9	66.7	3.8
AUC (95% CI)	0.84 (0.68-0.94)	0.64 (0.52-0.76)	0.63 (0.42-0.81)	n/a
p-value	<0.0001	0.031	0.22	n/a

*Hematoma expansion defined as an increase of >6mL or >30% from the baseline ICH volume in the 37 patients with a follow-up non-contrast CT. †Defined as mRS ≥4 at 3-month follow-up among the 26 survivors. ICH: intracerebral hemorrhage; mRS: modified Rankin Scale; n: number of patients within each rate of hemorrhage group; AUC: area under the curve after receiver operating characteristic analysis; CI: confidence interval; n/a: not applicable.

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Th MP45

The Impact of Blood Pressure Lowering on Perihematomal Edema Growth Measured by Serial Magnetic Resonance Imaging.

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Background: Spontaneous intracerebral hemorrhage (ICH) causes progressive perihematomal edema (PHE) formation, worsening mass effect and tissue shifts. Whether blood pressure (BP) lowering attenuates PHE volume (Ev) growth is unclear. **Objectives:** In this prospective study, we aimed to evaluate the influence of BP reduction on Ev measured on serial MRIs by randomizing patients to two different levels of BP lowering. **Methods:** Consecutive patients with a primary supratentorial ICH of >/= 5cc and GCS >/= 6 were prospectively enrolled < 24 hours of symptom onset, and underwent MRIs at pre-specified intervals: 48±12 hours and thereafter, weekly for up to 3 weeks when possible. Patients were randomized to a mean arterial pressure (MAP) goal of 70-90 or 90-110 mmHg for at least 72 hours. Intravenous nicardipine or esmolol were primarily used for BP lowering. Hematoma volume (Hv) and Ev were determined on FLAIR of the baseline MRI. Baseline Hv was used for subsequent Ev calculations. Eleven additional patients with a MAP goal of 90-110 mmHg and Hv (± 5 cc) matching the 70-90 mmHg group were used as controls. Mann-Whitney U and Wilcoxon signed ranks tests were used to compare the two randomized and the control groups. **Results:** Twenty-seven patients with 77 MRIs were included. Sixteen patients (median age 52 years) were randomized, seven to the MAP of 70-90 mmHg group. Patients in the 70-90 mmHg group had a strong trend towards smaller baseline Hv (16 vs. 38 cc, p=0.06) and Ev (29 vs. 41cc, p=0.07), and higher baseline relative PHE (rPHE=Ev/Hv: 1.78 vs. 1.28, p=0.02) compared to the 90-110 mmHg group. Despite the imbalance in baseline Hv, absolute Ev growth from baseline to peak was identical (19 vs. 19 cc, p=0.8) in the two randomized groups, and rPHE growth was greater in the 70-90 mmHg group (1.64 vs. 0.52, p=0.04). The control group (with MAP 90-110 mmHg) was similar to the randomized 70-90 mmHg group with respect to baseline Hv (16 vs. 15 cc, p=1), Ev (29 vs. 28 cc, p=0.2) and rPHE (1.8 Vs 1.8, p=0.3). However, the 70-90 mmHg group had more absolute Ev growth (10 vs. 8 cc p=0.06) and rPHE growth (0.8 vs. 0.5, p=0.03) than the control group.. **Conclusions:** Aggressive BP reduction does not attenuate and may worsen perihematomal edema growth measured by MRI in patients with spontaneous ICH.

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Th MP46

Reversible Cerebral Vasoconstriction Syndromes (RCVS): A comparison of Hemorrhagic and Non-Hemorrhagic forms

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Background: RCVS includes a group of conditions with reversible segmental constriction-dilatation of cerebral arteries. Nearly 90% present with thunderclap headaches, and upto 40% develop complications such as ischemic or hemorrhagic stroke. RCVS may be an important under-recognized cause of brain hemorrhage in young adults. '*Hemorrhagic*' RCVS has not been characterized, and it is unclear whether its clinical profile, mechanisms, and risk factors, differ from '*Non-Hemorrhagic*' RCVS. **Methods:** We analyzed the largest-ever RCVS case series based on the combined experiences of Mass. General Hospital (MGH) and Cleveland Clinic (CC). Diagnosis was based on published criteria. **Results:** We encountered 139 patients (84 at MGH; 55 at CC); mean age 42 yr; 81% women. The MGH and CC cohorts showed no major differences in clinical, laboratory or imaging features. Initial CT/MRI was normal in 45%, however ultimately 81% had abnormal brain imaging findings including infarcts (39%), convexity SAH (34%), lobar ICH (20%), and brain edema (38%). As compared to patients without hemorrhage (n=81), the group with any hemorrhage (ICH or cSAH, n=58) tended to be older (mean age 45±12 vs. 41±12, p=0.06), had a slightly higher frequency of women (88% vs. 76%, p=0.07), and a lower rate of normal CSF results (WBC≤5 cells/cmm in 71% vs. 93%, p=0.008, and protein level ≤60 mg% in 74% vs. 82%, p=0.20). There were no significant differences between hemorrhagic and non-hemorrhagic groups in the rates of prior migraine (45% vs. 36%, p=0.18); thunderclap headaches (90% vs. 82%, p=0.14); seizures (21% vs. 15%, p=0.25); or identified triggers such as vasoconstrictive drugs (52% vs. 48%, p=0.4) and pregnancy (5% vs. 11%, p=0.18). The 'hemorrhagic' group was significantly less likely to have a normal admission CT or MRI scan (31% vs. 73%, P<0.001) suggesting that ischemic complications occur later in the course of RCVS; however, both groups showed a similar rate of clinical neurological deficits (38% vs. 47%, p=0.19). Lobar hemorrhages were single or multiple, and (like ischemic strokes) were typically located in 'watershed' territories, suggesting reperfusion injury as the mechanism. Serial angiography showed no significant differences in the timing or reversibility of cerebral arterial irregularities between groups. Both groups had similar outcomes (mRS 0-3 in 91% vs. 88%, p=0.34). Similar results were found when restricting the analysis to patients with lobar hemorrhage versus ischemic stroke. **Conclusion:** Hemorrhagic and non-hemorrhagic/ischemic forms of RCVS have similar risk factors and clinical-angiographic features, although they may differ slightly in age, gender, and CSF profile. RCVS-associated brain hemorrhage develops earlier than ischemic stroke and carries a notably benign prognosis.

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Th MP47

Statin Use and Outcome after Intracerebral Hemorrhage: Case-control Study and Meta-analysis

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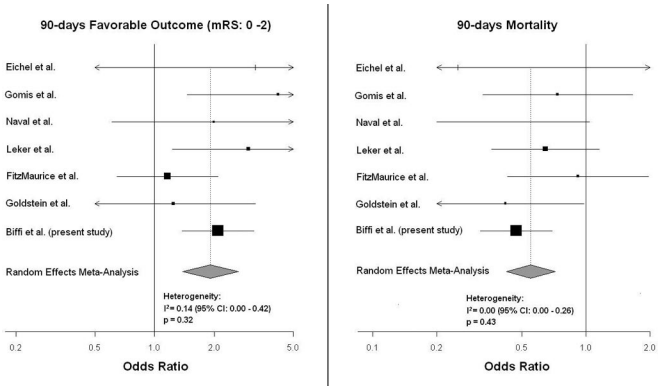
Introduction: Intracerebral hemorrhage (ICH) is a highly lethal disease of the elderly. The use of statins is increasingly widespread among the elderly, and therefore common in patients who develop ICH. While these agents may have neuroprotective effects, studies investigating association between antecedent statin use and ICH outcome have been conflicting. Hypothesis:

We analyzed unpublished data from our own institution and then performed a meta-analysis of all available evidence to determine whether antecedent statin use influences functional outcome after ICH. **Methods:** In our prospectively enrolled cohort, we investigated mortality as well as functional outcome (modified Rankin Scale score 0-2 vs. 3-6) in 238 pre-ICH statin cases and 461 statin-free ICH cases. We also compared outcomes for specific statin compounds: simvastatin (n = 93), atorvastatin (n = 102), pravastatin (n = 25) and lovastatin (n = 18). We use an inverse-variance weighted random effects model to conduct a meta-analysis of result from our cohort along with previously published studies. A total of 698ICH statin cases and 1823 non-statin exposed subjects was available for analysis. We evaluated meta-analysis heterogeneity by computing heterogeneity p-values and verified the absence of publication bias by performing the Begg and Egger tests. **Results:** Data from our center demonstrated an association between statin use before ICH and increased probability of favorable outcome (OR = 1.91, 95% Confidence Interval (CI): 1.38 - 2.65) and reduced mortality (OR = 0.55, 95% CI: 0.42 - 0.72) at 90 days (Figure). No compound-specific variations in effect size were identified for any tested statin. Meta-analysis of all published evidence confirmed the effect of statin use on good outcome (OR = 2.02, 95% CI: 1.42 - 2.90) and mortality (OR = 0.58, 95% CI 0.42 - 0.79) after ICH. We found no evidence of between-studies heterogeneity or publication bias in our meta-analyses (all p-values > 0.20). **Conclusion:** Antecedent use of statins prior to ICH is associated with favorable outcome and reduced mortality after ICH. This phenomenon appears to be a class-effect of statins. Further studies are required to clarify the biological mechanisms underlying these observations.



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Th MP48

Statin Discontinuation is Associated with Poor Outcomes Following Intracerebral Hemorrhage

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Introduction: Some studies suggest a protective role for statins following intracerebral hemorrhage (ICH). However, many failed to account for statin discontinuation following admission, did not include post-discharge outcomes, or were affected by loss to follow up. To address these limitations, we studied the relationship between pre-ICH statin use, in-hospital statin use, and 30-day mortality using a large stroke registry linked to population-based administrative data. **Methods:** Data were analyzed from 13 hospitals of the Registry of the Canadian Stroke Network. Primary outcomes were poor discharge mRS (defined as 4-6), and 30-day mortality. Continued statin use after admission was defined as any statin prescribed during the hospital stay. Multivariable logistic regression was used to determine the adjusted odds ratios (aOR) for statin use and outcomes, controlling for age, sex, stroke severity (measured by the Canadian Neurological Scale, CNS), elevated INR and other variables associated with the outcome in univariate analysis ($p<0.10$). **Results:** Data from 2466 consecutive ICH patients from 2003-2008 were analyzed: median age was 71 (IQR 58-80), 53.6% were male, and in-hospital mortality was 34.6%. Overall, 537 (21.7%) were taking statins prior to presentation: statin users were more likely to be older, to have medical comorbidities, and to be taking warfarin ($p<0.05$). Compared to non-users, statin users had similar rates of poor outcome (70% vs. 67%) and 30-day mortality (36% vs. 37%). Preadmission statin therapy was not associated with functional outcome (aOR for poor outcome 0.82, 95% CI 0.63-1.17, $p=0.14$) or increased mortality (aOR 0.88, 95% CI 0.68-1.15, $p=0.36$). Statins were discontinued on admission in 158/537 (29.4%); these patients were more likely to have severe stroke (CNS 0-4 in 65% vs. 27%, $P<0.01$), poor outcome by mRS (90% vs. 62%, $P<0.01$) and to have died by 30 days (71% vs. 21%, $P<0.01$). After adjusting for stroke severity, statin discontinuation was still associated with poor outcome (aOR 2.4, 95% CI 1.13-4.56, $P<0.01$) and higher mortality (aOR 2.0, 95% CI 1.30-3.04, $P<0.01$). These associations were also present after excluding palliative patients, and patients who died within 48 hours. **Conclusions:** We found no clear association between preadmission statin use and outcomes in ICH. However, statin discontinuation was independently associated with poor outcome and increased mortality. This may reflect a biological effect of statin withdrawal, although we cannot exclude the possibility of residual confounding by limitation of care, despite controlling for stroke severity, and excluding patients treated palliatively or who died early. A harmful effect of statin withdrawal has been reported from a randomized trial in ischemic stroke; our data suggest there may be a similar effect in ICH, and caution should be exercised when discontinuing statins soon after ICH.

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Th MP49

Stenting Or Angioplasty For Acute Stroke Due To Occlusion Or High Grade Stenosis Of The Extracranial Internal Carotid Artery Accompanying Intracranial Occlusions (tandem Lesions) In The Merci Registry: Incidence, Safety Profile And Clinical Outcomes

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Background: Endovascular therapy for acute stroke due to tandem occlusive disease (TOD) of the extracranial internal carotid artery (ICA) and intracranial arteries with proximal revascularization (angioplasty with or without stenting), before or after distal revascularization is increasingly being utilized. However, data on incidence, safety & clinical outcomes of this approach are scarce. We aimed to evaluate procedural results with this distinct endovascular stroke population in the Merci registry. **Methods:** The Merci registry is a prospective multicenter registry with 1000 patients enrolled from 37 centers. The only required inclusion criteria was the use of any Merci Retriever in patients with acute stroke. Clinical outcomes at 90 days were obtained prospectively with good outcomes defined as modified Rankin Score $\leq$ 2. Recanalization was reported using the TICI classification, with 2a, 2b & 3 considered as success. Patients with occlusion in the vertebrobasilar system were excluded. **Results:** A total of 746 patients were identified with completed 90d follow-up. Of those, 94 underwent proximal stenting with or without angioplasty and 37 underwent angioplasty alone. Table 1 outlines clinical, demographic & outcome data. **Conclusions:** With an incidence of 17.5% TOD is not uncommonly encountered during endovascular therapy for acute stroke in the anterior circulation. While patients with TOD tend to present later than those without TOD & are subjected to longer procedural times, a non significant trend towards higher recanalization rates, better clinical outcomes & lower incidence of sICH in TOD patients undergoing proximal stenting vs non TOD patients was observed. Proximal stenting is associated with better outcomes & lower incidence of sICH than angioplasty alone.

Table 1: Comparison of Stenting vs Angioplasty vs Others - Anterior Circulation patients only

Parameter	Prox. Stent (n=94)	PTA only (n=37)	All Others (n=615)
Age, mean	63.3	66.4	66.8
NIHSS, mean	16.8	18.0	17.6
Onset-to-Tx, mean	8.94†	4.78	5.47
Occlusion Location			
ICA	71.3%†	51.4%	26.5%
MCA–M1	28.7%†	48.6%	62.1%
MCA–M2	0.0%†	0.0%	10.4%
IIb/IIIa use	16.0%†	5.4%	4.6%
Proc dur., hr, mean	2.49†	2.20	1.76
TICI 2a+	84.0%	62.2%	77.2%
SICH, % (n/N)	1.6%(1/63)	10.0%(3/30)	7.7%(29/375)
90d mRS = 0-2	33.0%	27.0%	30.4%
90d Mortality	28.7%	40.5%	34.3%

† indicates statistically significant difference, in comparison with "All Others"

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Th MP50

Characterization of Clot Models for Preclinical Evaluation of Endovascular Recanalization Devices

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Introduction: Efficacy and safety of devices for the endovascular recanalization of acute ischemic stroke (AIS) are mostly validated in experimental vascular models and in-vivo animal models. Although critical for the evaluation, little is known about the mechanical similarities between these clot models and the human sources of embolic thrombi. The aim of this study is to explore the structure and mechanical properties of the cerebral emboli extracted from patients and model clots produced in-vitro. **Methods:** Nine thrombi were obtained from aspiration thrombectomy in AIS patients and 13 were collected during carotid endarterectomies (CEA). In-vitro embolus analogues (EAs) were prepared by simultaneously injecting whole

blood/ACD mixture and $CaCl_2$/thrombin solution into silicone tubing. Three variables of in-vitro clotting included species, thrombin concentration and addition of the radio-opaque component, barium sulfate. Dynamic mechanical analyzer was used to acquire the stress-strain behaviors of the clots in the controlled force mode, which gave an indication of clot hardness. Clot elasticity was analyzed from strain recovery experiments. Scanning electron microscopy (SEM) and Martius Scarlet Blue (MSB) stained sections were used to investigate the structure and composition of the specimens. **Results:** Two secant moduli that indicate clot hardness, designated as E1 and E2, are the slope of the stress-strain curve in the toe region (initial to 45% strain) and high strain (75%-95%), respectively. The softest clot material was obtained from AIS patients and was composed mainly of fibrin and erythrocytes ($E_{0\text{-}45\%}$= 0.026±0.0027MPa). Calcified thromboemboli showed the highest stiffness ($E_{0\text{-}45\%}$= 0.63±0.38MPa) followed by those that were cholesterol-rich ($E_{0\text{-}45\%}$= 0.17±0.039MPa). The histology and SEM results show that the EAs prepared in-vitro are mainly composed of homogeneously dispersed erythrocytes with several interspersed fibrin bands. Of the in vitro clots created in the lab, bovine EAs presented the highest stiffness and elasticity. The mechanical properties of the bovine EAs were not significantly altered by the addition of thrombin. Addition of thrombin at a concentration of 5 NIHU/ml blood resulted in increases in stiffness and elasticity of human and porcine EAs ($p<0.05$). The presence of barium sulfate significantly reduced the elasticity of all EAs ($p<0.05$). **Conclusions:** Endovascular device testing and development requires realistic EAs. The stiffness and elasticity of the cerebral emboli from AIS patients analyzed in this study were closely matched by recalcified porcine EAs and thrombin-induced human EAs. Stiffness of the CEA specimens was similar with that of the bovine EAs and thrombin induced porcine EAs.

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Th MP51

Careful Selection Of Patients with Stroke - On-Awakening Is Safe For Acute Recanalization Therapies

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Background: Approximately 10-25% of all acute ischaemic strokes (AIS) occur during sleepA proportion of these patients are likely to have suffered their stroke many hours into sleep and could be presenting to hospital within 4.5h of symptom onset. Tissue based methods of detecting salvagable patients are needed using imaging. We have treated selected patients with stroke-on-awakening at our centre using the good CT/occlusion paradigm. We aimed to study the safety of treatment and factors predicting outcomes for conservative,and thrombolytic therapy in this cohort.. **Methods:** The CT Angiography (CTA) database of the Calgary stroke program was reviewed for the period Jan03-Mar10. Patients with stroke-on-awakening, large artery occlusions on CTA, who received conservative, IV thrombolytic and/or endovascular treatment at discretion of the attending stroke neurologist were analysed. Time of onset was defined when patient was last seen or known to be normal. Baseline non-contrast CT scan ASPECTS => 7 was considered good scan in patients with anterior circulation strokes. Haemorrhage was defined on follow-up brain imaging using ECASS criteria. Independence (mRS≤2) at 3 months was considered a good clinical outcome. Standard descriptive statistics are used to report the data. **Results:** Among 532 patients with large artery occlusions, 70 patients (41 female) with stroke-on-awakening (13.1%) were identified. The median age was 69.5 (IQR 24), mean time from last seen normal to admission was 542 min (SD 186.2 min). 41 (58.5%) received anti-platelets only, 29(41.5%) received thrombolytic treatment [IV-12(17%),IV/IA-12(17%) and IA-5(7.1%)]. Locations of occlusions in tPA group were (M1 -8(17%),M2- 5(17%),M1+ICA-5(17%),M2+ICA-2(6%),Basilar - 9(31%). Asymptomatic ICH was observed in 3(7.3%) (HI1-1,HI2-2) patients in the conservatively treated group, and 3 patients (6.8%)(HI-1 -1, HI-2 -2) in thrombolytic group. No PH was seen in thrombolytic group One patient (2.4%) had a PH2 in the conservative treatment group. The median ASPECTS in tPA group was 8 (IQR7). Good outcomes were seen in 14/29(48.1%) patients treated with thrombolytic therapy as compared to 17/41(41%) treated conservatively ($p=0.806$).Unadjusted analysis showed that baseline NCCT ASPECTS <=7 ($p=0.002$) and higher NIHSS scores($p=0.018$) were associated with worse outcomes. Thrombolytic treatment did not predict good independent outcomes. In a multivariable model, baseline NCCT ASPECTS >7 (RR 2.9 CI_{95} 1.6-5.1), anti-platelet use (RR 1.7 CI_{95} 1.1-2.9) and age (RR 0.99 per year, CI_{95} 0.97-0.998) were predictors of good outcome, but not thrombolysis. **Conclusion:** When carefully selected by good scan (ASPECTS > 7) IV thrombolytic and/or endovascular treatment in stroke-on-awakening patients with large artery occlusions can be performed safely.Good Scans and premorbid use of antiplatelets may favour good outcomes.

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Th MP52

Progesterone Exerts Neuroprotection Against Permanent Focal Cerebral Ischemia In Rats By Activation Of The Akt-mediated Pathway

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Background: Studies continue to demonstrate the mechanisms and signaling pathways by which progesterone (PROG) provides neuroprotective actions. However, few data are available regarding PROG's effect on the Akt pathway after brain injury. Phosphorylation of Akt (pAkt), an important physiologic mediator of phosphoinositide 3-kinase (PI3K) signaling, activates several downstream targets of PI3K signaling. By negatively modulating genes that promote vascular permeability, apoptosis and inflammation, activation of the PI3K/Akt pathway protects vascular function. The effects of PROG on PI3K/Akt signaling may have important implications for regulation of the actions of growth factors such as vascular endothelial growth factor (VEGF) and brain-derived neurotrophic factor (BDNF). **Objective:** The present study sought to demonstrate the beneficial effects of PROG against brain injury following permanent focal cerebral ischemia (pMCAO) in rats, and the possible involvement of PI3K/Akt activation in neuroprotection. Method: Rats underwent pMCAO by electro-coagulation and received intra-peritoneal injections of PROG (8 mg/kg) or vehicle at 1h post-occlusion and then subcutaneous injections at 6, 24, and 48h. pAkt/Akt levels were analyzed by Western blot and immunohistochemistry at 24h post-pMCAO. VEGF and BDNF were analyzed at 72h post-pMCAO with Western blots. Infarct size was evaluated by cresyl violet 7 days after pMCAO. **Results:** Following pMCAO, treatment with PROG significantly ($P<0.05$) increased Akt phosphorylation compared to treatment with vehicle. Ischemic injury significantly ($P<0.05$) increased VEGF and decreased BDNF expression. PROG treatment significantly ($P<0.05$) attenuated both VEGF and BDNF expression after pMCAO. During the acute stage of ischemic injury, upregulation of VEGF in cerebral vessels increases blood-brain barrier (BBB) permeability, resulting in exacerbation of ischemic cell damage. PROG increased pAkt and reduced VEGF expression, suggesting that the acute reduction of VEGF prevents ischemic injury, which was confirmed by reduction (42.75%) in infarct size (% contralateral hemisphere). **Conclusions:** Post-treatment with PROG activates pAkt, decreases VEGF and increases BDNF expression, thus reducing ischemic brain damage. Taken together, our findings suggest that the PI3K/Akt pathway plays a role in mediating the neuroprotective effects of PROG in preventing ischemic injury. Additional experiments to investigate how Akt mediates the regulation of VEGF by PROG are needed.

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Th MP53

Transportation of Drip and Ship Patients with Acute Ischemic Stroke from Great Distances is Safe and Timely, Allowing Endovascular Therapy to Follow Intravenous Thrombolysis

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Introduction: Remotely-directed thrombolysis for acute ischemic stroke followed by transfer to a stroke center ("drip and ship") continues to gain broader utilization, with published data demonstrating safety. Drip and ship followed by endovascular therapy ("combined therapy") has potential to improve outcomes given the likely higher rates of endovascular therapy recanalization. Combined therapy should be assessed for safety and practicality, with evaluation of transfer systems for effeciency of transfers given the time-dependent nature of acute ischemic stroke therapies. Hypothesis: Air transport is faster than ground transport, and patients sent from great distances can meet time-based endovascular treatment guidelines. Drip and ship and combined therapy are safe with low rates of symptomatic intracerebral hemorrhage. **Methods:** We retrospectively reviewed consecutive records over an 18-month period for drip and ship patients. The time of stroke onset, time of tPA administration at the sending facility, time of arrival at the receiving facility, mode of transportation, use of endovascular therapy, and rate of symptomatic ICH were determined from medical records. Distance from the sending to the receiving facility was calculated by Google maps. **Results:** A total of 60 patients were treated by the drip and ship method. Thirty patients were transported by ambulance with 18 (60%) receiving combined therapy. Thirty patients were transported by air with 11 (37%) receiving combined therapy. Air transportation was from a mean distance of 154 miles (range 46-319) with mean 161 minutes from tPA administration to arrival. Ambulance transportation was from a mean of 50 miles (range 5-180 mi, mean 128 min from tPA administration to arrival). Mean transport time was 2.6 min/mi by ambulance and 1.0 min/mi by air ($p = 0.0001$). Ambulance transport reached the receiving facility within 7 hours from stroke onset in 27/30 events (90%) and air transport in 28/30 events (93%). For transfers of less than 100 miles there was no difference in transit times between air and ambulance transport (125 vs 117 min, p = NS). Three patients experienced symptomatic ICH (5%, 1 combined therapy and 2 treated with IV tPA alone). **Conclusions:** In this studied stroke network, transportation systems ensured timely arrival of acute stroke patients, allowing endovascular therapy to follow IV thrombolysis within recognized time guidelines, even from great distances. For shorter distances (< 100 mi) there was no benefit to air versus ground transport: this may have implications for cost consideration. It appears safe to transfer patients post IV thrombolysis from great distances.

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Th MP54

Robust Collateral Circulation on CT Angiography of Acute Stroke Patients with Proximal MCA Occlusion is a Strong Predictor of Small Admission MR Diffusion / MTT Infarct Size

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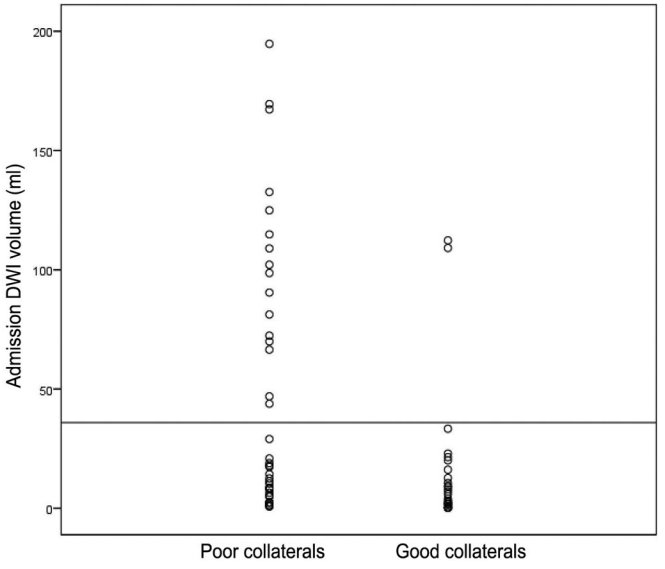
Background: Size of the admission DWI lesion is one of the most important factors in the decision for endovascular treatment of acute stroke patients, however, when MRI is unavailable or contraindicated, estimation of infarct core with CT can be unreliable. We hypothesized that

patients with robust collateral circulation on admission CT angiography (CTA) have small (< one third MCA territory) admission infarct volumes, and are therefore not excluded from intra-arterial stroke therapy. **Methods:** Consecutive patients with new onset acute stroke symptoms, admitted between April 2003 and April 2008, were screened for presence of unilateral M1 MCA occlusion on CTA. Only cases with available acute diffusion images (DWI) (<9h, mean 5h), and MR-perfusion (MRP) were included. We dichotomized patients into two groups: those with none-or-diminished collaterals, and those with equal-to-increased collateral circulation. Student's t-test was used to compare admission imaging and clinical variables between study groups (i.e. DWI-lesion volumes on admission, MR perfusion mean transit time (MTT) volumes, NIHSS score, and systolic blood pressure). We also performed a multivariate logistic regression to determine which of these variables are associated with robust collateral circulation. **Results:** We included 63 patients in our study, 26 were classified as having good collaterals and 37 as having poor collateral circulation. In the univariate analysis, we found that admission DWI volumes (16±5.7 ml vs. 51±9.2 ml, p= 0.002), and MTT volumes (131±13.7 ml vs. 183.2±75.7 ml, p= 0.016) were lower in those with good collaterals. Patients with good collaterals also had lower admission NIHSS scores (13±7 vs. 16±7, p=0.048). In the multivariate analysis, we found admission DWI lesion volume to be the only independent variable associated with status of collateral circulation on admission (p= 0.028). Based on ROC curve analysis, good collateral status on admission CTA was highly specific for small admission DWI volume (volume< 36 ml had 92% specificity and 43% sensitivity, area under the curve= 0.72; Figure). **Conclusion:** Robust collateral circulation on CT angiography of acute stroke patients with proximal MCA occlusion strongly correlates with small admission MR diffusion/MTT core infarct size. This may be of value in triage to intra-arterial therapy when MRI cannot be obtained.



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Th MP55

Education Improves Use of Thrombolytics for Ischemic Stroke

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Background: Two community based, non-academic, rural, primary stroke certified hospitals that treat 70 strokes per year reviewed data in 2004 that indicated thrombolytic medication was not being administered to ischemic stroke patients despite a defined drug protocol. In addition, 61% of ischemic stroke patients arrived within 3 hours of stroke symptom onset. Possible reasons for under-utilization of t-PA include non-standard information related to risks/benefits of t-PA as well as delayed arrival. **Purpose:** This intervention seeks to provide standardized patient education to improve patient and family response to stroke symptoms with earlier hospital arrival, and for t-PA candidates/families to receive standardized information on t-PA risk/benefits. The overarching goal was to achieve increased thrombolytic administration rates. **Method:** To address the concern of non-uniform information being presented to patients, we developed an educational DVD, designed for viewing by the lay public and potential t-PA candidates. After reviewing possible sources for an educational video, one was created in two 4 minute sections: the first part described stroke risk factors, signs/symptoms, and the second part discussed thrombolytic treatment risk and benefits. Four groups have been exposed to the DVD starting in late 2006. First, medical staff education was initiated, including the ED physicians to raise awareness of the studies and information upon which the video was based. In 2008, it was mailed to 30,000 households in Lenawee County. The DVD continues to be used in community screenings and events, and the video is shown to potential t-PA candidates/families in the ED. **Results:** The quality department tracks thrombolytic administration for all ischemic stroke patients as one measure of performance for primary stroke certification. Data demonstrates an increase in annual thrombolytic administration rate from 1.8% in 2004 to 6.5% of all ischemic stroke patients in 2009. Average arrival time from "last known well" has decreased from 327 minutes in 2007 to 259 minutes in 2009; in 2009 65% arrived within 3 hours. **Conclusion:** A standardized education tool (video) for medical staff, employees, patients and the community has been an important contributor to increased thrombolytic administration rate in this community hospital and a shortened time from stroke symptom onset to hospital presentation. More study is needed to demonstrate the relationship between the mailed DVDs and interval of symptom onset and ED presentation time. In conclusion, education and awareness has increased the use of thrombolytics in two community hospitals.

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Th MP56

The Mann Assessment Of Swallowing Ability Predicts Dysphagia After Stroke With High Specificity Compared To Video-Fluoroscopy

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Background: Dysphagia is a common medical complication of stroke that leads to aspiration pneumonia if not identified early. The videofluoroscopic swallow study (VFSS, also known as the modified barium swallow study) is the gold-standard for identifying dysphagia. In some clinical settings, the VFSS is limited by radiation exposure, high expense, and is not always available at all hospitals or on weekends. At times it would be optimal to have a validated clinical bedside assessment that supplants the VFSS on a short-term basis. While the use of a clinical swallowing assessment is standard practice, prior studies have not validated a clinical assessment tool with high specificity for dysphagia prediction. We hypothesized that the Mann Assessment of Swallowing Ability (MASA) would identify dysphagia in the stroke population with high specificity compared to the gold-standard. We tested the MASA against the VFSS to determine its sensitivity and specificity in detecting dysphagia. **Methods:** Patients were recruited from an urban, tertiary care hospital. Inclusion criteria were: an admission diagnosis of acute stroke, ability to participate in VFSS (defined by MASA alertness score of > 5), and age≥18. The MASA was administered by study coordinator within 8 hours prior to the VFSS and then the VFSS was conducted by a speech language pathologist blinded to the MASA results. A patient was scored to have dysphagia present or absent using the MASA criteria. A score < 178 indicated at least mild dysphagia while a score ≥ 178 was considered to reflect a normal swallow. The VFSS was scored utilizing the New Zealand Multidisciplinary Swallowing Index and a functional score was assigned using the Dysphagia Outcomes Severity Scale (DOSS). A DOSS score of < 5 was defined as "dysphagia", while a score of 6 or 7 was rated as "no dysphagia". Sensitivity, specificity, positive, and negative predictive values were calculated. **Results:** Our cohort included 216 subjects with suspected acute ischemic stroke. Mean age was 63 (22-97), 48% were female, 57% were Caucasian, and 42% were African-American. Mean NIHSS was 8.7. Sensitivity of MASA compared to VFSS DOSS was 90% and specificity was 87%. Positive and negative predictive values were 85% and 91%, respectively. **Conclusion:** The current state of practice in speech language pathology has the therapist conducting a clinical assessment of swallow function as an initial evaluation to determine the necessity for further evaluation or initiate oral intake. Previous studies have indicated that clinical assessments are not accurate when compared to the VFSS. This study, in addition to the initial study by Mann, provides evidence that the MASA has high specificity for dysphagia and should be considered the gold standard for clinical bedside assessments in the stroke population.

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Th MP57

A Systems Approach to Stroke Care: Increased Access to Tissue Plasminogen Activator Therapies

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Background and Purpose: In 1993, University Hospitals Case Medical Center (UHCMC) began its expansion from a single tertiary academic medical center to its current 9 hospital health system. In 2006, the University Hospitals Neurological Institute (UHNI) was formed with the vision of system integration to deliver the highest quality of care throughout the health system. In July 2008 the UH Stroke and Cerebrovascular Center (UHSCC) launched its System Stroke Program (SSP). One vision of the program was to increase access to lifesaving treatment with tissue plasminogen activator (tPA) for acute ischemic stroke patients in the fifteen counties surrounding Cleveland. **Methods:** Through a hub and spoke model, patients that present to community hospitals in the University Hospitals (UH) health system as well as other communities surrounding Cleveland have access to the same treatment options as those that present to the tertiary care center. The community hospital staff in the UH health system are provided with standard education including an acute stroke clinical practice guideline, National Institutes of Health Stroke Scale (NIHSS) training, dysphagia assessment training, and stroke pathophysiology and treatment module. Community emergency medicine teams triage patients, perform an NIHSS assessment, obtain an emergency computed tomography (CT) of the head, complete a tPA eligibility checklist, and consult with a stroke service attending at UHCMC to determine a treatment plan. Patients that are eligible for treatment with tPA have intravenous treatment initiated at the community hospital and are transferred to UHCMC for further care by stroke experts including intra-arterial (IA) tPA and clot retrieval procedures. **Results:** Since the launch of the UHSSP, UHCMC has seen a 9.1% increase in the number of ischemic stroke patients treated with tPA therapy from 2.4% in 2008 to 11.5% in 2009. The use of IA tPA has increased 18% from 25% in quarter one of 2008 to 43% in quarter one of 2010. **Conclusions:** The UHSCC has successfully increased access to life saving treatment with tPA for stroke patients in the fifteen counties surrounding Cleveland. Standardization of protocols, processes

and education allows for community hospital staff to accurately identify, assess, and treat patients who present with stroke symptoms. The system model provides patients with access to the same treatment options no matter where in the UH health system they present with stroke symptoms.

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Th MP58

Analysis Of Instrument Performance To Assess Depressive Symptoms In Stroke Survivors 0-3 Months Poststroke

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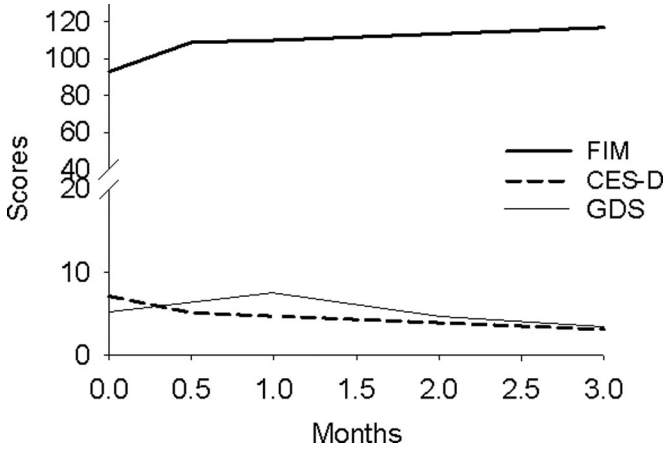
Background: Depression after stroke is common, affecting 185,000 U.S. stroke survivors a year. Assessing poststroke depression is challenging due to similarity of vegetative symptoms such as fatigues, lack of appetite and insomnia related to stroke to depressive symptoms. This is complicated by varying emotional disturbance poststroke that may be mistaken for depression such as apathy, pathologic crying and catastrophic reaction. Stroke researchers have utilized several instruments to assess depression; however, none have reliably been shown to reflect depressive symptoms in stroke patients. Purpose: To analyze and evaluate the application of two standard, commonly used depression instruments in a longitudinal study of stroke survivors. **Methods:** Using a prospective non randomized longitudinal design, a convenience sample of 23 ischemic stroke patients were assessed for depression, using 2 depression scales that have been validated for over-the-phone administration. The Center for Epidemiological Studies - Depression (CES-D) scale, and the Geriatric Depression Scale (GDS) were administered at baseline, 2 weeks, 1 month and 3 months poststroke. Subjects were additionally assessed on function (FIM), cognition (MMSE) and stroke severity (NIH stroke scale). **Results:** For majority of participants, depressive symptoms measured by CES-D improved significantly at time 2 and reached a plateau thereafter. The same pattern emerged with functional outcome measured by FIM. Patterns of GDS, however, did not have any similarity to the FIM (see sample graph below). Baseline mean and SD for the GDS was 2.69 (SD±2.12); scores remained under the published cutoff score for a positive screen for depression (a score of 5) at the 3 months follow-up, with a mean of 1.70 (SD ±1.69). The baseline mean for the CES-D was 7.09 (SD± 4.68); the mean also remained under the cutoff score for positive screen for depression (a score of 10) at the 3 months follow-up: mean 2.75 (SD±2.29). **Conclusion:** Several questions in GDS are more reflective of poststroke symptoms rather than depressive symptoms. These were represented by "*Do you feel you have more problems with memory than most?"; and* "*Do you feel full of energy"* The CES-D scale performed superior to the GDS in this longitudinal investigation. It is imperative to use a scale that truly measures depressive symptoms in stroke survivors. It is recommended that the CES-D, which was originally developed for use in a stroke population, be used in future studies including depressive symptom screening in longitudinal protocols involving stroke survivors.



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Th MP59

Recognizing Barriers That Decrease Adherence to Secondary Stroke Prevention

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Objective: Stroke Education includes stressing the importance of follow up after discharge for ongoing medical care. As patients with prior stroke and Transient Ischemic Attack (TIA) are at highest risk for recurrence, we established a Stroke Prevention Clinic with the expectation that all patients follow up 30 days after discharge to review the prevention plan, address control of risk factors, and obtain functional outcomes status. We sought to determine the barriers to meeting these goals. **Methods:** IRB-approved retrospective review of all hospital discharges from University Hospitals (UH) Case Medical Center with the primary diagnosis Ischemic Stroke or TIA from February 1- May 31, 2010 including patient demographics, insurance status, discharge disposition, primary care physician (PCP) listed at discharge, appointment made at discharge, and results of personal reminder call. **Results:** Of 212 eligible patients, 80 (37.7%) did not have documented follow up care; 20 (8.6%) had died or were in palliative care, 90 (42.5%) were seen in Stroke Prevention Clinic and 42 (19.8%) were seen with another UH Health System provider. Barriers to follow up included excessive distance or insurance carrier restrictions (12%), patient noncompliance (23%) and some "other" deficiency in the system for ensuring a follow up visit (65%). Non-compliant patients were less likely to have been discharged home (44 versus 57%, p=0.035) but were otherwise not significantly different from those who had documented follow up with respect to age (67 year), gender (40 vs. 44% male), race (33 vs. 38% African-American), insurance status (78 vs. 79%), or established with PCP (78 vs. 79%). The "Other" patients were slightly older (69.7 vs. 67.1 year), significantly more likely to be male (57 vs. 44%, p=0.034) and African-American, (44 vs. 38%, p=0.013) and less likely to have been discharged home (41 vs. 57%, p=0.001). They were as likely to be established with a PCP (72 vs. 79%) and more likely to have insurance (93 vs. 79%, p=0.026). **Conclusions:** Secondary stroke prevention is especially important for high-risk patients with prior stroke or TIA. Although patient noncompliance was a factor, the most frequent barrier to follow up care could be traced back to some inadequacy of the system for ensuring that visit. Vulnerable patients are more likely to be discharged to a facility, African Americans and male. Future research will explore how we can redesign the system to better meet the needs of vulnerable patients.

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Th MP60

Positive Impact of Electronic Reminders on Stroke Education

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Background and Issues: Stroke education for patients and/or caregivers has been a requirement for primary stroke centers since the inception of the Disease-Specific Care Certification Program for stroke. Our institution struggled to demonstrate consistent compliance with this standard. **Purpose:** To improve compliance with the Joint Commission stroke education requirement to ensure education of patients and/or caregivers. **Methods:** We performed chart audits to assess whether complete stroke education was performed and documented. The charts of patients who were admitted with ischemic or hemorrhagic stroke were audited from June 2008 through June 2010 (n = 797) for compliance with the Joint Commission stroke education requirements addressing all of the following: personal risk factors for stroke, warning signs for stroke, activation of emergency medical system, need for follow-up after discharge, and medications prescribed at discharge. To address inadequacies, we instituted inservices, verbal reminders during staff meetings, individual and group education, and reporting to the staff results of post-discharge chart reviews, but none of these strategies improved compliance. Nursing representatives then participated in development of first a paper form, then an electronic form that outlined the educational requirements. Unfortunately, neither of these provided the anticipated success. The nursing staff utilizes an electronic patient activity log (PAL) that is generated from provider orders and nursing protocols. We created an electronic pathway to connect a provider order or nursing protocol to the electronic reminder system, such that a nurse would be visually cued on the list of PAL tasks to provide stroke education and then, with just a click, be able to open the form and document the education. **Results:** Data findings in June 2008 demonstrated a 74% compliance rate, which dropped to a low of 29% in May 2009. Since the PAL reminder was instituted in August 2009, the compliance rate has been ≥84%, with a high of 96% in June 2010. **Conclusion:** Several interventions were instituted and monitored at our institution to improve compliance with the Joint Commission stroke education standard, but the action that achieved the most success was the implementation of a computer-based electronic reminder system.

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Th MP61

Risk-adjusted 30-day Intracerebral Hemorrhage Mortality Among The Elderly In The United States, 1993-2006

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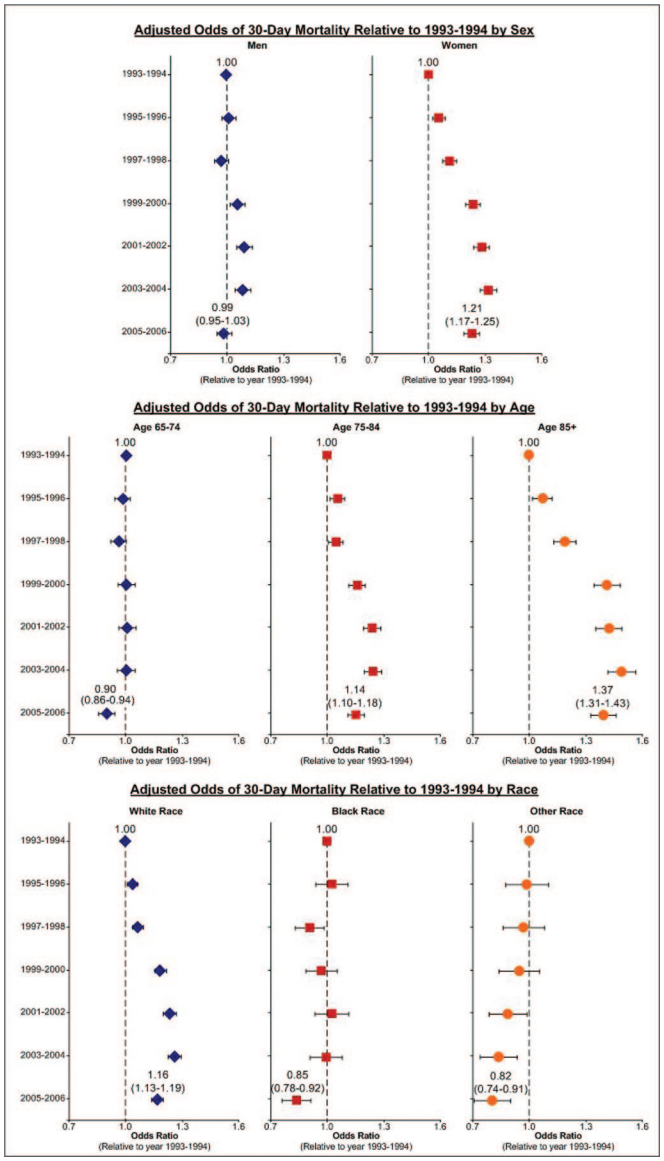
Background: National data reflecting parenchymal intracerebral hemorrhage (ICH) mortality rates in the US are limited due to the lack of a national surveillance system. **Purpose:** To assess temporal trends in 30-day risk-adjusted mortality rates following ICH by sex, age, and race in elderly Medicare fee-for-service (FFS) beneficiaries from 1993 through 2006. **Methods:** The study cohort included all fee-for-service (FFS) Medicare beneficiaries >=age 65 years hospitalized with ICH (ICD-9 primary discharge code 431) from 1993-2006 (combined in 2-year intervals). Patients discharged from non-acute facilities, transfers, or those with <12 months of continuous FFS status were excluded. Thirty-day mortality rates were determined by sex, age (65-74, 75-84, 85+), and race (white, black, other). Random effects logistic regression models compared annual mortality rates within subgroups using 1993-1994 as the referent time period, with risk-adjustment for demographic characteristics and comorbid conditions. **Results:** ICH hospitalizations decreased from 69,509 in 1993-1994 to 64,823 in 2005-2006.

Unadjusted in-hospital mortality decreased (33.3% to 30.3%), but 30-day mortality increased (38.8% to 42.3%) over time with an 11% increase in risk-adjusted odds of 30-day mortality (OR=1.11, 95% CI 1.09 to 1.14). Within each subgroup, relative to 1993-1994, risk-adjusted 30-day mortality in 2005-2006 was increased for women (OR=1.21, 95% CI 1.17 to 1.25) and older patients (OR=1.14, 1.10-1.18 for 75-84 year olds and OR=1.37, 1.31-1.43 for >85 years). Mortality also increased for white patients, but decreased for blacks and other race-ethnic groups (Figure). **Conclusions:** There was an increase in risk-adjusted 30-day mortality rates for elderly patients hospitalized with ICH from 1993 to 2006 despite a decrease of in-hospital mortality. The increase was more marked for women, older age groups, and white patients. Understanding the reasons for the relative increases in post-ICH mortality may help to eliminate these differences.



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Th MP62

Intracerebral Hemorrhage Specific Intensity of Care Quality Matrix

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Background: Intracerebral hemorrhage (ICH) care can vary among centers and previous studies have demonstrated differences in ICH outcome based on variations in patient care in various settings. The purpose of this paper is to present the design of an evidence-based dataset of elements of a new ICH specific intensity of care quality matrix. **Methods:** The articles were identified based on personal knowledge of the subject supplemented by data derived from multi-center randomized trials, and selected non-randomized or observational clinical studies. The information was identified with multiple searches on MEDLINE from 1986 through 2009. The current guidelines from American Heart Association (AHA)/American Stroke Association (ASA) Stroke Council and The European Stroke Initiative (EUSI) Writing Committee for management of intracerebral hemorrhage were reviewed extensively for identifying quality indicators and available scientific evidence. For certain elements where stroke-specific data was not available, data derived from other disease process with direct relevance was used. **Results:** A total of 27 quality indicators related to 18 facets of care with thresholds for quality response were identified. A pilot study was performed to asses and score 1350 (27 indicator per patientX25 patientsX2 raters) quality indicators. The minimum proportion of patients meeting quality parameter ranged from 44% to 100% depending upon the variable. The lowest performance scores were observed in the early intubation and mechanical ventilation, treatment of significant intracranial mass effect or transtentorial herniation, and timely acquisition of computed tomographic scan of head. The highest performance scores were seen in treatment of any seizure within two weeks of admission, status epilepticus, and prevention of gastric ulcer. **Conclusions:** The next step in development of a new ICH specific intensity of care quality matrix is validation and refinement of the quality indicators and thresholds presented in the current report. Future activities may include selection and validation based on consensus of experts and/or application of the system to a large series of patients with ICH and assessment of relationship of components in isolation and as a group to outcome after severity adjustment.

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Th MP63

The Comparative Mortality of Ischemic Stroke vs. Intracranial Hemorrhage On and Off Warfarin: The Anticoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study

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Background: When considering the net benefit of prescribing warfarin for atrial fibrillation, it is essential to compare the benefits associated with reducing ischemic stroke risk to the increase in intracranial hemorrhage (ICH) risk and severity. The impact of warfarin on stroke and ICH risk is relatively well studied, but the impact on event severity in atrial fibrillation is not. We compared 30-day mortality from ischemic stroke vs. ICH in a large community-based cohort of patients with atrial fibrillation. **Methods:** We followed a cohort of 13,559 patients with atrial fibrillation enrolled in an integrated healthcare delivery system over a median 6 years. Incident ischemic strokes and ICHs were identified from computerized databases and validated through medical record review. ICHs were categorized as intracerebral, subdural, or other ICH. Mortality was determined from healthplan databases and the State Death Index. We modeled the association of warfarin on 30-day mortality after ischemic stroke and ICH using multivariable logistic regression. **Results:** We identified 1025 ischemic strokes and 299 ICHs over ~65,000 person-years of follow-up. The annualized rate of ischemic stroke was 1.18% on warfarin and 1.97% off warfarin; the rate of ICH was 0.58% on warfarin and 0.32% off warfarin. Warfarin was associated with a substantially lower 30-day mortality rate after ischemic stroke, but higher mortality from ICH, particularly intracerebral hemorrhage (Table). ICHs occurring on warfarin were 1.6 times more lethal than ischemic strokes occurring while off warfarin. **Conclusions:** Warfarin not only reduces the risk of ischemic stroke from atrial fibrillation, but also reduces 30-day mortality from ischemic stroke. However, warfarin conversely raises both the risk and mortality associated with ICH. Because ICH on warfarin is less common than ischemic stroke off warfarin, anticoagulation continues to be indicated for appropriate patients with atrial fibrillation. However, both the rates as well as severity of events need to be incorporated into rational decision-making when considering warfarin treatment.

Table. Thirty-day Mortality after Ischemic Stroke and ICH by Warfarin Status

	On warfarin		Off warfarin		Odds of 30-day mortality associated with warfarin (95% CI)
	N	Deaths (%)	N	Deaths (%)	
Ischemic stroke	382	75 (19.6%)	643	178 (27.7%)	0.68 (0.48, 0.96)*
ICH (all)	193	88 (45.6%)	106	33 (31.1%)	1.69 (1.01, 2.83)**
Intracerebral	98	58 (59.2%)	41	17 (41.5%)	2.05 (0.98, 4.29)
Subdural	63	20 (31.7%)	38	8 (21.1%)	1.74 (0.68, 4.48)
Other ICH	32	10 (31.3%)	27	8 (29.6%)	1.08 (0.35, 3.29)

* adjusting for age, sex, prior stroke, hypertension, congestive heart failure, diabetes mellitus, coronary artery disease, and aspirin use
** adjusting for type of ICH (intracerebral vs. non-intracerebral)

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Th MP64

Prediction Of Very Early Stroke Or High-risk Stroke Mechanism In Patients With Transient Ischemic Attack From The Promapa Study. A Prospective Comparison Of Prognostic Risk Scores

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Background and Purpose: Several clinical scales have been developed for predicting stroke recurrence after a transient ischemic attack (TIA). We aimed to compare the very early predictive accuracy of the most relevant clinical scores (ABCD Score, ABCD2 Score, ABCDI Score, ABCD2I Score, California Risk Score [CRS], Essen Stroke Risk Score [ESRS] and Stroke Prognostic Instrument II [SPI-II]) among consecutive TIA patients. **Methods:** Between April 2008 and December 2009, we included 1255 consecutive TIA patients from 30 Spanish stroke centers (PROMAPA study). We determined the early short-term risk (7 and 90 days) of stroke and the composite end point consisting of stroke within 7 days or identification of atherosclerotic etiology (>50% stenosis in a vessel referable to symptoms). To evaluate the performance of each model, we calculated the area under the curve by receiver operating characteristic. **Results:** We could calculated clinical scales in 1136 patients (90.5%). The 7-day and 90-day stroke risk were 2.5% and 3.8% respectively. We confirmed an atherosclerotic etiology in 187 (16.5%) patients. The composite end point was observed in 205 (18.2%) cases. We could not confirm the stroke recurrence predictive value of the seven scores. However, only ESRS 0.62 (0.58-0.66) P<0.001 predicted the composite endpoint. **Conclusions:** In TIA patients, if we considered a composite end point, ESRS had a marginally superiority to identify patients requiring specific early intervention. According to our data, a new prognostic score is needed to better identify patients at higher risk.

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Th MP65

Is Acute Hospitalization Needed for Patients Presenting With a Transient Ischemic Attack? An Analysis of 400 Consecutive Patients

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Background: The Early Use of Existing Preventive Strategies for Stroke (EXPRESS) trial demonstrated that urgent use of existing preventive medical treatment after a transient ischemic attack or minor stroke cut the 90 day risk of recurrent stroke by approximately 80%. While the $ABCD^2$ score can be used to stratify patients who are at high risk of recurrence of stroke or transient ischemic attack (TIA) following an initial TIA, it remains unknown whether hospital admission is required for all patients with TIA. **Objective:** To determine whether acute hospitalization following a TIA identifies any new clinical conditions that require immediate medical treatment. **Methods:** A review of 400 consecutive patients with a pre-admission diagnosis of TIA (ICD-9 435.9) admitted to two University affiliated comprehensive stroke centers was performed. Data relating to vascular risk factors, pre-hospitalization medical treatment, in-hospitalization medical treatment, and investigations performed (telemetric monitoring, brain imaging studies), and discharge medications were collected. The main outcome was defined as the in-hospital recurrence or worsening of neurological symptoms and the identification of any new medical conditions that led to the initiation of a new treatment. **Results:** The data regarding events recorded during hospitalization among 400 patients with TIA (mean age ± standard deviation 67±15 years; 187 were men) is summarized in Table: 1. Table: 1

Pre-admission TIA patients	n=400
Length of stay (average)	3 days
Past medical history of atrial fibrillation,	19 (5%)
Sub-therapeutic INR (less than 2) on admission	
New diagnosis identified during hospital admission	
Atrial Fibrillation	8 (2%)
Atrial septal defect/patent foramen ovale	35 (9%)
Congestive heart failure	2 (0.005%)
Diabetes mellitus (Type II)	5 (1%)
Dyslipidemia	45 (11%)
Hypertension	18 (5%)
Infection	
• Urinary tract infection	5 (1%)
• Intra-abdominal abscess	1 (0.0025%)
Intracranial tumor	1 (0.0025%)
Non-ST elevation myocardial infarction	2 (0.005%)
Recurrent TIA	10 (3%)
Thrombus	
• Brachiocephalic artery	1 (0.0025%)
• Right internal carotid artery	1 (0.0025%)
• Left internal carotid artery	1 (0.0025%)
In hospital treatment	
Extracranial stent	4 (1%)
Intracranial stent	2 (0.005%)
Carotid endarterectomy	2 (0.005%)
Intravenous tissue plasiminogen activator	2 (0.005%)

Conclusion: A reassessment of need for acute hospitalization of asymptomatic TIA patients must be considered given the low rates of newly identified medical conditions that require emergent treatment. New emphasis on the outpatient work up of TIA patients, with the initial evaluation and initiation of existing preventive medical treatments performed in the emergency department is required.

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Th MP66

Impact of Stroke Clinical Prevention on Survival in Patients with Ischemic Stroke or Transient Ischemic Attack: A Propensity-Score Matching Approach

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Background: Propensity score methods are increasingly being used to reduce the impact of treatment-selection bias in the estimation of casual treatment effects using observational data. In the present study, we applied a propensity score matching approach to evaluate the impact of stroke clinical prevention (SPC) referral on survival in patients with ischemic strokes or transient ischemic attacks (TIA). **Method:** We analyzed data from 11 stroke centers in Ontario participating in the Registry of Canadian Stroke Network between July 2003 and March 2008, and linked this to provincial administrative databases to capture physician visits, procedures including carotid revascularization, medication prescriptions and mortality within one year of the index stroke hospitalization. We compared care and outcomes in patients referred to SPCs compared to those without such a referral. Because of the substantial differences in baseline characteristics between patients with an SPC referral and those without, the propensity score greedy matching technique was applied to create 1:1 matched pairs. Standardized difference was used to compare balance in baseline variables between SPC and non-SPC patients. A Cox proportional hazards model with robust variance estimator to account for matching was used to discern the affect of SPC referral on survival. McNemar tests and paired t-tests were used to test the binary and continuous outcomes, respectively. **Result:** The original cohort included 16,468 patients with ischemic or TIA, 7,700 (47%) of whom were referred to a SPC at discharge. Over 70% of SPC patients were matched with non-SPC patients (5,575 matched pairs, total N=11,150). In terms of standardized differences, the propensity-score matched cohorts were similar in demographic characteristics, stroke severity, medical history, in-hospital acute treatment and modified Rankin scores at discharge. However, 1-year all-cause mortality of SPC patients was significantly lower than that of non-SPC patients (7% vs. 11%; Hazards Ratio 0.66; 95% CI: 0.58-0.74). Within 1 year of discharge, compared to those without SPC referral, patients referred to SPCs had more physician visits (14 vs. 12, P<0.0001), were more likely to undergo carotid imaging (47% vs. 39%, P<0.0001), and were more likely to be prescribed anti-hypertensive agents (87% vs. 84%, p=0.0003) and lipid lowering agents (76% vs. 69%, P<0.0001). **Conclusion:** In a propensity-score matched cohort, patients referred to SPCs had more physician visits, investigations and medications prescribed and has greater survival compared with those without a referral to a SPC.

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Th MP67

Individual-level Barriers and Facilitators to calling 911 for Acute Stroke in an African American Community

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Background and Purpose: African Americans have nearly double the rate of ischemic stroke and are one-fifth as likely to receive acute stroke treatments compared with European Americans. We sought to determine knowledge of stroke warning signs and behavioral intent to call 911, self-efficacy with respect to seeking stroke treatment, barriers and facilitators to calling 911 and exposure to stroke health information in an African American Community. **Methods:** This was a community-based participatory research project conducted jointly by the University of Michigan stroke team and Bridges into the Future, a faith-based community organization in Flint, Michigan. In March 2010, an anonymous survey was distributed to adults and youth ages 11-14 at four African American churches in Flint. Descriptive statistics were used to summarize demographics of respondents, mean test scores, and frequencies of response options. **Results:** Of the 332 respondents, 250 were adults and 82 were youth. Ninety percent of adults and 85% of youth self-identified as African American. Females comprised 70% of adults and 51% of youth. Fifty six percent of adult had at least some college. Stroke warning signs were correctly identified in 51% (sd=0.32) of the vignettes by adults and 46% (sd=0.28) by youth (p=0.21). Adults would call 911 in 71% (sd=0.26) of the vignettes compared with 54% (sd=0.29) of youth (p< 0.01). With regards to stroke self-efficacy, 90 (36%) adults and 39 (48%) of youth believed they would be unable to recognize a stroke. Additionally, 106 (42%) adults and 32 (39%) youth respondents would not know what to do if they witnessed someone having a stroke. Barriers to calling 911 endorsed by over 10% of adult respondents included a belief that they could transport their loved one to the hospital faster than engaging an ambulance 40 (16%) and distrust of doctors 33 (13%). Cost, religious beliefs and embarrassment to have an ambulance arrive were not endorsed as barriers. Over two-thirds of adult and youth respondents reported no exposure to stroke health information in the past year. **Conclusion:** Behavioral intent to call 911 was high among an educated population of primarily African American adults and youth. This lends an optimistic eye toward improving recognition of stroke symptoms and self-efficacy to identify a stroke and take appropriate action. Few barriers to calling 911 were identified. Respondents had little exposure to stroke health information.

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Th MP68

A National US Telestroke Delivery System: Patient Characteristics and Frequency of Thrombolytic Therapy Delivery

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Background: Neurologic expertise at the bedside is essential for optimal acute stroke care but there are not enough neurologists locally available for emergent call to provide round the clock, in person, physical coverage for many rural and urban hospitals in the United States. Video telemedicine delivery of stroke expertise (telestroke) is an emerging solution to this challenge. Prior studies have described limited telestroke implementations within single states or regions by single academic medical centers rather than networks capable on a national scale. **Methods:** We reviewed the calendar year 2009 experience in emergent stroke consultation of the national Specialists on Call (SOC) telemedicine network, a national, Joint Commission certified telehealth provider. Spoke hospital addresses were geocoded and mapped to US 2000 US census data. **Results:** In 2009, the network provided telestroke consultations to 71 hospitals in 9 states. Consultations were performed by 42 different on call tele-neurologists, from both academic and community practices. Among the 6740 patients consulted upon, diagnoses were acute cerebral ischemia (ischemic stroke or transient ischemic attack) in 4076 (60.5%), intracerebral hemorrhage in 274 (4.1%), seizure in 441 (6.5%) and other in 1949 (28.9%). Among the patients with acute ischemic stroke, intravenous thrombolytic therapy within 3 or 4.5 hours was administered in 383 (9.4%). Geocoding analyses indicated that 90% of supported hospitals were in urban census tracts, 10% rural, and 0% frontier. Overall, 31.4 million individuals, 11% of the US population, resided within 30 minutes ground ambulance transport of an acute stroke ready hospital. **Conclusions:** National, multistate telestroke care is feasible. Stroke care can be provided to more than 4076 patients annually, including the delivery of thrombolytic therapy to 383. The system currently enables access to acute stroke therapy for 11% of the US population in regions where local, in person neurologic response is not available round the clock.

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Th MP69

Low Yield of Hospital Inpatient Stroke "Codes": Implications for Resource Allocation

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Background: Stroke rapid response systems (Stroke "codes") are intended to provide expeditious clinical expertise to support the evaluation and timely treatment of patients with acute stroke. This system was primarily intended for patients presenting to the Emergency Department (ED); however the same system can be used for hospitalized patients with acute stroke symptoms.The usefulness of inpatient stroke codes in uncertain.**Purpose:** We compared the proportions of in-hospital and ED stroke code patients having a stroke discharge diagnosis and the proportions treated with intravenous tPA or endovascularly based on current AHA/ASA Guidelines. **Methods:** Discharge diagnoses and management of in-hospital and ED stroke code patients were assessed retrospectively over 1 year at a Joint Commission Primary Stroke Center. **Results:** There were 93 in-hospital and 204 ED stroke codes (mean age 64.7±15.6 vs 65.5±17.2 yrs, p=0.70; 49% vs 43% men, p=0.27; 38% vs 41% African-American, p=0.31, respectively). In-hospital stroke code patients were less likely to have had a stroke (27% vs. 41%,pthrombolytics (3% vs. 14%, p=0.005). Stroke mimics not necessitating immediate neurologic attention accounted for 61% of in-hospital but only 31% of ED stroke codes (table). "Altered mental status" was the only presenting symptom and the reason for activating a stroke code in 48% of in-hospital but in only 10% of ED stroke codes (p=<.0001) and was associated with the diagnosis of a stroke mimic (OR 11.8, 95%CI (4.6-30.7), P<0.0001). Surgical services (39%) most commonly activated in-hospital stroke codes. **Conclusion:** The proportion of patients having acute ischemic stroke and the proportion treated with reperfusion therapy after activation of in-hospital stroke codes was small, and lower than in patients identified in the ED over the same time period. Targeted education of hospital staff may increase the yield of in-hospital stroke codes, potentially reducing the diversion of resources from other patient care activities.

Stroke code diagnosis	Hospital (N=93)	ED (N=204)	p-value
Focal ischemia (stroke or TIA)	25 (27%)	105 (51%)	<0.0001
Intracranial hemorrhage	5 (5%)	28 (14%)	0.03
Seizure	4 (4%)	7(3%)	0.74
Migraine	0 (0%)	8 (4%)	0.06
Metabolic/Infectious	39 (42%)	19 (9%)	<0.0001
Other	20 (22%)	37 (18%)	0.47

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Th MP70

Improving Rates Of IV tPA For Acute Ischemic Stroke: The Massachusetts Primary Stroke Service Experience, 2004-2008

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Background: Intravenous tPA (IV tPA) improves outcomes in patients with acute ischemic stroke (AIS). We sought to determine if IV tPA use in AIS patients increased in Massachusetts in association with the Primary Stroke Service (PSS) program, a statewide stroke center designation and quality improvement (QI) initiative. **Methods:** We reviewed prospectively acquired data from the Massachusetts Department of Public Health (DPH) between October 2004 and June 2008. Data from 10,045 consecutive de-identified ED-based AIS encounters arriving ≤3 hrs after stroke onset at 68 participating Massachusetts PSS hospitals, representing 97% of all hospitals in the state, were analyzed. We evaluated the characteristics associated with IV tPA use over time among *all* AIS patients arriving within 2 hours of symptom onset. **Results:** In univariate analysis, IV tPA use among *all* patients arriving within 2 hours of symptom onset increased steadily from 2005 (the first full year of the program) to 2008 (18.4%, 21.9%, 22.6%, 25.5%, P<0.003). Patients treated with IV tPA were more likely to be younger (72.3±14.1 vs. 74.7±14.0, P<0.001), to have presented to a teaching hospital (41% vs. 34%, P<0.001), larger hospital (median 223 beds vs. 205 beds, p=0.002), or after EMS re-routing in July 2005 (96% vs. 94%, p=0.009). Factors independently associated with use of IV tPA in multivariable analysis were older age (OR 0.8, 95%CI 0.7-0.9 *age 80-89*; OR 0.6, 95%CI 0.4-0.8 *age ≥90* vs. *age <80*) and increasing calendar year after 2004 (OR 1.1 *per year*, 95% CI 1.02-1.20) with a trend toward increased tPA use after EMS re-routing (OR 1.5, 95%CI 0.9-2.3). Twenty-eight hospitals participated in the AHA's Get With The Guidelines-Stroke (GWTG-S) program and received a performance achievement award during the study period. Patients arriving at those hospitals ≤2 hours after stroke onset were more likely to receive IV tPA after the hospital had received an award (32% vs. 20%, P<0.001). When award status was added to the multivariable model, it was independently associated with IV tPA use (adjusted OR

1.7, 95% CI 1.3-2.1) and calendar year was no longer significant (adjusted OR=1.01, 95%CI 0.9-1.1). **Conclusions:** In this nearly complete capture of statewide data, rates of IV tPA improved significantly in Massachusetts over the first 4 years of the state program. Hospitals that additionally earned a GWTG-S award during the program had higher IV tPA rates after award recognition; the post-award increase in IV tPA use at these hospitals accounted for much of the overall statewide increase in IV tPA per year. Further studies are needed to confirm that treatment disparities exist for older AIS patients, and to verify that hospital participation in local and national QI initiatives (such as GWTG-S, Joint Commission or state-based programs like the Coverdell Registry) is associated with increased rates of thrombolysis over and above secular trends.

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Th MP71

Age Stratification And Clinical Outcome Following tPA

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Background: Data suggests that elderly patients may not have the same benefit from tPA treatment compared to younger individuals. In addition tPA treatment is not readily administered to stroke patients > 80 y/o in some countries. **Objective:** To evaluate the clinical out come and disposition of patients treated with tPA stratified according to age. **Methods:** Retrospective chart review and analysis of 139 tPA cases at our hospital between 2009 - 2010. Patients were stratified into 3 age groups; < 60 (group 1), 60-80 (group 2), and > 80 (group 3). Stroke severity (NIHSS <7 mild, 7-14 moderate and >14 severe), door to needle time, clinical outcome (mRS 0-2 mild, 3-4, moderate, 5, severe and 6, dead) and post-hospitalization disposition [home, rehabilitation, or nursing home (NH)] was documented. **Results:** There were 27 (19%), 69 (49%) and 43 (31%) patients in groups 1,2 and 3 respectively. Admission stroke severity was: Group 1, mild 9/27 (33%), moderate 13/27 (48%) and severe 5/27 (18%); group 2, mild 18/69 (26%) moderate, 25/69 (36%) and severe 26/69 (37.6%); group 3, mild 6/43 (14%) moderate 20/43 (46%) and 17/43(39%) severe. Average door to needle time for tPA in each group was 90 min (group 1), 84 min (group 2) and 85 mins (group 3). While there were more deaths in the > 80 age group (28%) compared to the 60-80 (16%) and the < 60 (11%) age groups, these were not statistically significant. Similarly, there was no statistically significant difference in patient disposition (home vs rehab plus NH) among the survivors in the 3 groups. There was however a significant difference in clinical outcome (mRS, 0-2) for those < 60 vs >80 (p = 0.0059), but no significant difference in mild clinical outcome for 60-80 vs > 80 y/o (p = 0.2245). **Conclusions:** Compared to patients in the 60 - 80 age group there was no statistically significant difference in favorable clinical outcome, death or discharge disposition for elderly patients > 80 y/o treated with tPA.

Age	NIHSS at admission			mRS at discharge				Discharge Disposition		
	<7	7-14	>14	0-2	3-4	5	6	Home	Rehab	N-H
<60	9/27	13/27	5/27	17/27	5/27	2/27	3/27	16/24	7/24	1/24
60-80	18/69	25/69	26/69	28/69	24/69	6/69	11/69	31/58	21/58	6/58
>80	6/43	20/43	17/43	12/43	14/43	5/43	12/43	13/31	12/31	6/31

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Th MP72

Effect of Weekend Compared to Weekday Stroke Admission on Thrombolytic Use, In-Hospital Mortality, Discharge Disposition, Hospital Charges, and Length of Stay in the Nationwide Inpatient Sample Database: 2002-2007

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Background and Purpose: A stroke "weekend effect" on mortality has been demonstrated in other countries, with a possible slight effect in the United States. We studied stroke patients in the Nationwide Inpatient Sample (NIS) Database for a weekend effect on thrombolytic use, in-hospital mortality, discharge disposition, hospital charges, and length of stay. **Methods:** The NIS 2002-2007 was searched for all ER admissions for ICD-9 codes corresponding to ischemic stroke. Generalized estimated equations (GEE) for generalized linear models were performed, adjusting for gender, age, race, season, median income level, payer, comorbidity score, hospital region, hospital location, teaching status, bed size, and hospital annual stroke case volume to compare weekend versus weekday stroke admission incidence of thrombolytic use, in-hospital mortality, discharge disposition, hospital charges, and length of stay. The same analysis was performed using the ICD-9 codes for ischemic stroke AND transient cerebral ischemia to check internal validity for coding irregularities that may occur in differentiating stroke from transient ischemic attack. **Results:** There were 599,087 emergency room (ER) admissions for ischemic stroke: 159,906 weekend admissions and 439,181 weekday admissions. GEE For generalized linear model analysis was performed and demonstrated weekend compared to weekday stroke patients were more likely to receive thrombolytics (Odds Ratio=1.114; 95% CI=1.039 - 1.194; P=0.003); incur slightly higher total hospital charges (Effect Ratio=1.011; 95% CI=1.006 - 1.017; P<0.001); and have slightly longer lengths of stay (Effect Ratio=1.021; 95% CI=1.015-1.027.; P<0.001). There was no difference in in-hospital mortality or discharge disposition. **Conclusions:** There is a stroke weekend effect on thrombolytic use, and a slight effect on total hospital charges and length of stay, but no difference in in-hospital mortality or discharge disposition.

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Th MP73

Withdrawal of Antithrombotic Medication is Associated with More Severe Strokes at Baseline and Higher Mortality at 1-year

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Objectives: To investigate the relationship of antithrombotic use and withdrawal to baseline clinical characterstics and outcome in patients with ischemic stroke. **Methods:** Patient records from the population-based 2005 Greater Cincinnati / Northern Kentucky Stroke Study were reviewed to identify cases of ischemic strokes and determine the baseline clinical characteristics and outcome in three groups : 1) patients who had not taken any antithrombotic medication within 60 days of onset (Not on AT), 2) patients on antithrombotic medication at onset (On AT), and 3) patients who had withdrawal of antithrombotic medication (warfarin or any antiplatelet agent) within 60 days of onset (Stopped AT). **Results:** There were 2,255 ischemic strokes in 2142 subjects in the population for calendar year 2005, of which 1,750 (77.6%) were first-ever and 505 recurrent (22.4%). Of the 2142 stroke subjects, there were 116 (5.1%) in the Stopped AT Group, 1026 in the On AT group, and 1000 in the Not on AT Group. Of the 116 in the Stopped AT group, 50% had a stroke after stoppage of an anticoagulant and the remainder after stoppage of an antiplatelet agent. As compared to the On AT group, the Stopped AT group was more likely to have atrial fibrillation (41.4% vs. 22.1%), to be male (59.5% vs. 44.1%), have a larger baseline NIHSSS (7.4 ± 8.0 vs. 6.1 ± 6.9), and to be dead at one year (41.4% vs. 27.6%, Table 1). The Not on AT group was younger, more likely to be black, uninsured, and smokers with less prevalence of other stroke risk factors. **Conclusions:** Withdrawal of antithrombotic medication is associated with baseline atrial fibrillation, more severe strokes, and worse outcomes. Decreasing the frequency and poor outcome associated with withdrawal of antithrombotic medication is an important area for future study.

Table 1: Comparisons three groups of ischemic stroke subjects: Not on AT ≤ 60 days, on AT at time of stroke, stoppage of AT within 60 days of stroke.

	Not on AT medication ≤ 60 days N =1,000	On AT at time of stroke N =1,026	Stopped AT ≤ 60 days N =116	P value, 3-group comparison	P value, "On AT" vs. "Stopped AT ≤ 60 days"
Age in years (mean ± SD)	67.4 ± 15.6	73.4 ± 12.8	72.4 ± 10.9	< .0001	.44
Female (%)	55.6	55.9	40.5	.0057	.0022
Black (%)	25.0	18.2	13.8	.0001	.30
Atrial fibrillation (%)	8.7	22.1	41.4	< .0001	< .0001
Hypertension (%)	71.2	86.1	86.2	< .0001	1.00
Diabetes (%)	28.8	37.3	42.6	< .0001	.27
Current smoker (%)	32.2	19.8	22.5	< .0001	.53
History of MI (%)	6.5	18.8	19.8	< .0001	.80
Baseline NIHSS (mean ± SD)	6.0 ± 7.0	6.1 ± 6.9	7.4 ± 8.0	.109	.032
Pre-Stroke Rankin (median)	1	2	2	< .0001	.70
No medical insurance (%)	8.0	2.1	2.7	< .0001	.73
Discharge Rankin (median)	3	3	4	.0070	.025
1-Year Mortality (%)	24.4	27.6	41.4	.0004	.0025

Note: N's denote numbers of subjects. Subjects with more than one stroke during the study period are counted only once.

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Th MP74

Local Hospital Networks for Clinical Trials in Stroke

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Background: Clinical trials of stroke therapy have been hampered by slow rates of enrollment. PURPOSE. The purpose of this research was to validate a previously-

developed model for accelerating enrollment in clinical trials. The model uses a highly-coordinated, geographically-localized, multi-institution strategy for participant identification, screening, and enrollment. Methods: Among 70 US investigators participating in an NIH-funded trial of stroke prevention, five were invited to develop Local Identification and Outreach Networks (LIONs). The networks were based on a recently described model. Each LION comprised a coordinating center servicing multiple hospitals. Hospitals provided the names of patients with stroke or TIA to researchers at the coordinating center who initiated contact; patients were offered home visits for consent and randomization. Outcomes of the validation study were feasibility, enrollment, data quality and cost. **Results:** Five LIONs varied in size from 2 to 8 hospitals. All 24 hospitals we approached in the five sites agreed to participate. The average monthly rate of enrollment at the five research sites increased from 1.4 participants to 3.5 after expanding from a single institution model to the LION format (mean change=2.1, range 0.9-3.7). Monthly performance improved over time. Data quality was similar for LION and non-LION sites, except for drug adherence which was lower at LION sites. The average cost to randomize and follow one participant during the study interval was 2.5 times the cost under the per-patient, cost-reimbursement strategy at non-LION sites. The cost ratio declined from 3.4 in year one to 1.8 in year two. LIMITATIONS. The LION strategy requires unprecedented collaboration and trust among institutions. Applicability beyond stroke requires confirmation. **Conclusion:** LIONs are a practical, reproducible method to increase enrollment in stroke trial research. Twelve months were required for the average site to reach its potential. The per-participant cost at LION sites was higher than conventional sites, but declined over time.

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Th MP75

Cilostazol Surpasses Aspirin in Secondary Stroke Prevention: Combined Analysis of Randomized Clinical Trials, CSPS II and CASISP

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Objectives: The recent result of CSPS II showed superior efficacy of cilostazol versus aspirin in secondary stroke prevention. We performed a combined analysis of CSPS II conducted in Japan and CASISP in China, comparative trials of cilostazol and aspirin in secondary stroke prevention, to determine efficacy of cilostazol versus aspirin in a larger population with greater statistical power, and to examine differences in the main outcome and backgrounds of the two trials. **Methods:** Combined analysis of CASISP (n=719) and CSPS II (n=2672) data, involving 3391 patients (6907 person-years), was performed with the primary endpoint of first occurrence of stroke (cerebral infarction, cerebral hemorrhage, and subarachnoid hemorrhage) and secondary endpoints of: cerebral infarction; intracranial hemorrhage (cerebral hemorrhage, subarachnoid hemorrhage); and a cluster including stroke, TIA, MI and angina pectoris, both in the total population and in subgroups by stroke subtypes. Differences in the main outcome and patient characteristics between the two trials were also examined. **Results:** Primary endpoint rates were 2.82% per person/year in the cilostazol group and 3.89% in the aspirin group (p=0.0144). There were no significant differences for rates of cerebral infarction (p=0.3100) or cluster endpoint (p=0.0715) between cilostazol and aspirin. Cilostazol was significantly better than aspirin for preventing intracranial hemorrhage in the total population (p=0.0006), particularly in subgroup with lacunar infarction (p=0.0004). Examination of the patient backgrounds revealed that CSPS II included significantly higher rates of patients older than 65 years and patients with smoking/drinking habits, diabetes, hyperlipidemia, and hypertension, but not patients with BMI 25 or higher versus CASISP. As for outcome, rates of the primary endpoint tended to be higher in CASISP than CSPS II. **Conclusions:** Analyses of combined results confirmed that cilostazol is superior to aspirin in preventing stroke as well as intracranial hemorrhage especially in patients with lacunar infarction. CSPS II enrolled patients with higher risk versus CASISP, which might reflect more westernized life style in Japan versus China, however lower tendency of primary endpoint was seen, which might be attributable to more intensive control of risk factors in CSPS II versus CASISP.

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Th MP76

Angiotensin Converting Enzyme Inhibitors or Angiotensin Receptor Blockers Reduce Future Vascular Risk in Persons with a History of Stroke: A Meta-Analysis

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Background: Randomized clinical trials have shown that thiazide-based regimens reduce vascular risk in persons with known stroke. Although presumed efficacious, the impact of non-diuretic-based antihypertensives on vascular outcomes after stroke has been less well studied and is not convincingly proven. Specifically the totality of evidence regarding efficacy of renin angiotensin system (RAS) modulators in individuals with prior stroke is unclear. We assessed the efficacy of RAS modulators in persons with a history of stroke by conducting a systematic review and meta-analysis. **Methods:** Systematic literature search was performed. Inclusion criteria were 1) a randomized controlled trial; 2) participants with stroke history; 3) angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARB) as mandatory therapy in the active treatment group; 4) trials reporting cardiovascular events or just recurrent stroke as outcomes; 5) follow-up duration of at least 6 months. Studies were excluded if 1) mandatory ACE inhibitor or ARB used in control group; 2) additional treatment besides ACE inhibitor or ARB used in active group. **Results:** The search identified 7 randomized controlled trials comprising 28,805 participants with a history of stroke. Across all trials, RAS modulator therapy reduced cardiovascular events (relative risk 0.91, 95% confidence interval 0.86 to 0.96, P<0.001) (Fig 1). Across 6 trials with 25,791 participants with recurrent stroke reported as an endpoint, RAS modulator therapy marginally reduced stroke (relative risk 0.93, 95% CI confidence interval 0.86 to 1.00, P=0.05) (Fig 2). Heterogeneity existed between estimates of cardiovascular events (p<0.01, I^2 =65%) but not estimates of recurrent stroke (P=0.46, I^2 =0%). **Conclusions:** ACE inhibitor or ARB therapy modestly reduces the risk of future cardiovascular events in persons with a history of stroke. ACE inhibitor or ARB could be considered in patients with a history of stroke as add-on therapy, or in thiazide-intolerant patients.

Fig 1. Cardiovascular event

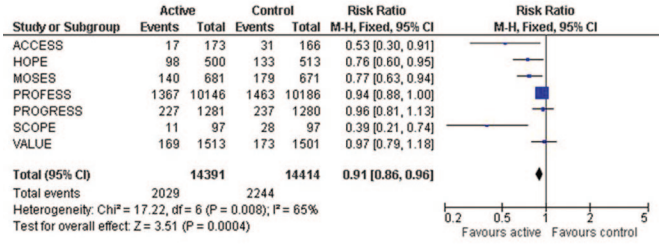
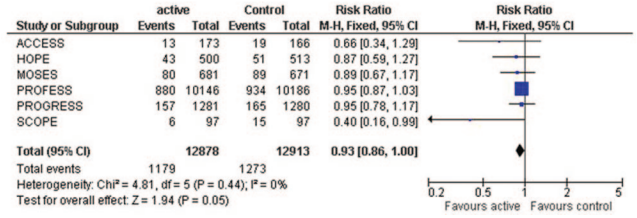


Fig 2. Recurrent stroke



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Th MP77

Small Vessel Disease As A Multisystem Disorder: Association Of Cerebral Microbleeds With Renal Impairment In A Cross-sectional, Hospital-based Study

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Objectives: In view of the close similarity between the vasculature of the brain and the kidneys, microvascular pathological changes in one organ could reflect or predict similar changes in the other, with relevance for vascular prevention. Cerebral microbleeds (CMBs) are a new MRI marker for small vessel disease in the brain, with potentially important diagnostic and clinical implications. We investigated the relationship between CMBs and renal impairment in a cross-sectional, hospital-based, cohort study. **Methods:** We studied consecutive patients referred to our specialist stroke service (stroke unit and associated neurovascular clinics). Patients with complete medical records, a satisfactory MRI study including T_2*-weighted sequence, and renal function tests (<4 weeks from the time of MRI) were included. We examined the MRI scans for the presence and number of CMBs and the presence of white matter changes (WMC) using validated scales, and estimated the glomerular filtration rate (eGFR) using the Modification of Diet in Renal Disease (MDRD) formula. Predictors of microbleeds presence in the brain were tested using regression analyses. **Findings:** One hundred and ninety-six patients were included, with a median age of 68.0 years. The prevalence of CMBs in the cohort was 18.9%. In univariate analysis, the only factor associated with the presence of CMBs was mean total WMC score (OR 1.09, 95%CI 1.02-1.17, p=0.009). Multivariate logistic regression analysis showed that for every unit decrease in eGFR, the odds of having one or more CMBs increased by 3.1% (OR 0.97, 95% CI=0.94-0.99, p=0.017), and this was independent of the severity of WMC. **Conclusions:** In this stroke cohort, the presence of CMBs, a marker of small vessel disease, is associated with impaired renal function as measured by the glomerular filtration rate. Our findings provide further evidence that cerebral small vessel disease may be part of a systemic microangiopathic disorder. Optimal prevention

and treatment of clinically silent chronic kidney disease may help to prevent the consequences of cerebral small vessel damage, including CMBs.

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Th MP79

The ALISAH Study: A Dose Escalation And Safety Study Of 25% Human Albumin Therapy In Subarachnoid Hemorrhage - Safety Results And Physiologic Response

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Background and Purpose: Several studies have suggested that 25% human albumin (HA) confers neuroprotection. We investigated the safety and tolerability of this therapy in patients with aneurismal subarachnoid hemorrhage (aSAH). **Methods:** The ALISAH (*Al*bumin *i*n *S*ubarachnoid *H*emorrhage) Clinical Trial was a multi-center, prospective, open-label, dose-escalation study. Subjects with aSAH (WFNS Scale I-III) received a 3-hour infusion of HA daily for 7 days beginning within 72 hours of symptom onset and after aneurysm treatment. Four successive HA dose tiers with 20 subjects each were planned ranging from 0.625 to 2.5 g/kg/day. Neurologic and cardiac function was sequentially monitored. The main safety outcome was severe or life-threatening heart failure up to 48 hours after treatment infusion. At 3 months the Glasgow Outcome Scale, Barthel Index, modified Rankin Scale, NIH Stroke Scale, and Stroke Impact Scale were measured. **Results:** Forty-seven subjects (mean age, 51 years) received HA at 2.2 +/- 0.7 days after aSAH onset (mean +/- standard deviation). Blood pressure increased after the first day of treatment and remained elevated thereafter. Serum osmolarity and creatinine were unaltered by HA treatment. Dose-related increases in plasma albumin and hemodilution were maximal at day 3 and were present 72 hours after termination of treatment. Heart failure to any degree requiring medical management was experienced by eleven patients (23%): 2 in dose tier 1 (0.625 g/kg); 3 in dose tier 2 (1.25 g/kg); and 6 in dose tier 3 (1.875 g/kg) with 2 severe or life-threatening events probably related to HA. Because of our pre-specified stopping rule the investigators and the DSMB agreed to terminate the study after 7 patients were enrolled in dosage tier 3. **Conclusion:** The ALISAH trial found that HA in doses ranging up to 1.25 g/kg/day x 7 days was tolerated by patients with aSAH without major dose-limiting complications. Because of the complexity and the amount of data a companion abstract presents neurologic outcome data and treatment effect analysis in these subjects.

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Th MP80

Elevated blood TNF-alpha and IL-6 are Associated with Poor 3-month Outcome following Subarachnoid Hemorrhage

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Background: Subarachnoid Hemorrhage (SAH) affects over 30,000 Americans per year and leaves over 50% of survivors with significant disability. Recent studies suggest SAH is associated with an inflammatory response which may mediate vasospasm and affect outcome. We hypothesize blood TNF-alpha and IL-6 levels are associated with vasospasm and SAH outcome, making them potential prognostic molecular biomarkers. **Methods:** We prospectively enroll consecutive SAH subjects, bank blood and CSF samples on post SAH days 0-3, 4-5, 6-7, and 10-14, and evaluate their 3-month modified Rankins score (mRS) via telephone follow-up. Angiographic vasospasm (VSP) is defined as $>$ 50% reduction in vessel caliber on angiography. Poor outcome is defined as mRS $>$ 2. We compared blood TNF-alpha and IL-6 levels by ELISA on post SAH days 0-3, 4-5, 6-7, and 10-14 in 32 SAH subjects with (n=17) and without (n=15) VSP and subjects with (n=22) and without (n=10) poor functional outcome at 3 months. **Results:** Poor outcome is associated with elevated mean TNF-alpha ($p=0.0005$) and IL-6 ($p=0.01$) averaged across all time points. Elevated TNF-alpha ($p<0.0001$) and IL-6 ($p=0.004$) on post SAH days 0-3 were most strongly associated with poor 3-month SAH outcome (Figure 1). After adjusting for SAH clinical severity (Hunt and Hess grade), elevated blood TNF-alpha ($p=0.003$) and IL-6 ($p=0.02$) remain independently associated with poor outcome at 3 months in a logistic regression model. Blood TNF-alpha and IL-6 levels are not associated with VSP at any time point. **Conclusion:** Elevated blood TNF-alpha and IL-6 levels on post SAH days 0-3, 4-5, 6-7, and 10-14 are strongly and independently associated with 3-month SAH outcome and may be potential predictive biomarkers for SAH outcome. Differential associations between TNF-alpha and IL-6 with respect to VSP and functional outcome suggest these inflammatory cytokines may play a divergent role in SAH-related pathogenesis. Further studies in larger cohorts are necessary to determine the role of TNF-alpha and IL-6 in SAH clinical outcome.

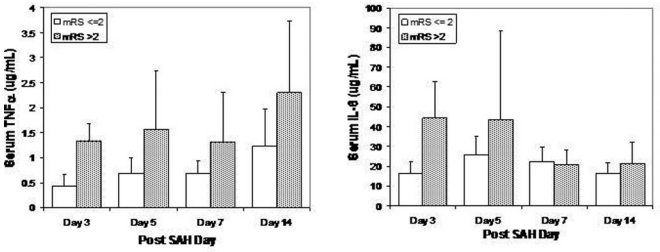

Figure 1: Blood TNF-alpha and IL-6 and 3-month Functional Outcome following SAH.

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Th MP81

Plasma-type gelsolin (pGSN) is reduced in Human Blood and Cerebrospinal Fluid following Subarachnoid Hemorrhage

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Background: Subarachnoid Hemorrhage (SAH) causes 27% of stroke-related potential life-years lost below age 65 and leaves over 50% of survivors with significant disability. Recent studies suggest SAH is associated with acute systemic inflammatory responses. A substrate of metalloproteinases (MMP), pGSN may play an important role in modulating actin-mediated inflammation and cell injury. Clinically, blood pGSN predicts mortality from critical illness. We previously found pGSN in plasma proteomic screening of patients with neurovascular injuries. In this study, we hypothesize pGSN is reduced in blood and CSF following SAH, and explore MMP activity as potential etiology for pGSN reduction. **Methods:** We prospectively enroll consecutive SAH subjects and bank blood and CSF samples on post SAH days 0-3, 4-5, 6-7, and 10-14. Controls subjects are consecutive non-vascular patients who undergo elective lumbar-drain trial. Blood and CSF in control subjects are banked on days 0-3 post lumbar drain placement. We compared blood and CSF pGSN levels in 30 SAH subjects with 20 controls and performed pGSN ELISA, pGSN Western blot, and MMP zymography. **Results:** Mean blood pGSN was higher in control subjects compared to SAH subjects at all time points ($p<0.0001$). Median CSF pGSN was lower in SAH compared with non-SAH controls ($p=0.0009$), and this effect was strongest on post SAH day 4-5 ($p=0.02$). Western blot on selected SAH and control subjects demonstrated that the SAH subjects had novel bands at 50 kD, which represents potentially cleaved pGSN fragments. Gelatin zymography in these subjects showed CSF MMP-9 activity was higher in SAH compared with controls (Figure 1), and a trend towards higher CSF MMP-9 activity with lower CSF pGSN ($r2=0.92$; $p=0.18$). **Conclusion:** SAH is associated with reduced blood and CSF pGSN compared with normal control subjects. In SAH subjects, lower CSF pGSN levels correlate with higher MMP-9 activity, suggesting MMP-9 may cleave pGSN. Novel cleaved pGSN fragments are present in CSF of SAH subjects but not control subjects on Western blot. The molecular weight of these fragments corresponds to cleaved product we previously reported in the plasma of stroke patients. To our knowledge, this is the first report of pGSN fragments in CSF of SAH. From these preliminary findings, we hypothesize that pGSN reduction in SAH may be secondary to cleavage by MMP-9. Further studies of total pGSN, pGSN cleaved products, and MMP-9 activities in blood and CSF in larger patient cohorts with long-term outcome data are needed to understand the mechanism of pGSN in SAH.

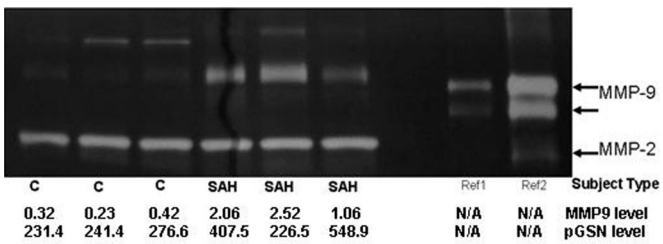

Figure 1: MMP-9 Zymography and pGSN Levels in CSF of SAH and Control Subjects.

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Th MP82

An Admission Prediction Model for Cerebral Vasospasm in Patients with Aneurysmal Subarachnoid Hemorrhage

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Introduction: Cerebral vasospasm (VSP) is a leading factor for morbidity and mortality in patients with aneurysmal subarachnoid hemorrhage (SAH). Well-defined risk factors delineate the likelihood of VSP; however, there is a paucity of available prediction models, which, in contrast, allow cumulative integration of each individual SAH patient's clinical, laboratory, and imaging data to produce a "personalized" VSP risk profile. Method A retrospective analysis of a prospective aSAH database was performed (admission days 0-3). Data included: A) clinical profile: age and gender, median BP and ICP; Hunt and Hess grade (HHG), conventional VSP risk factors (HTN, DM, smoking, ethanol intake, antiplatelet therapy, illicit drug use); B) imaging profile: initial CT (Fisher grade [FG]); CTA; CTP (quantitative CBF, CBV, MTT maps (mean days 1.5±1); location, size, multiplicity of aneurysm; TCD (mean days 2.5±0.7); C) laboratory profile: white and red cell blood counts; serum Na, K, Ca, Mg and albumin concentrations. Multivariate linear regression analysis was performed to create the VSP prediction model. **Results:** Of 75 patients the mean HHG was 2.25+1.03 and FG 2.89+0.78. Angiographic VSP occurred in 35% (26/75) and clinical vasospasm 31% (23/75) at a mean of 7.5±2.2 and 5.8±2.1, respectively. Of 31 patients diagnosed by TCD with flow abnormalities during days 1-3, 42% (13) developed clinical and 48% (15) angiographic VSP. Of 25 patients with CTP abnormalities during days 1-3, 64% (16) developed clinical/angiographic VSP. Notably, the following test showed a strong correlation with VSP development: FG ($p=0.006$), CTP deficit ($p<0.00$), and abnormal TCD ($p=0.03$). No other admission profiles showed a VSP correlation. The overall value to predict VSP was R2=0.363 using (0.484xCTP deficit)+(0.227xTCD abnormality)+(0.047xFG)-0.825. The likelihood ranged for patients with both normal CTP and TCD and a FG of 1 (best scenario) was -0.067, while those with both abnormal CTP and TCD and a FG of 4 (worst scenario) had 0.785. **Conclusion:** Using the presented prediction model and the results of 3 admission factors (CT Perfusion, TCD, and Fisher grade) we were able to delineate a range of likelihoods for developing VSP after aneurysmal SAH. This model will help to risk stratify SAH patients for VSP early on in their disease course.

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Th MP83

Symptomatic Large Vessel Vasospasm after Aneurysmal Subarachnoid Hemorrhage is Associated with Low Pulsatility Index on Transcranial Doppler

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Background: Vasospasm occurs in 30-70% of patients with aneurysmal subarachnoid hemorrhage (aSAH) and can result in severe disability or death. Elevated mean flow velocity (MFV) on Transcranial Doppler (TCD) predicts vasospasm of the large intracranial arteries, although sensitivity and specificity are variable. The Pulsatility Index (PI), derived from the spectral doppler, is defined as- (Peak Systolic Velocity - End Diastolic Velocity) / MFV and is a measure of distal vascular resistance. Distal vascular resistance, and therefore the PI, may be low when there is compensatory distal vasodilatation following hypoperfusion caused by large vessel vasospasm. Low PI may predict critical lower limb ischemia in the setting of peripheral vascular disease. **Objective:** To study the predictive value of low Pulsatility Index for symptomatic large vessel vasospasm (SLVVS) after aSAH. **Method:** Medical records of patients admitted with aSAH between January 2007 and April 2009 were reviewed. Patients with poor acoustic windows and those who died within 72 hours were excluded. TCD was performed daily through transtemporal windows while the patient was in the ICU. Patients who suffered acute neurological decline underwent non-contrast CT followed by catheter angiography or CT angiography when no other cause was readily identified. **Results:** There were 79 patients with aSAH admitted in the study period. 21 of 79 (26.6%) had neurological decline associated with moderate or severe large vessel vasospasm on angiography. Median lowest recorded PI was 0.65 (95% CI 0.60-0.69), range 0.41-1.09. An ROC curve of lowest recorded PI in predicting SLVVS revealed an optimal PI of 0.58- sensitivity 66.67% (95% CI 43-85.4%); specificity 84.48% (72.6-92.7%), Area Under Curve 0.725; P(Area=0.5)=0.0045. Odds Ratio for PI<0.6 in predicting SLVVS was 8.54 (95% CI 2.79-26.19, $p=0.0002$). All values of PI<0.6 in patients with SLVVS were recorded in vessels seen to be moderate or severe vasospasm on angiography. An ROC curve of highest recorded MFV in predicting SLVVS revealed optimal MFV of 139cm/s- sensitivity 85.71% (63.7-97.0%); specificity 70.69% (57.3-81.9%), Area Under Curve 0.774; p(Area=0.5) <0.0001. Odds Ratio for MFV> 140cm/s in predicting SLVVS was 14.47 (95% CI 3.76-55.63, $p=0.0001$). Regression analysis between PI and MFV revealed a coefficient of determination $R^2=0.32$, residual standard deviation 0.14. The equation was y = 0.88 + -0.0014 x; coefficient of the slope 0.0014 (95% CI 0.0018-0.0009), standard error 0.0002, P<0.0001. **Conclusion:** Pulsatility Index <0.6 on TCD, in addition to MFV>140cm/s, predicts symptomatic large vessel vasospasm after aneurysmal SAH. This may reflect compensatory distal vasodilatation in the setting of ischemia. The presence of low Pulsatility Index on Transcranial Doppler should increase the level of concern for impending symptomatic ischemia from vasospasm after aSAH.

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Th MP84

Diagnostic Yield of CT and MR Angiography in Patients with Catheter Angiography Negative Subarachnoid Hemorrhage

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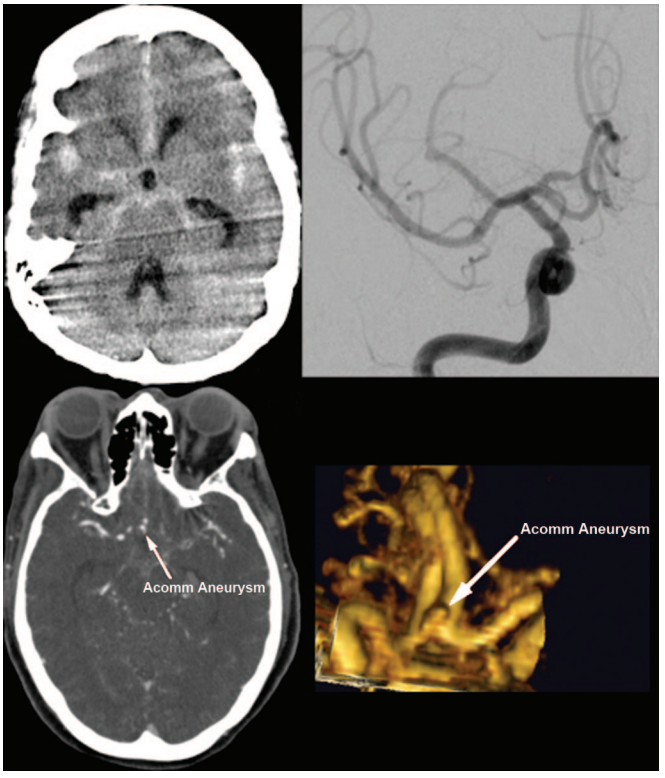
Purpose: To determine the yield of CT and MR angiography for the detection of causative cerebral aneurysms in patients with subarachnoid hemorrhage (SAH) who have a negative initial catheter angiogram. **Methods:** From January 1st, 2005, until July 31st, 2010, we instituted a prospective protocol in which patients who presented with SAH documented by non-contrast CT (NCCT) or cerebrospinal fluid (CSF) xanthochromia and had a negative initial catheter angiogram were also evaluated with CT and MR angiography to assess for causative cerebral aneurysms. Two neuroradiologists evaluated the NCCTs to determine the pattern of SAH (perimesencephalic or not) and the CT and MR angiograms (CTA, MRA) to assess for the presence of causative cerebral aneurysms. Differences in reader interpretation were resolved by consensus. **Results:** 76 patients were included in our study, with a mean age of 53.4 years (median 54 years, range 19-88 years). 49 patients were female (64.5%) and 27 male (35.5%). 72 patients had SAH by NCCT (94.7%) and 4 patients had CSF xanthochromia (5.3%). Among the former, 29 patients had perimesencephalic SAH (40.3%) and 43 had non-perimesencephalic SAH (59.7%, kappa 0.91, 95% CI 0.89-0.93). CTAs were performed in all patients and MRAs were performed in 71 patients (93.4%). Mean time interval between the initial catheter angiogram and the CTA was 1.05 days (median 1 day, range 0-7 days), and the MRA was 1.28 days (median 1 day, range 0-5 days). CT angiography demonstrated a causative cerebral aneurysm in 4 patients (yield of 5.3%, kappa statistic 0.88, 95% CI 0.86-0.9), all of which had non-perimesencephalic SAH (yield of 9.3%). Aneurysm locations were 1 anterior communicating artery (Figure 1), 1 posterior communicating artery, 1 right posterior inferior cerebellar artery, and 1 distal left posterior cerebral artery. Mean aneurysm size was 2.6mm (median 2.45mm, range 2.1-3.3mm). Two of the aneurysms underwent surgical clipping and two endovascular coil embolization. MR angiography only showed 1 of these aneurysms because 2 patients underwent treatment immediately after the CTA and in 1 patient the field of view did not include the aneurysm. No causative aneurysms were found in patients with perimesencephalic SAH or CSF xanthochromia. In 1 patient the CTA and MRA demonstrated a 2mm anterior communicating artery aneurysm that was found to be a fenestration in a repeat catheter angiogram. **Conclusion:** CT angiography is a valuable adjunct in the evaluation of patients with non-perimesencephalic SAH who have a negative initial catheter angiogram, demonstrating a causative cerebral aneurysm in 9.3% of patients.



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Th MP85

Patterns of Cerebral Amyloid Binding in Acute Ischemic Stroke

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Background: Dementia affects survivors of ischemic stroke at a greater rate than the general population, suggesting interaction between vascular lesions and neurodegenerative disease. If post-stroke dementia (PSD) reflects unmasking of preclinical Alzheimer's disease (AD), it might be predicted by increased binding of beta-amyloid (Abeta) in a typical AD pattern. Alternatively, other patterns of Abeta binding, reflecting cerebral amyloid angiopathy (CAA) or ischemia-induced Abeta deposits may be important determinants of PSD. Principal component analysis (PCA) is a multivariate technique that extracts patterns explaining the variance in data and is thus an ideal tool to explore the distribution of Abeta binding after acute ischemic stroke (AIS). **Methods:** We analyzed ^{11}C-PIB PET scans from 39 cognitively normal elderly individuals with hemispheric AIS enrolled in a longitudinal study investigating the use of PIB to predict PSD. PCA was performed on the voxels in non-infarcted hemisphere (to avoid effects of reduced blood flow on PIB uptake in infarcted hemisphere) from filtered, masked images normalized to cerebellar gray matter, aligned to MRI, and co-registered to Talairach atlas space using an affine transform. Mean cortical binding potential (MCBP) values for PIB were calculated as the average of binding potentials in regions of interest drawn in prefrontal cortex, precuneus, laterotemporal cortex, and gyrus rectus, excluding areas of infarct. **Results:** ^{11}C-PIB binding was elevated (MCBP$>$0.18) in 13 (33%) individuals with AIS (age 76$\pm$8 years) compared to 90% of 21 individuals with AD (age 77$\pm$7 years, CDR 1-2) and 31% of 76 healthy controls (age 75$\pm$6 years, CDR 0). PCA showed that the first 2 eigenvectors explained 70% of the variance among AIS participants; the subsequent 3 eigenvectors accounted for the bulk of the remaining variance. Eigenvector 2 was highly correlated with MCBP (r=0.85), reflecting the binding patterns characteristic of healthy controls and AD. A third eigenvector identified a pattern of posterior cerebral uptake particularly in lateral occipital lobe in 9 participants, 5 of whom had normal MCBP. Lobar microbleeds were seen in 2 of these participants (5 in 1; 1 in the other). **Conclusion:** ^{11}C-PIB binding followed an AD pattern in one-third of elderly individuals with hemispheric AIS, a similar rate as seen in normal controls. In addition, PCA identified at least 1 other pattern of uptake in a subset of participants. This pattern of prominent posterior binding suggests CAA, though only 2 of the participants with this pattern met MRI criteria for possible or probable CAA. Longitudinal data are needed to determine whether any PIB binding pattern is predictive of PSD.

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Th MP86

Effect of Apixaban on Covert Stroke and Cognitive Function: AVERROES MRI-Brain Assessment Trial

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Covert stroke is common in patients with atrial fibrillation, proposed to occur about five-times more often than clinical stroke. Cognitive impairment is a prominent consequence of covert stroke. However, it is not known whether anticoagulant therapy prevents covert stroke to a similar extent as clinical stroke. In the AVERROES trial, we evaluated the effect of apixaban on; 1) covert stroke (MRI of brain) and; 2) cognitive function. **Methods:** The AVERROES trial compared apixaban to antiplatelet therapy for prevention of stroke in patients with atrial fibrillation who failed or were considered unsuitable for warfarin, and was recently terminated early by the DSMB because of superiority of apixaban. In the MRI study, a baseline MRI of brain has been completed (FLAIR, DWI, T1, T2 and GRE sequences) in 1,184 participants, and we measured the prevalence of cerebral infarction, white matter hyperintensities (WMH) and microbleeds (MRI Lab, Essen, Germany). Follow-up MRI scans are expected to be complete by Nov 2010. Participants underwent cognitive assessment, with modified-Montreal Cognitive Assessment (m-MoCA), Digit Symbol Substitution test and Trails Making test-B. **Results:** In the 1,184 participants who completed baseline MRI (mean age 69 years), covert infarction was recorded in 25.6% of participants. In those without a history of clinical stroke (n=1,059), covert infarction was present in 20.1%. WMH were observed in most participants (84.6%), reported as mild in 45.3%, moderate in 29.3% and severe in 10.0%. Microbleeds were recorded in 9.9% of participants. Mean m-MoCA was 9.1 (SD 2.5) in patients with covert infarct, 8.9 (SD 2.7) in patients with severe WHD and 10.1 (SD 1.9) in those without covert infarction or WMH. In Feb 2011, we will present the effect of apixaban on rates of new covert stroke and cognitive decline (compared to antiplatelet therapy) and, the prognostic importance of baseline covert ischemia and microbleeds on clinical outcomes (ischemic and hemorrhagic stroke and cognitive decline). **Conclusion:** Covert stroke is common in patients with atrial fibrillation and associated with impaired cognitive testing. AVERROES-MRI will be the first large study to determine the effectiveness of anticoagulant therapy on the incidence of covert stroke.

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Th MP87

Acute Ischemia in Left Angular Gyrus Impairs Comprehension of Syntax

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Background: Studies from chronic stroke and fMRI have emphasized the role of Broca's area (left Brodmann's area 44 and 45) in syntax processing and working memory. However, conflicting results have been reported; many patients with lesions in Broca's area have no deficits in either syntax comprehension or working memory, perhaps because they have recovered through reorganization of structure-function relationships. Additionally, it is likely that both functions rely on more widespread cortical networks. We sought to identify other regions that when damaged acutely disrupt syntax comprehension and working memory, and investigated the relationship between them. **Method:** A series of 49 patients had tests of syntax processing and working memory and MRI within 24 hours of acute ischemic left hemisphere stroke, before extensive reorganization. Language tests included sentence-picture matching and enactment of sentences with both syntactically complex and simple sentence structures, and forward and backward digit span. MRI scans were analyzed by a technician masked to language results for ischemia on DWI and/or PWI in each of 11 Brodmann's areas (BA). We identified associations between dichotomous variables using chi square tests after Bonferroni correction, evaluated differences in means between groups using ANOVA, and identified correlations between tests using Spearman's rho. **Results:** There was a strong association between ischemia in BA 4, 6, 44, and 45 and impaired working memory defined by backward digit span $\leq$2 (X^2 = 6.7 - 19.9; p$<$ 0.0001- 0.009). Patients with acute ischemia in these posterior frontal regions had significantly reduced backward digit spans (e.g. mean 1.0 vs 4.0; P$<$0.002 for BA 6) compared to patients without ischemia in these regions, but did not have significantly impaired comprehension of syntactically complex sentences. In contrast, patients with acute ischemia in left BA 39 (angular gyrus) had significantly lower backward digit span (mean 1.6 vs 3.9; p=0.008) than those without acute ischemia in BA 39, but also had significantly impaired comprehension of only syntactically complex sentences. For example, they were impaired in sentence picture matching with semantically reversible object cleft sentences (eg. " It was the niece that the father kicked") compared to patients without ischemia in BA 39 (mean 77.6% correct vs 92.8% correct; P$<$0.04). Patients with acute ischemia in BA 20, 21, 22 were impaired in understanding all sentence types (syntactically simple and complex). Forward and backward digit span were correlated (r^2=.42; P$<$.0001), but there were no significant correlations between complex sentence comprehension tests and measures of working memory. **Conclusion:** Left angular gyrus has a critical role in comprehension of syntactically complex sentences that does not appear to be explained only by its role in working memory, and needs further investigation.

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Th MP88

White Matter Hyperintensity Burden is Associated with Cognitive Decline in a Stroke-free Cohort: the Northern Manhattan Study

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Background: A heavy burden of white matter hyperintensities (WMH) is a risk factor for vascular cognitive disorders - cognitive impairment and dementia where vascular damage plays a role - but few large prospective population-based studies have used volumetric methods to examine the effect on cognitive decline. Also, many studies have been limited to non-Hispanic white participants, and the effect of WMH on cognitive decline among black and Hispanic people is not clear, even though they are at greater risk of stroke and dementia than whites. **Methods:** The Northern Manhattan Study (NOMAS) includes a stroke-free sample that underwent brain MRI. We used quantitative methods to assess WMH volume (WMHV) blind to participant characteristics and cognitive performance, and adjusted for intracranial volume (ICV) to correct for differences in head size. The modified Telephone Interview for Cognitive Status (TICS-m) has been collected annually in NOMAS. We examined cognitive change over time using mixed models, with an interaction term between quartiles of WMHV (Q4=highest, Q1=lowest and reference) and time between baseline and each subsequent TICS-m, adjusting for relevant sociodemographic and vascular risk factors. **Results:** There were 1,099 NOMAS participants with both brain MRI measures of WMHV and subsequent TICS-m assessments available (mean (SD) age 71 (8.5), 61% women, 67% Hispanic, 18% black, 15% white). The mean WMHV was 0.67% of ICV (interquartile range 0.22-0.77% ICV). There was no significant difference in baseline TICS-m scores between those in different WMHV quartiles. Examining the dose effect of WMHV on cognitive decline with Q1 as the reference, scores on the TICS-m declined in a linear fashion for Q2 (-0.07 points/year) and Q3 (-0.11 points/year) but showed a steeper decline for Q4 (-0.33 points/year), and only Q4 had significantly lower TICS-m scores over time adjusting for age, sex, race-ethnicity, education, alcohol use, physical activity, peripheral vascular disease, and systolic blood pressure (P=0.006). Examining the change in adjusted mean TICS-m scores across years of follow-up, scores of those with WMHV in Q4 declined steadily, and were significantly lower at five years (adjusted mean difference=1.6 points, P=0.0006). **Conclusions:** Despite similar baseline cognitive performance, we found that NOMAS participants with a WMH burden greater than 0.77% of ICV showed more cognitive decline than those in the lowest quartile in this multi- ethnic stroke-free community-based cohort. Prospective studies in diverse samples with more sensitive neuropsychological tests are needed to clarify the domains impacted by WMH in vascular cognitive disorders.

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Th MP89

MRI Correlates Of Vascular Cognitive Impairment: Effects Of Microbleeds, Lacunes, Cortical Infarcts, And White Matter Changes On Frontal-executive Function In A Large, Hospital-based Stroke Cohort

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Objectives: Vascular cognitive impairment (VCI) is an increasing healthcare challenge, but the underlying mechanisms remain poorly understood. VCI is characterised by frontal-executive impairment, attributed to small vessel damage. Cerebral microbleeds (CMBs) are a new MRI marker of small vessel pathology, including cerebral amyloid angiopathy (CAA). However, the functional effects of CMBs are difficult to investigate because they are associated with other cerebrovascular MRI findings, especially lacunes and white matter changes (WMC). We investigated the associations of CMBs, lacunes, territorial cortical infarcts and WMC with cognitive function in a large, hospital-based, cross-sectional study. **Methods:** Consecutive patients referred to a single hospital stroke service (1999-2007) had standardized clinical assessment, detailed neuropsychological testing and standardized MRI including FLAIR, T1, T2 and T2* gradient-echo sequences. CMBs, WMC, lacunes and territorial cortical infarcts were identified by 2 trained observers. Patients with intracerebral haemorrhage were excluded. Predictors of frontal-executive impairment were tested in logistic regression. **Findings:** Four hundred and forty-five patients were included (84 with, 361 without CMBs). Frontal-executive impairment was more common in patients with CMBs than without (36% vs 22%; p=0.012). In univariate analysis, predictors of frontal-executive impairment were: presence of strictly lobar CMBs (odds ratio [OR] 2.32, 95%CI 1.15-4.68, p=0.019) and mean WMC (OR 1.04, 95%CI 1.00-1.08, p=0.05). In multivariate analysis, presence of strictly lobar CMBs (OR 2.19, 95%CI 1.08-4.45, p=0.029) remained independent predictors of frontal-executive impairment, but not WMC. Territorial cortical infarct presence and severity of WMC predicted impairment in multiple cognitive domains. **Conclusions:** In this cohort of patients from a hospital stroke service cohort, strictly lobar CMBs were independently associated with frontal-executive impairment. Subclinical CAA may contribute to frontal-executive impairment in stroke patients. CMBs may be a useful addition to radiological criteria for VCI.

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Th MP90

Infectious Burden and cognition: The Northern Manhattan Study

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Background: A composite measure of several chronic infections (infectious burden, or IB) is associated with risk of stroke and carotid atherosclerosis in our cohort. The association of IB with cognitive impairment and dementia remains mostly unexplored, however. We hypothesized that a measure of IB associated with vascular risk would also be associated with cognition and cognitive decline in a prospective cohort study. **Methods:** Cross-sectional and prospective analyses among stroke-free community participants in the multi-ethnic Northern Manhattan Study were performed. Cognition was assessed using both the Mini Mental State Exam (MMSE) at enrolment and the modified Telephone Interview for Cognitive Status (TICS-m) during annual telephone follow up . IB was calculated based on a composite measure of serologies against microbial agents previously shown to be associated with risk of stroke and carotid plaque (i.e. Chlamydia pneumoniae, Helicobacter pylori, CMV, HSV1 and 2). Linear and logistic regression were used to measure the magnitude of association between IB and cognition after adjusting for other risk factors, and generalized estimating equation models were used to evaluate associations with TICS-m and its change over time. **Results:** Both serologies and cognitive assessments were available in 1623 participants (mean age 68.5+/-10.1 yrs, 64.9% women). Median MMSE was 27 (interquartile range (IQR) 24-29) and median TICS-m 32 (IQR 27-36). In the unadjusted model IB index was associated with MMSE and TICS-m (both P<0.0001; see table). These effects were attenuated after adjusting for demographics, and there was little change after further adjusting for vascular risk factors. The effect of IB remained significant for TICS-m (p<0.0001; see table). IB was associated with MMSE =<24 (adjusted OR 1.22, 95% confidence interval 1.03-1.45). However, IB was not associated with cognitive decline over time (p=0.07). **Conclusion:** A measure of infectious burden that is associated with vascular disease risk was independently and inversely associated with cognitive performance in this multi-ethnic cohort, though it was not associated with further cognitive decline. Past infection and associated inflammation-related vascular damage may contribute to cognitive impairment in the elderly.

Table

	Unadjusted	Adjusted for demographics*	Adjusted for demographics & risk factors**
MMSE *change per SD* in IB (p)	-0.77 (p<0.0001)	-0.16 (p=0.08)	-0.15 (p=0.11)
TICS-M *change per SD* in IB (p)	-1.89 (p<.0001)	-0.66 (p<.0001)	-0.63 (p<.0001)
MMSE≤24 *OR* (95% CI)	1.58 (1.36-1.82)	1.23 (1.04-1.45)	1.22 (1.03-1.45)

* adjusted for age, gender, race-ethnicity, insurance status, education
** adjusted for age, gender, race-ethnicity, insurance status, education, alcohol consumption, physical activity, smoking, diabetes mellitus, hypertension, coronary artery disease, and lipid lowering medication use

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Posters

W P1

Time To Recanalization And Risk Of Symptomatic Intracerebral Hemorrhage In Patients Treated With Intravenous Thrombolysis

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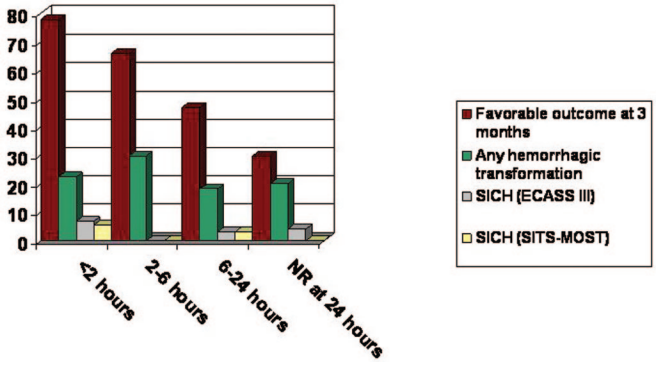
Introduction: The risk of symptomatic intracerebral hemorrhage (SICH) after intravenous thrombolysis (IVT) has been related to the persistence of arterial occlusion >2h as well as to delayed recanalization (>6h). It remains however unknown whether time to recanalization implies a progressive increase in the risk of SICH. Objetive: To study the relationship between the risk of SICH and time to recanalization evaluated by serial transcranial Dupplex monitoring within 24 hours of IVT (1, 2, 6, 12 and 24h), in a cohort of 151 patients with acute ischemic stroke due to large artery occlusion in the anterior circulation treated with i.v. alteplase. **Methods:** Patients were classified in 4 groups according to the time to complete recanalization (TIBI 4 or 5) as follows: <2h (n=58), 2-6h (n=10), 6-24h (n=33) and no recanalization (NR) at 24 hours (n=50). SICH was defined following the ECASS-2 criteria (any hemorrhagic transformation with NIHSS score worsening ≥4 points) and according to SITS-MOST criteria (parenchymal hematoma type 2 with neurologic worsening). Favorable outcome was considered when the modified Rankin score ≤2 at 3 months. **Results:** There were no differences among groups in localization of the occlusion (MCA/ICA 56/3, 10/0, 30/3, 44/6, p=0.37) or in stroke severity (median NIHSS 11 [8-18], 15 [8-19], 13 [9-17] y 16 [11-20], p=0.13), however, the patients from the NR group were significantly older than the other groups (68.7±10.4, 65.2±14.5, 64.8±12.8, 72.2±11.3, p=0.039). SICH (ECASS/SITS-MOST) was observed in 6.9%/5.2% of the patients who recanalized <2h, in 0%/0% of the patients who recanalized between 2-6h, in 3%/3% of the patients who recanalized within 6-24h and in 4%/0% of those patients who did not recanalize at 24h. The rate of favorable outcome was 78%, 66%, 47% and 30% (p<0.001). **Conclusions:** Our findings are in line with the literature showing a relationship between time to recanalization and functional outcome. Based in the results of this study, a progressive increase in the rate of SICH with time to recanalization cannot be concluded.



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W P2

Two Hour Improvement Of Patients In The NINDS t-PA Trials And Prediction Of Final Outcome

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Background: Ongoing clinical trials are using the early response to intravenous t-PA (IV t-PA) to stratify patients into endovascular therapies. Little is known about the likelihood of ultra-early recovery after IV t-PA and its correlation with final stroke outcome. Using previously unpublished data points, we investigated the likelihood of neurological improvement 2 hours after IV t-PA compared to placebo in the NINDS IV t-PA studies. **Methods:** The two NINDS t-PA studies were randomized and placebo controlled; published in 1995 and proved that IV t-PA within 3 hours after stroke improved patient outcome at 3 months. Details regarding patient baseline demographics and study methods were published elsewhere. The NINDS t-PA dataset was obtained from a publicly accessible data repository. We analyzed patients by improvement of $\geq$4 points on the NIHSS at 2 hours after study drug or placebo bolus administration; and correlated this 2 hour improvement with the likelihood of good outcome (modified Rankin Scale 0 or 1) at 3 months. We adjusted for multiple confounders, including t-PA treatment. **Results:** Two hour improvement was seen in 112/312 (35.9%) of t-PA treated patients and 71/312 (22.7%) in the placebo groups ($p<0.0001$)). Smokers ($p=0.012$) and patients treated under 90 min ($p=0.008$) were more likely, diabetics ($p=0.023$) less likely to show improvement at 2 hours. The baseline NIHSS (mean$\pm$SD) of patients with improvement was 16.1$\pm$6.5 versus 14.3$\pm$7.4 ($p=0.001$). Good outcome was achieved in 68/112 (60.7%) t-PA treated patient who had 2-hour improvement and 65/200 (32.5%) without (placebos groups 30/71 (42.3%) versus 53-241 (22.0%)). When adjusting for age, admission NIHSS, history of diabetes and t-PA treatment the odds for a good outcome in patients with 2 hours improvement was 7.69 (95% CI: 4.63, 12.76; $P<0.0001$). **Conclusion:** Early improvement was more common in t-PA treated patients compared to placebo, and was associated with good 90 day outcome. The use of early improvement after t-PA to predict final stroke outcome shows value.

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W P3

Gender and Race Interact to Influence Outcome of Ischemic Stroke After Treatment with rt-PA

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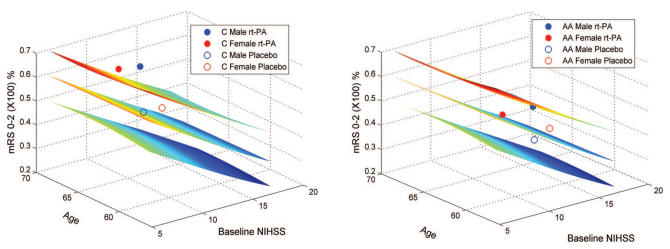
There is considerable interest in identifying differential subgroup effects of rt-PA, however often with discrepant results, especially regarding gender. Group imbalances in factors associated with outcome may contribute to discrepancies. Conventional statistical means by which imbalances are usually adjusted are based on assumptions of relationships between these factors that may not be valid. Subgroup analyses are especially vulnerable to imbalances as their numbers dwindle or issues such as recruitment bias emerge. We have developed new methods that accommodate imbalances and applied them to assess the influence of gender and race on rt-PA outcomes. **Methods:** pPREDICTS©(Mandava and Kent, Stroke 2009) is a method in which an outcome model based on placebo arms of multiple trials is generated with multi-dimensional statistical intervals to assess whether a population differs from expected outcome at similar baseline conditions (see figure; $\pm$ $p=.05$ prediction intervals bound the outcome surface). pPAIRS© (Mandava et al Stroke 2010) is an algorithm by which subjects within groups are matched in Euclidean space for baseline factors and outliers eliminated. We applied both methods to the NINDS rt-PA dataset and examined outcomes based on gender and race. **Results:** There were major imbalances among the gender and race rt-PA and placebo groups at baseline, reinforcing the need for an assumption-neutral analysis method. Predicts©: The figure shows % achieving good outcome (mRS$\leq$2) compared to baseline NIHSS and age using the entire dataset. Placebo outcomes were close to the model for all groups. In Caucasians (C), significant improvement in functional outcome was seen for both genders (Fig 1a; note both rt-PA outcomes are above the $p=.05$ interval). Overall, African Americans (AA) showed about half the degree of improvement, and this was explained by essentially no improvement for AA females, while AA males showed improvement that was only slightly below the $p=.05$ interval (Fig. 1b). Pairs©: Simultaneous matching for gender, race, baseline NIHSS, age, glucose and stroke subtype indicated that functional outcome after rt-PA in AA females was considerably worse than C females at similar baselines (e.g. median NIHSS 15.5 vs 15; mRS 0-1: 39% for AA vs 65% for C; $p=.023$) and mortality was 3X higher (27% vs 8%). **Discussion:** We were able to clarify the role of gender and race in treatment outcome that has been complicated by imbalances. We found good response to rt-PA regardless of gender in Caucasians, marginally less in AA males and poor in AA females. Factors that may explain this poor response are under investigation.



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W P4

Tissue Plasminogen Activator Use May be Associated with Increased Diffusion-Weighted Imaging Lesion Volume in Malignant Middle Cerebral Artery Syndrome

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Objective: Tissue plasminogen activator (tPA) has been shown in animal and human studies to induce blood brain barrier opening and reperfusion injury. We hypothesized that in patients with malignant middle cerebral artery syndrome (MMCA), prior use of IV tPA may contributed to infarct expansion and cerebral edema increasing the need for hemicraniectomy (HC). We compared the MRI-DWI lesion volumes in patients with MMCA that necessitated (HC) who had received IV tPA (+ tPA) within 3 hours of symptom onset versus patients who did not receive IV tPA (- tPA). **Methods:** We retrospectively reviewed our registry from 07/03 to 02/10 and identified consecutive patients diagnosed with MMCA infarctions that underwent HC and had preoperative brain MRI performed within 24 hours of admission. The DWI volumes were calculated using a validated GUI (Graphical User Interface) tool developed in MATLAB R2010a software (by one of the author -MK). Relevant clinical data was gathered by chart review. **Results:** We identified 46 patients meeting our criteria (+ tPA = 24 and - tPA = 22). Demographics and risk factors are shown in the table. The mean MRI-DWI lesion volume in the + tPA group was 213ml (SE=29) and mean MRI-DWI lesion volume in the - tPA group was 160ml (SE=29) with $p=0.10$. The + tPA group also had 5 hemorrhagic transformations compared to 0 in the - tPA group ($p=0.05$). There was no statistical difference in clinical outcome defined by discharge mRS. The rates of patients that underwent intra-arterial therapy (+ tPA = 29% vs - tPA= 27%, $p=1.00$) and recanalization (partial or complete) rates (+ tPA = 41% vs - tPA =20%, $p=0.19$) did not differ between the two groups. **Conclusion:** IV-tPA therapy may be associated with increased MRI-DWI infarct volumes in patients who develop MMCA and undergo HC. One possible reason may be that tPA increases the blood brain barrier permeability leading to increased edema formation and infarct expansion. Other potentially confounding variables such as baseline NIHSS, time to MRI and intra-arterial therapy were balanced between the two groups. However, our study is limited by its retrospective nature with a small sample number (n=46).

Table: Demographics, Risk Factors and Clinical Data

	+ tPA(n=24)	-tPA (n=22)	P Value
Mean Age (Years) ± SD	54 ± 12	51 ± 18	NS
Male Sex (%)	58	36	NS
Median Admission NIHSS (Range)	15.5 (6-25)	17 (9-40)	0.11
Atrial Fibrillation (%)	17	9	NS
Hypertension (%)	54	59	NS
Coronary Artery Disease (%)	8	14	NS
Diabetes (%)	21	27	NS
Smoking (%)	21	36	NS
Hyperlipidemia (%)	8	9	NS
Median Discharge mRs (Range)	5 (2-6)	5 (4-6)	0.45
Intra-arterial Therapy (%)	29	27	NS
Partial or Complete Recanalization* (%)	41*	20†	0.19
Mean Onset to MRI-DWI (min) ± SD	934 ± 516	970 ± 561	NS
Any Hemorrhagic Transformation (%)	21%	0%	0.05

*Data only available for 22/24 patients. †Data only available for 21/22 patients

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W P5

64 Slice Computed Tomography Perfusion (CTP) Imaging Predicts Outcome in Acute Ischemic Stroke Patients Who Receive IV Thrombolysis with rt-PA

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Background: Some MRI based studies have suggested a role of perfusion imaging in identifying candidates for thrombolysis. However, CTP is far more accessible and new techniques allow whole-brain coverage using conventional 64 slice CT, potentially improving utility. We sought to determine the feasibility and utility of routine 64 slice CTP in rt-PA treated stroke patients, and to correlate the CTP results with follow-up MRI. **Methods:** Retrospective study of all consecutively treated IV rt-PA patients between 7/2006-6/2010 who received pretreatment 64 slice CTP. Pretreatment NCCT, CTA and CTP were compared with post treatment MRI including DWI and FLAIR. Outcome was determined by pretreatment and discharge NIHSS. Safety was evaluated by symptomatic ICH (sICH) rate and mortality. **Results:** 117 patients had a pre-treatment CTP. 50% demonstrated perfusion mismatch (pre- and post-average NIHSS 10.3, 6.9); 42% no perfusion defect (NIHSS 7.5, 3.1); 8% matched defect (NIHSS 8.8, 9.9). 92 patients had a follow-up MRI; 37 (42%) patients had equal infarct size on CTP and MRI, 31 patients (34%) had smaller infarct size on MRI as compared to the area at

risk on CTP, and 24 patients (26%) had an infarct on MRI when the CTP appeared normal (8 multifocal embolic, 8 posterior fossa, and 8 subcortical infarcts). 8 patients received rt-PA at >4.5h (range 275-390 min); none had a matched perfusion defect. In these patients, follow-up MRI demonstrated reduced final infarct volume as compared to area at risk seen on CTP in 4/8 patients, and 7/8 showed improved/stable NIHSS. Overall, 2 of 117 patients had sICH, both occurring contralateral to their perfusion defects. **Conclusions:** CTP is feasible in determining eligibility for IV rt-PA. Perfusion mismatch and lack of initial perfusion defect may be predictive of improved clinical outcome post thrombolysis. Areas of CTP mismatch generally correlate with final infarct on MRI, with the exception of small lesions. CTP may be useful in expanding the time window for IV rt-PA administration, by identifying patients with high probability of improvement and low risk of bleeding complications. Further comparison of MRI and whole brain CTP images, using a larger cohort, is warranted.

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W P6

A Modified Method for Ischemic Extent Evaluation, ASPECTS+W on DWI, Accurately Predicts Intracranial Hemorrhage

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Introduction: Patients with extensive early ischemic change are at risk of intracranial hemorrhage (ICH) after iv-tPA therapy. Although Alberta Stroke Program Early CT Score (ASPECTS) being widely used for evaluation of early ischemic change on CT and diffusion weighted imaging (DWI), no comparison was made whether ASPECTS on CT or DWI could predict ICH risk regardless of iv-tPA therapy. We aimed to establish an accurate tool for ischemic extent evaluation in terms of predicting ICH in patients with acute ischemic stroke. **Methods:** In total, 164 consecutive patients with hyperacute anterior circulation ischemic stroke were enrolled. All patients underwent both MRI and CT within 3 hours of symptom onset. On DWI, presence of high intensity in the deep white matter (DWI-W) was evaluated. ASPECTS+W (ASPECTS11 on DWI) was defined as 11-point method by combination of 10 ASPECTS regions and DWI-W. The relationship between CT-ASPECTS, DWI-ASPECTS, ASPECTS+W, and ICH within the initial 36 hours was assessed. **Results:** Among all, 36 patients (22%) were treated with iv-tPA. Follow-up CT was obtained in 159 patients and 19 (12%) had ICH. Patients with development of ICH had higher NIHSS score on admission (median, 25 vs. 13, p=0.010), higher rate of tPA therapy (42% vs. 20%, p=0.041), lower grade CT-ASPECTS (median, 7 vs. 10, p=0.008), lower grade DWI-ASPECTS (median, 6 vs. 9, p=0.001), lower grade ASPECTS+W (median, 6 vs. 9, p=0.001), DWI-W lesion (74% vs. 47%, p=0.048) and ICA or M1 proximal occlusion more frequently (68% vs. 32%, p=0.004) than those without development of ICH. Multivariate logistic regression analysis demonstrated that lower ASPECTS+W (OR 0.75, 95% CI 0.58-0.96, p=0.027) and presence of iv-tPA therapy (OR 9.13, 95% CI 2.15-46.21, p=0.004) independently predicted development of ICH within the initial 36 hours, respectively. Neither CT-ASPECTS nor DWI-ASPECTS predict development of ICH on multivariate logistic regression analysis. **Conclusions:** ASPECTS+W (ASPECTS11 on DWI) is a useful tool to predict development of ICH independently from iv-tPA therapy.

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W P7

Computerized Tomography Perfusion Predictors of Clinical Outcome in Acute Ischemic Stroke Patients Treated with Intravenous Tissue Plasminogen Activator

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Objective: Computerized Tomography Perfusion (CTP) is used to assess physiological brain tissue parameters in patients with acute ischemic stroke (AIS). Its utility for patients presenting within the 3 hrs time window is unknown and questionable given possible delay of thrombolytic administration and additional exposure to radiation. We addressed whether parameters on CTP for AIS patients treated with IV t-PA within 3 hrs of onset are predictive of good or bad outcome. **Methods:** We retrospectively identified patients from our stroke registry (7/07 to 2/10) who presented with AIS and underwent CTP and then received tPA within 3 hrs of symptom onset. Patients that underwent intra-arterial therapy were excluded. A neuroradiologist blinded to outcome performed CTP measurements on a commercially available Siemens Neuro PCT workstation. Total perfusion deficit was defined as the area of infarct territory with a relative time to peak greater than 4s compared to the contralateral side (TTP). Nonviable tissue (NVT) was defined as the area of infarct territory with absolute cerebral blood volume (CBV) less than 2ml/100g. Penumbra was defined as the area of TTP minus the area of CBV. Good clinical outcome (GCO) was defined as mRS 0-2, and poor clinical outcome (PCO) was defined as mRS 5-6 at hospital discharge. Clinical perfusion mismatch (CPM) was defined as admit NIHSS ≥ 8 and NVT ≤25cm^2. **Results:** We identified 44 patients with a mean age of 68 years , median NIHSS on admission of 13 and median discharge mRS of 4. NVT was statistically different in those with poor outcome (Table 1) and a strong predictor of poor outcome when NVT was greater than 50 cm^2 (OR=6 , 95%CI: 1.05-34, p=0.044). TTP was statistically different in patients that achieved and did not achieve GCO (Table 1; OR=0.97, 95%CI: 0.95- 1, p=0.037). There was no statistical correlation between penumbra area, percentage penumbra, and CPM with GCO in univariate analysis. Younger age and lower admission NIHSS were associated with GCO and higher NIHSS was associated with PCO. Using multivariate logistic regression controlling for age and admission NIHSS, none of the CTP parameters were statistically associated with outcome measures. **Conclusion:** CTP parameters derived from commercially available software and published thresholds do not provide useful value beyond the NIHSS for predicting good outcome for AIS patients treated with IV tPA within 3 hours of onset but may be useful in predicting poor outcome if the area of non-viable tissue is greater than 50 cm^2. Our study is limited by its retrospective nature with a small sample and lack of standardization of CTP thresholds.

Table: CTP Parameters

	Baseline	Good Outcome				Poor Outcome			
Univariate Analysis	(n=44)	Yes (n=9)	No (n=35)	OR; 95% CI	P value	Yes (n=18)	No (n=26)	OR, 95% CI	P Value
Mean TTP (cm^2) ± SD	71 ± 40	45 ± 18	78 ± 41	0.97; 0.95-1	**0.037**	81 ± 39	64 ± 39	1.01; 1-1.03	0.18
Mean NVT (cm^2) (cm^2) ± SD	24 ± 25	7.5 ± 6	28 ± 26	0.91; 0.82-1	0.075	35 ± 29	16 ± 19	1.03; 1-1.06	**0.022**
Mean Penumbra (cm^2) ± SD	47 ± 29	37 ± 19	50 ± 30	.98; 0.95-1	0.24	46 ± 29	48 ± 29	1 ; 0.98-1.02	0.776
Mean Penumbra (%) ± SD	71 ± 21	81 ± 14	68 ± 21	1.04; 0.99-1.1	0.12	61 ± 24	78 ± 15	0.96; 0.92-0.99	0.011
Mean Age ± SD	68 ± 15	58 ± 16	71 ± 14	0.94; 0.89-1	**0.033**	71 ± 15	66 ± 15	1.02; 0.98-1.07	0.259
Median Admission NIHSS	13 (1-40)	5 (1-13)	16 (2-40)	0.78; 0.64-0.94	**0.01**	23 (3-40)	9 (1-22)	1.25; 1.1-1.42	**0.00**

Multivariate Analysis	Good Outcome		Poor Outcome	
	OR; 95% CI	P Value	OR; 95% CI	P Value
TTP (cm^2)	0.985; 0.95-1.02	0.355	0.99; 0.97-1.01	0.388
NVT(cm^2)	0.924; 0.82-1.04	0.209	1.01; 0.98-1.05	0.542
Penumbra (cm^2)	0.994; 0.96-1.03	0.765	0.97; 0.94-1	0.129
Penumbra (%)	1.04; 0.94-1.11	0.331	0.97; 0.93-1.01	0.145

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W P8

Is There An Association Between The First Moment Method MTT And Tmax Based Mismatch Estimates In Acute Ischemic Stroke?

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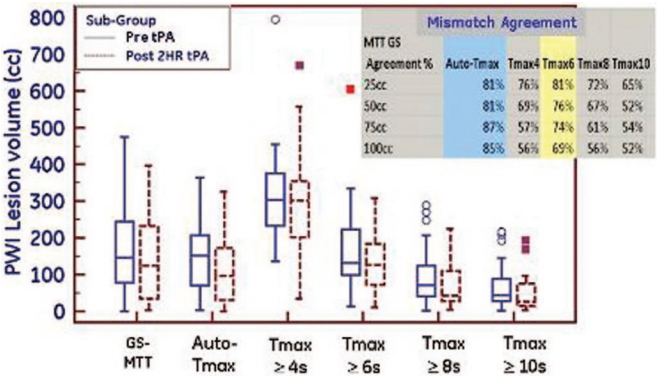
Background: In MRI of acute ischemic stroke (AIS), salvageable tissue is approximated as the diffusion (DWI) - perfusion (PWI) mismatch. The choice of PWI maps, such as first moment method MTT or deconvoluted Tmax, and segmentation approach can impact the estimated mismatch volume and thus the selection of patients for therapy. In this study, we compared the PWI lesion and mismatch volumes determined using MTT maps segmented manually, to those obtained using Tmax and an automated segmentation algorithm. The resulting binary classification of "presence=true" based on minimal cutoff volume was compared across methods. **Methods:** Twenty-seven IV-tPA treated patients having pre- and 2hr post-treatment MRI were included. A trained imaging scientist manually segmented lesions on DWI and MTT maps to form the gold standard (GS). An in-house tool, PANDA, was used to compute Tmax by AIF deconvolution and perform automated lesion segmentation and mismatch classification using: i) an automated algorithm (Auto-Tmax) based on lesion location knowledge, contralateral differences, and morphology and ii) basic thresholding Tmax maps at ≥4s, ≥6s, ≥8s and ≥10s, with no additional processing. For both approaches, CSF pixels were removed using the ADC maps generated from DWI images, to remove bias from elevated Tmax in ventricles. Patients were classified as "mismatch=true" if mismatch volume exceeded a range of cutoff values of 25cc, 50cc, 75cc, or 100cc. Agreement with GS was compared across technique and cutoff value. **Results:** For both pre and post tPA treatment MRI, Auto-Tmax and basic thresholding Tmax ≥6s were found to provide similar volume estimates to those of GS. With Auto-Tmax, the mismatch agreement with GS was stable (~83%), independent of cutoff value. For Tmax ≥6s, the best agreement was 81% at >25 cc and dropped off with increasing cutoff value. The error rates for mismatch agreement were higher with basic threshold segmentation compared to Auto-Tmax and worsened as the mismatch volume cutoff value was increased. **Conclusion:** We conclude that both Auto-Tmax and basic Tmax threshold of ≥6s provides a similar estimate of perfusion volume and mismatch detection to that of manual segmentation. However, Auto-Tmax resulted in a more robust classification independent of cutoff value, providing an automated method for mismatch detection that could eventually be used to select patients prior to therapy.



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W P9

Complete Reperfusion On MRI 5 Days After IV tPA Treatment Is Indicative Of Early Reperfusion: Evidence From The Lesion Project

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Background/Purpose: Reperfusion is the physiological goal of thrombolytic therapy. Despite different times of assessing reperfusion on post-treatment MRI, both DEFUSE (3-6 hours post-treatment) and EPITHET (3-5 days post treatment) studies reached similar positive conclusions about the effects of reperfusion in patients receiving tPA within a 3-6 hour time window. We assessed the relationship of reperfusion at 5 days to that at earlier time points in a tPA-treated cohort. **Methods:** From the NINDS Stroke Branch Registry LESION project, we selected all patients (N=62) treated with IV tPA who had (1) pre-treatment PWI data showing focal ischemia and (2) evaluable PWI studies at all of 3 follow-up time points: 2 hours, 24 hours, and 5 days post-treatment; N=62. Qualitative reads of reperfusion as recorded in the registry were used to determine whether the patients had partial or complete reperfusion relative to the pretreatment scan. The proportions of patients with complete reperfusion at 5d vs reperfusion at 2 hours and at 24 hours was compared by the McNemar test. **Results:** Median time to tPA was 154 minutes. Median times tPA to follow-up MRIs were 112 min, 23.9 hours, 4.7 days. 5 day reperfusion (accuracy= 69%) was indicative of any reperfusion at 2 hours (71%) and of complete reperfusion at 24 hours (60%), and did not differ on the McNemar test. Compared to any degree of reperfusion at 2 hours, 5 day complete reperfusion had 77% sensitivity, 50% specificity, and 79% PPV. **Conclusion:** Complete reperfusion on 5 day MRI is indicative of early reperfusion as seen 2 hours post treatment. These observations suggest that a 5 day MRI reperfusion measure is informative about 2 hour reperfusion and supports the combination of 5 day reperfusion results with those from earlier timepoints.

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W P10

Multi-modal CT: Diagnostic Yield And Changes In Management In Patients Presenting With Suspected Stroke Or Tia

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Introduction: Patients presenting emergently with suspected cerebrovascular ischemia are first screened with non-contrast head CT to rule out hemorrhage. Multi-modal CT imaging (CT perfusion, CT angiography and contrast-enhanced CT) can be obtained immediately following the non-contrast CT, in an emergent setting, or at a later time. An advantage to multi-modal CT imaging is immediate access to diagnostic information that may influence patient management in the acute setting. **Objective:** To determine the diagnostic yield of multi-modal CT imaging for patients presenting in the ED with suspected stroke or TIA and to determine changes in patient management attributable to multi-modal CT imaging. **Methods:** This is a retrospective analysis of prospectively collected data at our hospital from March through May 2010 (n=128). Patients with hemorrhagic stroke were excluded. Diagnostic yield was determined from the multi-modal CT images. Physicians were queried about changes in patient management according to pre-specified categories. Diagnostic yield for emergent conditions was defined as (a) previously unknown arterial dissection, (b) intraluminal thrombus, (c) intracranial occlusion, (d) extracranial occlusion and (e) CT perfusion assessment of tissue viability. Acute changes in management were defined as (a) decisions regarding emergent intra-arterial revascularization, (b) anticoagulation for thrombus or dissection, or (c) change in level of care (admission to an intensive care unit or step-down unit). **Results:** The prevalence of critical diagnostic yield was 24%. The total diagnostic yield for other conditions which could have been identified outside of the acute setting, such as aneurysm or extracranial stenosis, was 46.1%. Multi-modal CT led to acute changes in management in 9.4% of the total sample while 7.8% underwent a non-acute change in management (e.g. carotid revascularization, aneurysm clipping or coiling). **Conclusion:** Multi-modal CT imaging of patients with suspected cerebral ischemia has a demonstrable diagnostic yield for acute conditions and may be instrumental in patient management. Further data are needed to better identify individuals with a higher prevalence of critical diagnostic findings who would ultimately benefit from immediate multi-modal CT.

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W P11

Risk of Hemorrhage in patients on Coumadin who are treated with Tissue Plasminogen Activator for Acute Ischemic Stroke

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Background: Tissue plasminogen activator (t-PA) remains the only proven treatment for ischemic stroke but concurrent use of warfarin at the time of stroke poses a potential risk for symptomatic intracerebral hemorrhage (sICH). Few studies have addressed this risk. We studied all patients admitted to our service who were on warfarin at the time of their acute ischemic stroke and were treated with IV t-PA in order to define incidence and risk factors of sICH. **Methods:** Retrospective chart review of patients was conducted from our stroke registry from January 2003 to June 2010. We evaluated consecutive patients who received IV tPA within 0-3 hours while on warfarin. Patients who were off their warfarin were excluded. We collected demographics, National Institute of Health Stroke Scale (NIHSS) on admission, rates of symptomatic intracerebral hemorrhage (sICH), and discharge modified Rankin Scale (mRS) outcomes. **Results:** Among 61 patients, 13 patients (21%) had sICH. Comparing those patients who bled with those who did not have sICH, there were no significant INR level nor warfarin dose differences. There was no statistical difference in all BP parameters measured between the two groups. Four patients (31%) died in the hemorrhage group compared with 2 patients (5%) in the non-hemorrhage group. There was a statistical difference in mRS at discharge and mortality between the two groups. However, when corrected for baseline NIHSS and age, the ORs for either outcome were not statistically different (1.1, 95% CI: 0.2-7.3, p=0.9) and (0.2, 95%CI: 0.02-1.6, p=0.13), respectively. Although the percentage of hemorrhages decreased with lower INR levels, neither higher INR level nor warfarin dose predicted hemorrhage as the ORs were 0.2 (95%CI: 0.02-2.2, P-value=0.6) and 0.9 (95%CI: 0.6-1.4, P-value: 0.2). No patients with INR less than 0.9 had hemorrhagic changes. **Conclusion:** Our data suggest that patients on warfarin have a higher risk of symptomatic hemorrhages after receiving IV-tPA compared to the overall known risk of 6% for sICH in patients who receive IV t-PA within 3 hrs. There was no correlation between INR level or the warfarin dose and the risk of sICH. There were worse outcomes and higher rates of death in the patients who had hemorrhages. However, worse outcomes in patients who bled could have been more related to the severity of the stroke at initial presentation. Further studies are therefore needed to evaluate the safety of IV- t-PA with concurrent warfarin use with respect to admission NIHSS score. Our study is limited by the small sample size.

Table 1: Demographics, Risk Factors, Clinical Data and Outcomes

	Hemorrhage (N=13)	No Hemorrhage (n=48)	P Value
Demographics			
Mean Age (Years) ± SD	71±12	72±12	NS
Female Sex (%)	46	52	NS
Risk Factors			
Hypertension (%)	92	67	NS
Diabetes (%)	23	23	NS
Hyperlipidemia (%)	23	15	NS
Clinical Data			
Pre-tPA NIHSS (Median)	19	13	0.002
Post-tPA NIHSS(Median)	22	9	0.001
INR (Mean) ± SD	1.3±0.2	1.4±0.3	NS
INR (Range)	0.9-1.7	0.99-2.16	NS
Warfarin dose mg(Mean) ±SD	3.6±2	3.8±1.5	0.04
Pre-tPA systolic BP(Mean) ±SD	162±16	158±21	NS
Pre-tPA diastolic BP(Mean) ±SD	91±14	83±13	NS
Max systolic BP ±SD	183±23	179±16	NS
Max diastolic BP ±SD	97±15	94±15	NS
Hemicraniotomy	0	0	NS
Ventriculostomy	1	0	NS
Outcomes			
Median Discharge mRS	5	3	0.03
Median Discharge mRS ≤2 (%)	15	34	NS
Death (%)	31	5	<0.01
Median LOS(days)	5	5	NS
Correlation Between INR Levels and Hemorrhages			
INR≥2.00 (%)	0	4	NS
INR=1.71-1.99 (%)	0	9	NS
INR ≤ 1.7 (%)	92	87	NS
INR ≤ 1.6 (%)	77	73	NS
INR ≤ 1.5 (%)	77	65	NS
INR ≤ 1.4 (%)	77	52	NS
INR ≤ 1.3 (%)	77	50	NS
INR ≤ 1.2 (%)	38	31	NS
INR ≤ 1.1 (%)	15	17	NS
INR ≤ 1.0 (%)	8	2	NS
INR ≤ 0.9 (%)	0	0	NS

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W P12

Reversal of Infarcts Determined by Cerebral Blood Volume on Computed Tomography Perfusion Imaging with Intra-arterial Thrombolysis

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Background: Mismatch between Mean Transient Time (MTT) and blood volume on computed tomography perfusion (CT-P) scan in acute ischemic stroke patients has been used to identify salvageable tissue, with areas with low CBV identifying an ischemic core. There is no current literature on whether or not areas of low cerebral blood volume (CBV) are reversible. **Objective:** To evaluate whether CT-P infarct size (based on CBV) can be decreased or reversed with endovascular treatment in acute ischemic stroke patients. **Methods:** We retrospectively reviewed consecutive patients treated with endovascular thrombolysis for acute ischemic stroke between January 2006 and June 2010. All patients that had CT-P imaging on initial stroke admission and had follow-up CT scan or MRI, within 24 hours - 7 days, were included. CT-P images were reviewed by two of the authors and stratified into two groups based on whether or not there was any salvage of the area with decreased CBV on initial perfusion scan, with third investigator as a tie breaker. Clinical characteristics, National Institutes of Health Stroke Scale score (NIHSSS) (admission, 7day or discharge), modified Rankin Score (mRS) on discharge and complication rates were collected. **Results:** We identified 27 patients with decreased CBV on initial perfusion scan that underwent endovascular therapy, mean age of 66.8 $\pm$ 13 years and NIHSS score of 15.7 $\pm$ 5.4. There were 9 (33%) patients who had smaller final infarct sizes on follow-up imaging. When compared to the group with no reversal, they had a higher age (70.7 years versus 64.8), similar initial NIHSS (15.4 versus 15.8), higher rate of good outcome based on mRS 0-2 at discharge (56% vs 16%), and similar rates of IV thrombolysis (56% versus 53%). **Conclusion:** Ischemic brain identified by qualitative inspection of CBV perfusion scans can be salvageable by endovascular reperfusion therapy. Triaging patients with ischemic stroke for interventional reperfusion therapies based on CT perfusion MTT-CBV mismatch should not be adopted until further study.

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W P13

Early Reduction of Lesion Volume is Associated with Complete Early Recanalization in Stroke Patients Treated with Intravenous tissue-Plasminogen Activator Therapy

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Background and Purpose: Intravenous tissue plasminogen activator (IV t-PA) can improve clinical outcome in acute stroke patients. Early arterial recanalization has been recognized to salvage a vulnerable brain tissue in the diffusion-perfusion mismatch area, and thus believes as a predictor of good outcome. Indeed, and we are certain of the hyper-intense lesion on diffusion-weighted imaging (DWI) as brain tissue with irreversible damage. However, thrombolytic reversal or reduction of initial ischemic lesion on DWI has been reported in several recent studies. Thus, our aim is to investigate the frequency of stroke cases with DWI lesion decline after thrombolysis and to examine the association between clinical backgrounds including early recanalization and DWI lesion volume reduction. **Methods:** From January 2005 to June 2010, we prospectively enrolled patients with occluded artery of anterior circulation on initial magnetic resonance angiography (MRA) who were admitted to our stroke center within 3 hours of onset. All patients were treated with IV t-PA, and received magnetic resonance imaging study including DWI and MRA on admission and immediately (within 30 minutes) after IV t-PA. DWI lesion volume was measured manually using image analysis software (ImageJ 1.38, developed by the National Institutes of Health). Reduction of DWI lesion was defined more than 30% decrease of lesion volume from initial to follow-up MRI. Recanalization status was evaluated on follow-up MRA according to Thrombolysis In Myocardial Infarction (TIMI) flow grade. Complete recanalization was defined as TIMI grade 2 or 3. All patients were classified into two groups based on reduction of DWI lesion; reduction group (RD group) and no reduction group (non-RD group). We compared the clinical characteristics including complete recanalization between two groups. **Results:** Ninety-five patients (median age; 77, median initial National Institute of Health Stroke Scale; 16, 50 men) were included in this study. Reduction of DWI lesion was observed in 7 (7%) patients (RD group). In the RD group, initial glucose level (113mg/dl [interquatile range; 100-125mg/dl] vs. 139mg/dl [116-175mg/dl, p=0.009) was lower and complete recanalization was more frequently (86% vs. 10%, P<0.001) observed than non-RD group. There was no difference of other factors including age, sex, and interval from onset to initial MRI or IV t-PA between the groups. **Conclusion:** The frequency of early decrease of DWI lesion after IV t-PA therapy was 7%. Reduction of infarct volume should be associated with early complete recanalization after thrombolysis.

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W P14

Presence of MRI 'Mismatch' and Infarct Growth in Different Time Windows After Stroke Onset: a cross-sectional study

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Background: The 'mismatch' between MTT and DWI lesion volumes (MTT-DWI) is believed to reflect salvageable tissue and is often used as a selection criterion in clinical trials. In patients serially imaged, 'mismatch' is known to reduce over time. The frequency of mismatch and the evolution of 'mismatch' tissue into infarction in different time windows, is not known. **Methods:** The study cohort included 274 ischemic stroke patients who received DWI/PWI <12 hr after onset (i.e. last known well) and follow-up MRI on day 5 or later. Of these, n=230 had analyzable DWI and MTT lesion volumes; these patients were grouped by time from onset to MRI (0-3, 3-6, 6-9, 9-12 hr). Chi-square or ANOVA was used as appropriate. **Results:** Mean age, gender, vascular risk factors, mean admission BP, temperature, glucose, NIHSS score, and stroke etiology were not significantly different among time windows (ANOVA, p>0.05 for all). The groups showed no significant difference in mean admission DWI and MTT lesion volumes (Table). The frequency of any mismatch and >30% mismatch was >75% in all groups, with substantial volumes of mismatch (>70 cc) in each group. There were no differences in mismatch frequency or mismatch volumes. The frequency of 90-day mRS 0-2 was highest (85%) in the 6-9 hr group and lowest (54%) in the 9-12 hr group. Infarct evolution as measured by absolute lesion growth, or penumbral salvage [(admission MTT- chronic FLAIR)/(admission MTT- admission DWI)], was similar among groups; percent lesion growth was significantly different, with decreasing growth in later time windows (p=0.04). Similar results were obtained when the analysis was restricted to patients with (a) onset witnessed or <1 hr since last seen well, (b) hemispheric lesions, (c) no thrombolysis. **Conclusion:** In patients undergoing DWI/PWI upto 12 hr after onset, we found a high frequency of patients with persistent mismatch. This may be explained by selection bias (e.g. clinical perfusion-MRI more likely to be performed if CTA shows arterial occlusion), and reflect limitations of MR techniques for estimating 'mismatch' during the earlier time frames of this study (e.g. no delay compensation). However, the similarities in ischemic lesion evolution in different time windows is notable. Multivariate analysis with potential confounders (e.g. thrombolysis, MRI technique) is needed to fully understand lesion growth in these cohorts. These data may impact clinical trials using MTT-DWI mismatch for patient selection, and call for an interrogation of techniques used for estimating mismatch.

Patient characteristics (n=230)	0-3 hrs (n=31)	3-6 hrs (n=91)	6-9 hrs (n=70)	9-12 hrs (n-38)	P value
Admission DWI volume (cc)	37±62	24±35	24±30	28±49	0.51
Admission MTT volume (cc)	125±133	107±102	106±92	99±102	0.76
Any mismatch	87%	89%	90%	87%	0.95
Mismatch >30%	87%	86%	86%	79%	0.73
Penumbra volume (cc)	89±95	83±93	80±78	71±82	0.85
Infarct growth in pts with mismatch (n=202)	**(n=27)**	**(n=80)**	**(n=62)**	**(n=33)**	
Volume of Infarction expansion (cc)	31±59	30±62	25±57	17±38	0.72
Percentage of infarction expansion (%)	246±440	201±335	106±189	78±165	0.04
Percentage of Penumbra salvage (%)	51±41	48±41	41±40	41±44	0.55
90-day Rankin Score (n=166)	**(n=24)**	**(n=69)**	**(n=47)**	**(n=26)**	
mRS=0-2 (n=111)	63%	61%	85%	54%	0.02

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W P15

Therapeutic Impact of "Rapid MRI" During a Stroke Code

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Introduction: In patients with suspected acute ischemic stroke, a head CT is most often the only neuroimaging necessary prior to treatment with IV t-PA. Occasionally, the history or clinical examination may raise the suspicion of an alternative diagnosis (stroke mimic). Hypothesis: We assessed the hypothesis that in some stroke code cases the use of rapid MRI might alter management by diagnosing stroke mimics in patients otherwise eligible for acute therapies such as IV t-PA. **Methods:** We retrospectively reviewed the charts of the 377 "stroke code" patients in 2008 at our comprehensive stroke center. Of those patients, 30 had "rapid MRI" (FLAIR, DWI, ADC, and GRE) to assist in the diagnosis. We further reviewed those 30 charts to determine if management was altered after the MRI. **Results:** Among 377 stroke codes in 2008, 30 (8%), underwent rapid MRI. The mean age and gender were similar between the patients who had emergent MRIs and those who did not (mean age 61.1 and 61.0 years, respectively; gender was 67% women and 56% men, respectively, p = NS for both). All patients except one presented within the time period for acute treatment: 21 within 3 hrs, 5 within 4.5 hrs and 3 within 8 hrs. The most common presenting symptoms were: weakness (63%), aphasia (40%), dysarthria (17%), and altered mental status (13%). At the time of the stroke code, 17 of the patients were inpatients (11 of which were peri-procedural), and 13 were ED cases. Of the 30 patients, 19 had acute strokes on MRI and 11 were diagnosed as stroke mimics. Eight of the 19 acute stroke patients were treated (2 received IV t-PA, 6 underwent IA therapy). We refrained from acutely treating 22 of the 30 patients (11 mimics and 11 stroke patients in whom a contraindication was detected). Of the 11 mimics detected by MRI, 6 would have been eligible for t-PA within the 3 hr window and 1 patient was within 4.5 hrs. The reason for not using t-PA in 2 of the 11 stroke patients was directly due to MRI findings on the gradient echo sequence that were not detected on the non-contrast CT; 1 had multiple microhemorrhages and one had GRE+ metastases. Almost one-third of the patients (9 of 30) would have been potential candidates for IV t-PA but were excluded based on the MRI findings. **Conclusions:** In our series of "stroke code" patients who had rapid MRI out of concern for a possible stroke mimic, the majority did not receive thrombolytic therapy based on the MRI results. The test was useful in definitively selecting appropriate patients for acute intervention as well as in avoiding the unnecessary and potentially harmful treatment of patients with stroke

mimics. In conclusion, this demonstrates the utility of rapid MRI for a select group of patients and shows the potential to improve patient selection and safety.

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W P16

Intravenous Thrombolysis for Acute Ischemic Stroke in Asia: a Meta-analysis

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Background: Despite the proven benefits of intravenous tissue plasminogen activator (IV-TPA) in acute ischemic stroke (AIS), treatment rates remain low even at established centers. Data regarding thrombolysis in Asia are scarce and only a small percentage of patients are thrombolyzed. The dose of IV-TPA in Asia remains a controversial issue. Randomized controlled trials in Asia included only Japanese patients and suggested the clinical efficacy and safety of low-dose IV-TPA (0.6mg/Kg body weight; max 60mg) as comparable to standard-dose (0.9mg/Kg body weight; max 90mg). Reduced treatment cost, lower symptomatic intracerebral hemorrhage (SICH) risk and comparable efficacy encouraged many Asian centers to adopt low-dose or even variable-dose IV-TPA regimens. We aimed at evaluating various Asian studies on thrombolysis as compared to the SITS-MOST registry and Japanese and NINDS trials. **Methods:** We searched the published literature on AIS thrombolysis in Asia. We included studies published in English, with at least 10 patients, reported functional outcomes at 3months and SICH rates. The studies were reviewed independently by 2 investigators. Unadjusted relative risks and 95% Confidence intervals were calculated for each study. Eventually, the pooled estimates from random effects models were used because the tests for heterogeneity were statistically significant in all analyses. **Results:** We found a total of only 17 publication regarding AIS thrombolysis in Asia. Of the 44 countries in Asia, only 9 (total number of patients1808) reported their results (4 each from Japan and India; 2 each from Thailand, China and Taiwan; 1 each from Singapore, Vietnam and Pakistan). Owing to ethnic differences, stroke severity, small number of cases in individual reports, outcome measures and TPA dose-regimens, it is difficult to compare these studies. In general, the functional outcomes were almost similar (to Japanese studies) when lower-dose TPA was used in non-Japanese populations across Asia. Interestingly, with standard-dose IV-TPA regimen, considerably better functional outcomes were observed, without increasing SICH rates. **Conclusions:** Variable dose-regimens of IV-TPA are used across Asia without any reliable or established evidence. Based on Japanese studies, recommending the use of low-dose TPA across Asia is difficult since there has never been a head-to-head comparison of variable dose regimens. Establishing a uniform IV-TPA regimen is essential since the rapid improvements in health-care facilities and public awareness are expected to increase the rates of thrombolysis in Asia. A large randomized controlled trial is not feasible and hence, we propose an Asia-side ischemic stroke thrombolysis registry to address the prevailing confusion about the IV-TPA dose.

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W P17

Number Of Neurohospitalists Impact On The Rate Of Iv recombinant Tissue Plasminogen Activator Usage In Ischemic Stroke

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Background: Currently in the US IV recombinant tissue Plasminogen activator (t-PA) is given to 1.8-2.1% of ischemic stroke patients. There has been a very minimal increase in number of patients getting IV t-PA since its approval. As Neurohospitalists provide hospital-based on-site neurological care to patients with stroke and other serious neurological disorders, they may increase the t-PA usage. Limited or no data exists to determine the impact of Neurohospitalists on IV t-PA usage in ischemic stroke. The purpose of this study was to compare the rate of IV t-PA usage in ischemic stroke patients treated by Neurohospitalist service with IV t-PA usage by community based neurologists. **Methods:** We did a retrospective chart review of all ischemic stroke patients treated at the Baylor University Medical Center from January 2009 to June 2010. We divided them into two groups. From January to August 2009, there were only 1-2 Neurohospitalists on call and the majority of t-PA was given by community based neurologists. The second evaluation period was from November 2009 to June 2010 when there were 4 Neurohospitalists on-call. The primary data reviewed was rate of IV t-PA per month during these two time periods. Secondary measurement was Door to needle time in IV t-PA patients. **Results:** Overall between January to August 2009 a total of 465 strokes were treated at an average of 58 strokes per month. IV t-PA was given in 38 of these cases for an average rate of 4.75 per month. Between November and June 2010 a total of 407 were treated on average 51 strokes were treated per month with IV t-PA given to 65 patients in total and for an average rate of 8.125 per month. This translates into t-PA usage of 8% and 16% respectively. Mean Door to Needle time for IV t-PA given by Community based Neurologists was 98 minutes +/- SD of 32 minutes. Mean Door to Needle time for Neurohospitalists was 89 minutes +/- 32 minutes. There was no statistically significant difference (Two sided t test $p=0.13$). **Conclusion:** We found that an increasing number of Neurhospitalists led to an increase in IV t-PA treatment rates and also trends towards earlier treatment of ischemic stroke patients with IV t-PA at our center. The increased utilization of Neurohospitalists may lead to an increase in number of patients being treated with IV t-PA.

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W P18

Clinical Characteristics Of Acute Brain Infarction During Anti-coagulation Therapy With Warfarin -the Fukuoka Stroke Registry (FSR)

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Background and Purposes: Anti-coagulation therapy using warfarin is commonly done in patients with atrial fibrillation to prevent cardioembolic events. Intensity of anti-coagulation is recommended to be prothrombin time-international normalized ratio (PT-INR) 1.6-2.6 for elderly subjects with non-vulvular atrial fibrillation according to Japanese Guidelines, which is lower than that in Western countries (PT-INR 2-3), because the frequency of intracranial hemorrhage is significantly higher in Japanese. Here we examined the characteristics of patients developing ischemic stroke during oral anti-coagulant therapy. **Methods:** We designed Fukuoka Stroke Registry (FSR), a multi-centered prospective study for acute stroke, in Japan, which started registration at June 2007 (UMIN000000800). As of May 2010, 2,834 acute brain infarction (BI) have been enrolled. BI was classified into 4 subtypes according to the TOAST classification: atherothrombotic (AT), lacunar (Lac), cardioembolic (CE), and unclassified (Unc) infarction. **Results:** Two hundred and forty four BI patients (8.6%, mean 75 years) were taking warfarin at onset. CE (65.6%) was predominant, followed by AT (11.1%), Lac (10.2%), and Unc (13.1%), and 46.3 % patients had the history of BI. There were no differences in age and gender among the subtypes. Median PT-INR values were 1.28 (interquartile range (IQR) 1.09-1.59) in CE, 1.70 (1.33-2.17) in AT, 1.73 (1.40-2.43) in Lac, and 1.76 (1.36-2.12) in Unc. The PT-INR values in CE were significantly lower than those in other subtypes ($p< 0.001$). The median PT-INR was 1.50 (IQR 1.24-1.86) in recurrent BI patients, which was significantly higher than that in first-ever BI (1.30 (1.10-1.69)) ($p<0.01$). Seventeen percent of CE had fair PT-INR values (1.6-2.0), and 7.6% had good PT-INR ($\geq$ 2.0). In the good PT-INR group, the frequency of valvular heart disease (VHD) was significantly higher than that in other groups ($p< 0.01$). Systolic blood pressure on admission was significantly lower with the increase in the intensity of PT-INR ($p< 0.01$). Neurological severity on admission, as assessed by NIHSS, was less in patients with PT-INR $\geq$1.6 (NIHSS 4 (IQR 2-10)) than in those with PT-INR $<$ 1.6 (NIHSS 7 (3-16)) ($p< 0.01$). **Conclusions:** CE during anti-coagulation therapy is often associated with lower PT-INR values, while it can develop in spite of good PT-INR values in patients with VHD. The other subtypes of BI can occur even when anti-coagulation is effective. Neurological severity may be alleviated in patients with higher PT-INR values ($\geq$1.6) on admission.

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W P19

Longer Treatment Duration is Associated with Better Functional Outcome of Counterpulsation-treated Ischemic Stroke Patients

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Objectives: External counterpulsation (ECP) is a non-invasive method used to augment cerebral blood flow. We aim to identify the predictors of good functional outcome for ECP-treated acute ischemic stroke patients. **Methods:** We retrospectively analysed our ECP registry of acute ischemic stroke patients with cerebral large artery stenosis who underwent ECP therapy at the Prince of Wales Hospital. A standard treatment protocol consisted of 35 daily 1-hour therapy sessions. We included 192 patients who completed at least 10 hourly sessions of ECP. 155 patients successfully completed 3 months follow up. Patients were divided into to good outcome group (modified Rankin Scale [mRS] at 3 months 0-2) and bad outcome group (mRS 3-6). We compared the differences in the two groups in terms of demographics, medical history and ECP treatment duration time. **Results:** Good outcome was found in 99 (63.87%) patients. Univariate analysis showed age, previous TIA history, time since stroke onset, admission NIHSS, admission systolic blood pressure, total cholesterol levels and ECP duration were significant factors. Multivariate logistic regression showed that ECP duration (OR 0.938, 95%CI 0.885~0.993, $p=0.029$), admission NIHSS (OR 1.344, 95%CI 1.189~1.520, $P<0.001$) and admission systolic blood pressure (OR 0.977, 95%CI 0.962~0.992, $p=0.003$) were independent predictors. **Conclusion:** It is the first time that the duration of ECP therapy is found to be an important predictor for stroke recovery, in addition to the well-known prognostic factors such as admission NIHSS and blood pressure.

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W P20

Shortening Of Onset-to-arrival Time After Approval Of Intravenous Rt-pa Therapy And Its Influence On Stroke Outcome

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Background and Purpose: In Japan, intravenous recombinant tissue plasminogen activator (rt-PA) for acute stroke patients within 3 hours of stroke onset was approved in October 2005 and altered the environment for acute management of stroke then. Our purpose was to determine whether the onset-to-arrival time changed after the approval and the change affected the outcomes of stroke patients. **Methods:** Prospective multicenter observational

studies were conducted at 27 hospitals twice, from January 2005 through March 2007 (Period A) and from January 2008 through December 2009 (Period B). Stroke patients who presented to hospitals within 24 h of symptom onset were registered. The primary outcome was independent activity of daily living (ADL) corresponding to a modified Rankin Scale (mRS) score ≤1 at discharge. The outcome was compared between two periods in total and in three subgroups classified by the onset-to-arrival time (≤2.5h, 2.5 - 4.0h, 4.0 - 24.0h). **Results:** 2663 patients (1596 men, 71.0±12.6 years old, 1783 ischemic stroke and 880 intracerebral hemorrhage [ICH]) from Period A and 3144 patients (1885 men, 72.0±12.4 years old, 2066 ischemic stroke and 1078 ICH) from Period B were enrolled into this study. The onset-to-arrival time of Period B was shorter than that of Period A (median 150 minutes vs. 180 minutes, $P<0.001$) and more patients arrived within 2.5 hours from the onset in Period B compared to Period A (50.5% vs. 39.9%, $P<0.001$). In overall patients, the initial NIHSS score and the mRS score at discharge were not different between 2 periods. In ischemic stroke patients of the earliest-arrival subgroups (≤2.5h), the initial NIHSS score tended to be low (median 8 [IQR 3-16] vs. 9 [3-17], $P=0.063$) and the mRS score at discharge was lower (median 2 [IQR 1-4] vs 3 [1-5], $P=0.024$) in Period B than Period A. Independent ADL was 1.34 times (95% CI 1.01 - 1.78, $P=0.044$) more common in patients in Period B than Period A after adjustment for age, sex and the initial NIHSS score. In ischemic stroke patients of the other two subgroups and in ICH patients of any subgroups, no significant differences were observed in the initial NIHSS score and the mRS score at discharge between 2 periods. **Conclusion:** The onset-to-arrival time in stroke patients became shorter and the outcome of the ischemic stroke patients arriving within 2.5h of stroke onset improved in recent years in Japan. The 3-hour rt-PA rule may cause the limited improvement of outcomes only in the earliest-arrival subgroup of ischemic stroke patients.

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W P21

Extending Therapeutic Window for Intravenous Thrombolysis to 4.5 hours Remains Safe and Effective in Asian Acute Ischemic Stroke Patients

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Background: Intravenously administered tissue plasminogen activator (IV-TPA) remains the only approved therapy for Asian acute ischemic stroke (AIS) patients within 3 hours of symptom-onset. The meta-analysis IV-TPA trials demonstrated that the therapeutic benefit could exist up to 270 minutes and this was confirmed recently in a randomized clinical trial (ECASS-III) as well as multicenter registry (SITS-MOST). Treatment rates for AIS remain low in Asian populations. Patients' late arrival and higher anticipated bleeding-risk are the major contributing factors. We aimed at evaluating the safety and efficacy of IV-TPA therapy in an extended therapeutic window among Asian patients in Singapore. Methods- Data from consecutive AIS patients treated with IV-TPA, in a standardized protocol, from Jan 2007 to March 2010 were included in the prospective thrombolysis registry at our tertiary care center. All patients received standard-dose of IV-TPA (0.9mg/Kg body weight) Efficacy of IV-TPA was assessed with functional outcomes at 3-months (modified Rankin Scale (mRS) score, dichotomized as good outcome (mRS 0-1) and poor outcome (mRS 2-6). Safety of IV-TPA was assessed by rates of symptomatic intracranial hemorrhage (SICH). SPSS 16.0 was used for statistical analysis. **Results:** Of the total of 2271 AIS patients admitted to our center, 224 (9.9%) eligible cases were treated with IV-TPA during the study period. Baseline data included mean age 63±12 years; 131 (59%) males; mean onset-to-treatment time 157±38 minutes and median NIHSS 16 points. 190 ( ) patients were treated within 3 hours while 34 received IV-TPA in an extended therapeutic window. Hypertension was the commonest vascular risk factor in 170 (76%) while 73 (33%) patients suffered from atrial fibrillation (AF). Strokes involved anterior circulation in 189 (84%) as compared to 35 (16%) posterior circulation. Overall, 115 (51%) patients achieved good functional outcome (mRS 0-1 at 3 months). Female gender, AF, pre-TPA NIHSS score and HMCAS on follow-up CT scan were associated with poor functional outcome. Although, higher proportion of patients treated after 180 minutes had poor outcomes at 3 months (62% versus 46% in 0-180 minutes group), the difference was not statistically significant (OR 1.87;95%CI 0.88-3.96, p=0.097). SICH occurred in a total of 9 (4.01%) patients. Although, higher proportion of patients treated in an extended window developed SICH (9.7% versus 3.3%), the difference was not significant (p=0.141). **Conclusion:** Intravenous thrombolysis in an extended therapeutic window is effective as well as safe in the treatment of acute ischemic stroke in our multiethnic Asian population in Singapore.

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W P22

Long Term Follow-up Of Incidentally Found Intracranial Aneurysms In Patients With Acute Ischemic Stroke

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Background: Sometimes intracranial aneurysms are incidentally found in patients with acute ischemic stroke, in whom long term anti-thrombotic therapy is essential for secondary stroke prevention. In these cases, natural history of intracranial aneurysms has not been well identified. Regarding this, we performed two years follow-up of clinical outcome and CT angiographic findings in acute ischemic stroke patients with incidentally found intracranial aneurysms. **Methods:** We consecutively included acute ischemic stroke patients within 7 days of onset. Demographics, risk factors, clinical outcome (modified Rankin Scale), aneurysm type, and maximum diameter of aneurysm were identified. Clinical characteristics of patients with aneurysm were compared to those without aneurysms. CT angiography was performed on admission and at least two years after the initial exam in order to evaluate the change of the aneurysms. The development of aneurysmal rupture and hemorrhagic complications directly due to intracranial aneurysm were checked. **Results:** Incidental intracranial aneurysms were found in 19 (6.1%) of the total 314 patients. The female sex and old age were associated with the presence of incidental intracranial aneurysms (patients with aneurysms vs. those without; 13/19, 68.4% vs. 109/295, 36.9%, p=0.006; 72.2±13.1, 65.5±13.4 years, mean, SD, p=0.043). The most common site of aneurysm was at the distal internal carotid artery (n=11), followed by the middle cerebral artery (n=6) and basilar artery (n=2). The diameters of the aneurysms ranged from 1.84 to 8.06 mm. All the patients except one who had cancer have been taking anti-thrombotics. No aneurysm rupture or subarachnoid hemorrhage has occurred during the two years of follow-up. In 7/19 patients, follow-up CT angiography could be performed. Six of them showed no change regarding aneurysm shape and size. In one, the aneurysm disappeared. Eight patients could not perform follow-up CT angiography because of death (5), refusal (1) and disability (2). The remaining four patients are supposed to perform follow-up CT angiography and the results are pending. **Conclusions:** There was no aneurysm rupture or subarachnoid hemorrhage during the two years of follow-up period even with the continuing long term anti-thrombotic treatment. On the follow-up CT angiography, the diameter and shape of aneurysms mostly did not change.

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W P23

Comparison Between Mr Angiography At 3t (3d Time-of-flight And Contrast-enhanced) With Flat Panel Digital Subtraction Angiography In The Assessment Of Embolized Brain Aneurysms

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Introduction: The endovascular treatment with detachable coils has become an established technique for the treatment of intracranial aneurysms. Despite all the advances in the techniques of embolization, it is known that 14.7% to 33.6% of aneurysms embolized are subjected to any type of recurrence. It is important the imaging surveillance of coiled aneurysms, to identify any recurrence of aneurysm reperfusion, to determine the need for retreatment. Traditionally, this control has consisted of repeated digital subtraction angiography (DSA). However, this method has a risk of neurological complications. Thus, many authors have advocated the use of noninvasive imaging methods, considering the magnetic resonance imaging (MRI) as a viable option in terms of safety and image quality. **Material and Methods:** This prospective study compared the magnetic resonance angiography (MRA), including time-of-flight (TOF) and contrast-enhanced (CE-MRA) techniques in relation to DSA in the evaluation of embolized cerebral aneurysms. We studied 30 patients, harboring a total of 43 embolized cerebral aneurysms. Thirty-four (79.1%) aneurysms were located in the internal carotid artery, 6 (13.9%) in vertebral-basilar system, two (4.7%) in middle cerebral artery and 1 (2.3%) in the anterior communicating artery. The size of the aneurysms was small in 15 cases (34.9%), medium in 12 (27.9%), large in 12 (27.9%) and giant in 4 (9.3%). The endovascular technique applied was: simple technique in 13 cases (30.2%), balloon remodeling in 21 cases (48.8%) and stent remodeling in 9 cases (20.9%). Two interventional neuroradiologists, with experience in both methods, interpreted the results independently. The status of aneurysm occlusion was assessed according to the Raymond scale. **Results:** There was full interobserver agreement in all evaluated methods. Intertechnical agreement, assessed by k statistics, was excellent, between TOF-MRA and CE-MRA (k=0,98). Disagreement occurred in only one case (2.3%), corresponding to a small aneurysm treated by balloon remodeling, located in the internal carotid artery, which was classified as Class I (Raymond scale) by TOF-MRA and class II by DSA and CE-MRA. Agreement between CE-MRA and DSA was perfect (k = 1). In three aneurysms, treated by stent remodeling, parent-artery intraluminal stenosis was seen within the stent, which was not confirmed by DSA. **Conclusions:** Our study shows that DSA and both MRI techniques (TOF-MRA and CE-MRA) have excellent intertechnical and interobserver reproducibility for the assessment of aneurysm occlusion after embolization. However, in cases treated with stent remodeling, DSA may still be necessary to confirm an eventual parent artery stenosis identified by MRI.

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W P24

Proteomic Analysis of Aneurysm Healing Mechanism after Coil Embolization: Comparison of Dense Packing with Loose Packing

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Background and Purpose: In clinical practice, durability of occlusion following coil embolization is superior in densely packed as compared to loosely packed aneurysms. We probed, in a rabbit model, the biological mechanisms associated with densely packed, well healed, durably occluded aneurysms compared to loosely packed, poorly healed, imperfectly occluded aneurysms following embolization. **Methods:** Elastase-induced, saccular aneurysms were created in rabbits and were allowed to mature, after which aneurysms were either densely packed (Group 1, packing density>30%) or loosely packed (Group 2, packing density<20%) with platinum coils. After 2 weeks (n=6 for both groups) and 4 weeks (n=6 for both groups) of implantation, aneurysm samples harboring coils were harvested. Soluble proteins were extracted from the necks and domes of aneurysms and proteins were identified using mass

spectrometric techniques. **Results:** Ninety proteins in the neck and 294 proteins in the dome of 2 week aneurysms and 64 proteins in the neck and 139 proteins in the dome of 4 week aneurysms were differentially expressed in Group 1 aneurysm compared to Group 2 aneurysm. Specific pathway analysis revealed that, compared to Group 2, Group 1 aneurysms were associated with upregulation of cell adhesion molecules, cytoskeleton and extra cellular matrix remodeling at 2 weeks. Conversely, at 4 weeks Group 1 aneurysms showed a decrease in the expression of cell adhesion and an elevated expression of transcription factors as compared to Group 2 aneurysms. **Conclusion:** These findings may focus efforts on specific targets aimed at improving the long-term healing of intracranial, saccular aneurysms

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W P25

Heparin Dosing is Associated with DWI Lesion Load Following Aneurysm Coiling

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Background: Diffusion-weighted (DWI) lesions post aneurysm coiling is common. Heparinization protocols differ among operators and centres for coiling procedures. The goal of this study was to determine whether intra-procedural heparinization protocols affect the frequency and type of DWI lesions post-coiling. **Methods:** A retrospective review of 277 aneurysm coilings performed in 240 patients at a single centre was performed. Patients were excluded if there was no follow-up MRI performed within 10 days post-op or due to incomplete heparinization records. This resulted in 135 coiling procedures in 127 patients. The following baseline characteristics were collected: age, sex, aneurysm size, neck:dome ratio and rupture status. Procedural data including length of procedure, number of coils used, balloon or stent assistance and identity of operator was also collected. The procedures were either assigned as having received a bolus dose of heparin (>2000 U at any one time) or small aliquots of heparin (<2000 U doses). The total time to achieve adequate heparinization (activated clotting time (ACT) of 250 $\pm$ 20 s) was calculated. Post-procedure DWI were reviewed and the number and size of the DWI lesions were classified as small (<5mm), medium (5-10mm), large (>10mm) or macro infarcts (>4 cm^2). The cases were then classified into Group 1 (<5 small lesions) or Group 2 (>5 small lesions, or any larger lesion). Macro infarcts caused solely by technical complications were excluded. Statistical differences in baseline and procedural variables between Group 1 and Group 2 were calculated. A P-value of <0.05 was considered significant. **Results:** There were 78 procedures and 74 patients in Group 1 and 55 procedures and 55 patients in Group 2. Overall, there were 39 cases (29%) with no infarcts, and 94 cases with infarcts (71%) but 59 of these (44 %) consisted of 0-2 small lesions. Two macro infarcts (2 procedures in 2 patients) were excluded from further analysis. There was no significant difference in baseline characteristics between Group 1 and Group 2, including rupture status. Patients who received small aliquots (N=37) vs boluses of heparin (N=96) intra-procedurally had a greater frequency and size of DWI lesions (57% vs 35% in Group 2) (P=0.03). The mean time to achieve an ACT >230 s and the proportion of cases achieving this ACT did not differ significantly between the two groups. None of the procedural variables: duration of the procedure, operator, number of coils used and use of balloon or stent assisted techniques were found to be statistically different between the two groups. **Conclusions:** Ischemic lesions are frequently seen on DWI post-coiling. A greater frequency and size of DWI lesions was associated with small aliquots of heparin dosage compared with bolus doses. In the future, preferential regimen of bolus heparin could decrease ischemic load in aneurysm coiling.

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W P26

Vascular Mineralcorticoid Receptor Antagonism Combined With A Decrease In Salt-intake By Eplerenone Inhibits Cerebral Aneurysm Without Affecting Blood Pressure

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The pathogenesis of cerebral aneurysms is multifactorial and obscure. As epidemiological data show a high incidence of cerebral aneursyms in postmenopausal women, we established a new cerebral aneurysm model in female rats subjected to estrogen deficiency, increased hemodynamic stress, and hypertension and studied the relationship between their aneurysms and endothelial tight junctions, oxidative stress and inflammation in the vascular wall. To examine the pathogenetic contribution of mineralocorticoid receptor (MR) we used the MR antagonist eplerenone and the MR agonist deoxycorticosterone acetate in saline (DOCA-salt). Compared to sham-operated rats, at the aneurysm site of experimental rats we observed a reduction in the tight-junction proteins occludin and ZO-1 and an increase in nicotinamide adenine dinucleotide phosphate-oxidase subunits, inflammatory-related molecules, and angiotensin II expression. In rats treated with eplerenone, opposite findings were made and the incidence of cerebral aneurysms was decreased; angiotesin II level in their vascular wall was decreased via the down-regulation of angiotnesin-converting enzyme (ACE) without affecting the blood pressure and their salt-intake was reduced. In contrast, the formation of cerebral aneurysms was increased in rats implanted with DOCA pellets as were their ACE levels in the vascular wall and their salt intake. Our results provide new insights into the formation of cerebral aneurysms in rats subjected to hypertension and hypoestrogenicity that the activation of MR combined with an increase in salt-intake is associated with the activation of the vascular renin-angiotensin system, thereby at least partly contributing to the formation of cerebral aneurysms independent of hypertension, and that eplerenone may represent an agent for the prevention and/or treatment of cerebral aneurysms.

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W P27

Quantitative Analysis Of Coil Embolization Of Brain Aneurysms: Multi-center Study Using Auto Measurement Software

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Background and Purpose: Endovascular coil embolization has recognized as acceptable treatment for intracranial aneurysms. Despite of importance of precise morphological evaluation to anticipate stability of treated aneurysms and advancement of modern three dimensional imaging technology, no scientific evaluation method of morphological outcome has been established. Therefore, novel objective morphological evaluation system is mandatory. The aim of this study is to identify whether initial volume embolization rate (VER)correspond to long term stability of treated aneurysm measured by newly developed auto measurement software. **Methods:** This is a multi-center, prospective analysis for coil embolization using volume measurement software (NeuroVision, KGT, Tokyo, Japan). Between April 2009 and May 2010, 295 patients with unruptured aneurysms were enrolled in the study. Sixteen centers were participated. The aneurysms were treated predominantly using Matrix2 coils in combination with or without GDC bare platinum coil. Follow-up catheter 3D angiography at 12 months was performed. Pre, post embolization, and follow up 3D angiography DICOM data was recorded and evaluated at independent core lab using new measurement software. Special attention was paid for pre, post, and follow up embolization aneurysm volume and VER. Clinical outcomes were assessed using a modified Rankin scale. Factors related for aneurysm recurrence was statistically analyzed. **Results:** Two hundred fifty seven aneurysms were anterior circulation and 38 were posterior circulation. All aneurysm volume and VER were calculated automatically with NeuroVision. There was no morbidity and mortality after the treatment. Average volume (size) and VER were 165.2mm3 (6.1x5.8mm) and 25.5% respectively. Posterior circulation was better VER (29.8%) than anterior circulation (25.5%). Aneurysm location was not related to VER in the anterior circulation (ICA 25.3%; MCA 25.1%; ACA 25.2%) aneurysms also demonstrated equally good VER outcomes. The average VER of participated centers were range between 20 and 28%. **Conclusions:** This report is first multi center study using quantitative analysis after coil embolization of brain aneurysms without human bias. Using this software more scientific evaluation of coil embolization can be conducted. Mid term anatomical result will be reported.

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W P28

Should We Treat Unruptured Intracranial Aneurysms? - Evaluation Of Clinical Outcome Between Conservative Management And Therapeutic Intervention

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Background and Aim: management of unruptured aneurysm is controversial. We analyzed relationship between aneurysm size and clinical benefit of treatment in comparison to outcome of conservatively observed UIAs. **Methods:** Between March 2003 and April 2009, 876 patients with 1111 UIAs were referred to our institution. After informed consent, 326 patients with 370 aneurysm agreed either endovascular coiling or surgical clipping. 9 patients received both coiling and MC due to multiple aneurysms. The remaining 603 patients with 741 aneurysms were conservatively observed with 3D CTA evaluation. **Results:** In the treatment group, overall morbidity and mortality were 3.1% and 0.3%. In the observation group, 26 aneurysms ruptured (1.8%/year: 1405.7 person-year) during follow up. Of these, 10 patients were dead (38.5%) and 6 patients (23.8%) were disabled status (mRS 3-5). Treatment benefit was confirmed when aneurysm size was more than 6mm if morbidity was defined as modified Rankin scale 2(P=0.0021). However, treatment benefit were only confirmed the aneurysms more than 8mm if morbidity was defined as mRS 1(P=0.031). **Conclusion:** The patients with UIA need accurate and multi factorial information about therapeutic benefit before treatment.

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W P29

Contributing Factor For Incomplete Clipping Of Cerebral Aneurysm Detected By Indocyanine Green Video Angiography

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Objective: Delayed blood filling detected by ICG-VA following aneurysm clipping has rarely been reported. This study was conducted to assess the factors contributing to complete

occlusion after clipping of intracranial aneurysms. **Methods:** From October 2008 to December 2009, 135 patients with intracranial aneurysms were treated by clipping at the hospital that the author is affiliated with. After we were convinced that the intracranial aneurysms had been completely clipped, intravenous indocyanine green (ICG, Dong In Dang Pharm. Co., Shihung-Si, Korea) injection was conducted in all cases. The delayed-filling group was defined as filling of ICG into the aneurysm dome until the venous phase. We assessed the clip force, the size of the aneurysm neck and dome, the parent artery diameter, and atherosclerosis of the aneurysm neck between the delayed-filling and no-filling group. Aneurysms with domes that could not be identified in surgical view and were less than 3mm in size were excluded. **Results:** Eight cases of all 31 aneurysms in 29 patients showed delayed blood filling upon ICG video angiography. Four Yasargil miniclips (Aesculap AG & Co., Tuttlingen, Germany), one Sugita mini clip and three Sugita standard clips (Mizuho Medical Co., Tokyo, Japan) were used in the delayed-filling group. Only clip force and neck atherosclerosis differed significantly between the delayed-filling and no-filling group ($p<0.05$). We repositioned a clip, applying a booster clip in the delayed-filling group due to atherosclerotic change in the aneurysm neck and insufficient passage of a tip of the aneurysm clip. No aneurysm dome was observed upon postoperative CT or digital subtraction angiography. **Conclusion:** ICG videoangiography is a valuable tool for confirmation of complete occlusion of aneurysm surgery. Our results also suggest that low closing force of clip, atherosclerotic aneurysm neck, the position of clip tip and the presence of remnant slit are important factors for incomplete occlusion of intracranial aneurysm.

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W P30

Stent - assisted Coil Embolization of Complex, Wide-necked Bifurcation Cerebral Aneurysms using the "Waffle Cone" Technique

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Background and Purpose: Endovascular treatment of complex, wide-necked bifurcation cerebral aneurysms is challenging. A variety of techniques have been used to treat these aneurysms. Intra/ Extra- aneurysmal stent placement, the so-called "Waffle Cone" technique, has the advantage of using a single stent to prevent coil herniation and does not involve stent delivery to the efferent vessel. However, the published data on the use of waffle cone technique is limited. We present here our initial and followup experience with stent-assisted coiling of cerebral aneurysm to evaluate the durability of the waffle cone technique. **Subjects and Methods:** We retrospectively identified 10 consecutive patients who underwent stent-assisted coiling of an aneurysm using the waffle cone techniques from July 2009 to June 2010. Demographic, clinical, angiographic and procedural data were reviewed. Six month clinical and angiographic follow up were available in 6 cases. **Results:** Conventional stent assisted coiling was not performed in all cases because efferent artery anatomy precluded stent placement across the aneurysm neck. The Neuroform3® stent was used in 9 cases and the Enterprise stent was used in one. Complete or near complete occlusion of the aneurysm initially was achieved in all cases. No intraoperative aneurysm rupture occurred. No coil herniation was observed and the afferent and efferent vessels were patent at procedure completion. One patient developed thrombosis of an efferent artery 24 hours after treatment without permanent deficit. In one patient with Grade V subarachnoid hemorrhage, care was withdrawn after successful coiling of the aneurysm. Clinical and radiographic followup in the remaining 9 patients (mean 5.4 month) revealed no subsequent rebleeding or ischemic complications. Follow-up angiography performed six months after treatment demonstrated the aneurysm remained obliterated in 5 of 6 patients. The aneurysm recurred in one patient who had been treated using an Enterprise stent and received repeat coiling. All stents were patent without in-stent stenosis or thrombosis. The afferent and efferent vessels remained widely patent in all cases. **Conclusion:** Our preliminary experience suggests that stent-assisted coiling of aneurysm using the waffle cone technique is safe and effective. This stent placement strategy is a useful alternative for complex, wide-necked aneurysms when the anatomic configuration of efferent artery is unfavorable for conventional stent placement.

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W P31

Increased Packing Volumes of Endovacular-Treated Intracranial Aneurysms Correlates with Reduced Aneurysm Recurrence

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Background: Endovascular repair of intracranial aneurysms is a safe and effective treatment modality. However, concerns of endovascular treatment include durability of therapy and aneurysm recurrence. We hypothesized that increased packing volumes during coil embolization was associated with decreased aneurysm recurrence, and conversely, that lower packing volumes were associated with increased aneurysmal recurrence. Therefore, we correlated aneurysm packing volumes with aneurysm recurrence. **Methods:** The study population included 61 sequential aneurysm patients, (47 female, 14 male), admitted to a University Hospital from 2007-2010. Fifteen patients were excluded for incomplete data or pseudo-aneurysm. The remaining 46 patients, with 55 aneurysms, were placed into two groups. Group A, n=38, included those with a single coiling procedure and without recanalization (29 female, 9 male, median age 55 years, 40 procedures). Group B, n=8, included those with one or more coiling procedures and demonstration of aneurysm recanalization (6 female, 2 male, median age 51.5yrs, 18 procedures). Aneurysms were categorized according to presentation, location, shape, number of coils used, coil types, and immediate angiographic outcome. Using AngioCalc, an online program for cerebral aneurysm analysis, we determined aneurysm volumes, coil volumes, and total packing volume percentages for each aneurysm. **Results:** Aneurysm locations were: AcoA (n=18), ICA (n=1 right, n=3 left), Cavernous ICA, (n=1 right, n=2 left), Paraclinoid ICA (n=1 right), Ophthalmic ICA (n=3 right, n=3 left), Hypophyseal ICA (n=2 left), Supraclinoid ICA (n=2 right, n=2 left), PCoA (n=4 right, n=3 left), MCA (n=3 right), A1 ACA (n=1 right, n=1 left), Pericallosal ACA (n=1 left), P1 PCA (n=1 right), PICA (n=1 left), and Basilar Apex (n=2). AngioCalc analyses of these 55 aneurysms revealed similar average volumes between groups: Group A: 442.59mm3, (median 65.45mm3, range 5.58 - 4,849.05mm3), Group B: 428.65 mm3, (median 72.99 mm3, range 4.87 - 3,053.63 mm3). The average packing volume percentages were markedly different: Group A, 25.66%, Group B, 12.03%. **Conclusion:** Our data strongly indicates that for endovascular-treated intracranial aneurysms of similar volumes, packing volumes of ~25% are associated with reduced aneurysm recurrence rates compared to aneurysms with packing volumes of ~12%. This analysis is limited by AngioCalc's assumption of perfect shapes such as a sphere, cylinder, or ellipsoid. Future studies using CT angiography data will account for shape imperfections and may improve calculations of packing volume percentages.

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W P32

Derived Biomorphometric Criteria Can Predict Aneurysm Rupture Status: A CT Angiographic Analysis

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Introduction: Subarachnoid hemorrhages (SAH) occurring after rupture of an intracranial aneurysm has an overall morbidity and mortality rate of 50 to 60%. SAH affects young and healthy patients, creating economic and social effects. Determining variables to formulate an equation which can predict which aneurysms are more likely to rupture would allow better stratification of patients that may benefit from invasive procedures such as coil embolization and microsurgery. Prior studies have assessed several biomorphometric parameters which have variably correlated with rupture status. The objective of this study is to assess whether the ostium area and surface area of an aneurysm can potentially be used to predict the rupture status for intracranial aneurysms. **Methods:** Patients presenting to the University Hospital of UMDNJ with the diagnosis of ruptured or unruptured aneurysms were evaluated. CT angiography was performed according to standard protocol, which included 150 cc injection of contrast at 4cc per second. Images were obtained at 0.625mm thickness on the GE 16 slice scanner and processed with the GE Advantix Workstation. Biomorphometric variables such as aneurysm height, width and neck diameter were obtained in planes parallel and perpendicular to the flow of blood from 3-D reconstructions. The ostium area was calculated using the measured neck diameters in the formula to calculate area of an ellipse. Surface area calculations were obtained by isolating the region of interest, the aneurysm, in all axial sections, and importing these images into Adobe Photoshop for surface area calculations. Results were analyzed using Levene's Test for Equality of Variances. **Results:** Twenty consecutive patients with ruptured aneurysms and 20 patients with unruptured aneurysms were analyzed. Statistically significant differences were identified in ostium area, surface area to ostium area and volume to ostium area for the aneurysm. Neck diameter, parallel to flow, correlated positively with rupture status. Binary logistic regression of these individual parameters was then applied which demonstrated that the most significant predictors of rupture status were neck diameter in a plane parallel to flow and volume-to-ostium area with a predictive accuracy of 87.8 %. **Conclusions:** Although surface area assessment was statistically significant by the independent samples test, multi-variable regression suggests that volume-to-ostium area and neck size are more predictive of rupture status. Though no biophysical data is available with this mathematical study, these data strongly suggest that future studies are warranted in a larger population of patients.

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W P33

Change of Hemodynamic Situations of Elastase Induced Aneurysms with Arterio-venous Fistula Creation in Rabbits

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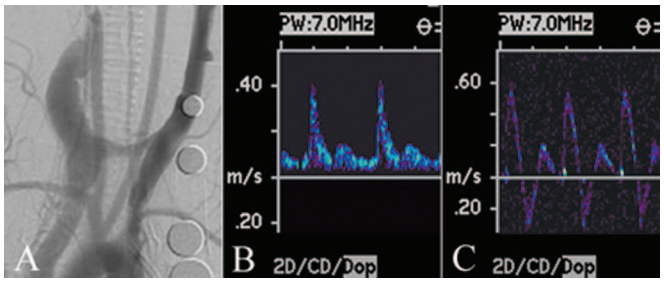
Purpose: To explore if creation of arteriovenous fistula (AVF) can change the hemodynamic situations of elastase-induced aneurysms in rabbits. **Materials and Methods:** Right common carotid artery (RCCA) elastase-induced aneurysms were created in 10 rabbits (Group 1) 4 weeks after RCCA-REJV (right external jugular vein) fistula creation (Figure 1A), which involved end to side anastomosis of REJV to RCCA. Ten other aneurysms (Group 2) were created without AVF creation. Ultrasound examination and digital subtractive angiography (DSA) were performed 3 weeks after aneurysm creation. Doppler waveform features in the parent artery of aneurysms were evaluated. Occurrences of different features between two groups were compared using Fisher's Exact Test. **Results:** Persistent (through both systolic and diastolic) antegrade flow waveform in parent artery was shown in 7 (70%) of the aneurysms in group1 (Figure 1B), which was not shown in any aneurysms in Group 2. Systolic antegrade flow and diastolic reversal of flow were shown in all the aneurysms (100%) in Group 2 (Figure 1 C), which were shown in only 3 (30%) of the aneurysm in Group 1. Occurrence of persistent antegrade flow in Group 1 was significantly higher than that in Group 2 ($p < .01$). **Conclusion:** Persistent antegrade flow can be induced in the elastase-induced aneurysms with arterio-venous fistula creation, which is more close to the cerebral blood flow patterns in patients.



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W P34

Stent-Assisted Coil Embolization of Unruptured Middle Cerebral Artery Aneurysms

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Background: Aneurysms of the middle cerebral artery (MCA) are frequently wide necked and incorporate important branches. These anatomical features have proved challenging for endovascular management, and have led many clinicians to favor neurosurgical clipping of aneurysms at this location. Stent-assisted embolization may increase the likelihood of successful endovascular treatment. **Methods:** We retrospectively reviewed all cases of stent-assisted coil embolization of unruptured MCA aneurysms performed at our institution and assessed procedural success, procedural complications, durability of treatment, and complications during follow-up. **Results:** Treatment was attempted in 23 patients and successful in 22/23 (96%). The median age was 61 years (mean 62). Aneurysm size was: $<$5 mm in 5/22 (23%); 5-9 mm in 14/22 (64%); and $\geq$10 in 3/22 (14%). There were 4 periprocedural complications, none of which resulted in either transient or permanent neurological morbidity or mortality. Angiographic follow-up was available in 18/22 (82%) and clinical follow-up in 19/22 (86%). On angiographic follow-up at a median of 1 year (mean 1.2 years), aneurysm occlusion was complete in 12/18 (67%). A neck remnant was present in 3/18 (17%). Persistent aneurysmal filling was present in 3/18 (17%) requiring retreatment in 1/18 (6%). In-stent stenosis of 50%, which was asymptomatic, occurred in 1/18 (6%). After a median clinical follow-up period of 1 year (median 1.2 years), no subarachnoid hemorrhage occurred. There were two ischemic events (one TIA and one lacunar stroke) both likely unrelated to the procedure. **Conclusions:** In this small series, the technical success rate was 96%, there were no transient or permanent neurological complications, and complete aneurysmal occlusion was achieved in two thirds of treated aneurysms on follow-up angiography. These results suggest that in selected patients, stent-assisted coil embolization of middle cerebral artery aneurysms can be performed with a high degree of technical success, a low procedural risk, and acceptable durability.

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W P36

Stent-Assisted Coil Embolization of Brain Aneurysms Produces Safe and Durable Occlusion

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Introduction: Stent-assisted coiling techniques have improved the endovascular treatment of wide-necked (neck $\geq$ 4 mm or dome-to-neck ratio $<$ 2) and fusiform intracranial aneurysms. We prospectively evaluated the safety and efficacy of a new generation neurovascular closed-cell stent (CCS) approved for the treatment of wide-necked intracranial aneurysms. We hypothesize that CCS-assisted coiling improves the durability of endovascular aneurysm treatment. **Methods:** Between June 2007 and March 2010, 107 wide-necked and fusiform/dissecting intracranial aneurysms were treated endovascularly in 99 patients using CCS. Fifteen (14%) aneurysms were located in the posterior circulation. The aneurysms were defined as wide-neck complex (81%), dissecting or fusiform (12%) or blister (7%). Ten (9%) were treated acutely following subarachnoid hemorrhage. Aneurysms that recanalized following primary coiling (21%) or clipping (2%) were also included. The mean aneurysm diameter and neck size was 5.9mm (2-25mm) and 4.8mm (2-15mm), respectively. Follow-up angiography was obtained for 67 patients (68%) at a mean of 10 months (5-21months). Immediate post-procedure control and follow-up angiograms were evaluated using the Raymond[1] scale by a core lab. Clinical evaluations were performed using a modified Rankin scale (mRS). **Results:** Immediate control angiography demonstrated total aneurysm occlusion in 39 (36%), neck filling was seen in 37 (34%), and dome filling was seen in 34 (32%) aneurysms. All serious adverse events occurring within 30 days were: 2 TIA, 4 minor strokes, 1 major stroke and 2 access site complications requiring surgical intervention. Permanent morbidity, defined as any increase from baseline mRS, and mortality during the follow-up period were 9% and 3%, respectively. Of the 2 patients that expired, one was due to rebleeding from a dissecting posterior-inferior cerebellar artery aneurysm 6 days after embolization, and the other due to an embolic stroke. In the small cohort of ruptured aneurysms, only 1 of 9 surviving patients has persistent neurological impairment. Procedure-related permanent morbidity and mortality during the follow-up period was 3% and 1.5%, respectively. Angiography at follow-up demonstrated total occlusion in 54 (77%), 14 neck remnants (20%), and 2 residual aneurysms (3%). The recanalization and retreatment rates in this series were 8.6% and 5.7%, respectively. **Conclusion:** Complex, wide-neck aneurysms may be successfully obliterated with CCS-assisted embolization. Recanalization rates for CCS-assisted embolization compare favorably to historical controls (20% reported in the literature[2] and 13% from our own data[3]). Caution should be exercised and further evaluation is required in using CCS-assisted coil embolization for acutely ruptured aneurysms. 1. Stroke 2001;32:1998 2. Stroke 2009;40:e523 3. Am J Neuroradiol AJNR 2007; 28:1395

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W P37

The Incidence And Mechanisms Of Postoperative Cerebral Infarction After Clipping Surgery For Non-ruptured Intracranial Aneurysms - A Multivariate Analysis Study

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Background: There are few studies that denote the incidence and underlying mechanisms of cerebral infarction after clipping surgery for non-ruptured intracranial aneurysms. In this study, herefore, we evaluate the incidence and risk factors of silent or symptomatic cerebral infarction after clipping surgery. **Subjects and Methods:** This study included 198 patients who underwent clipping surgery for non-ruptured aneurysms in the anterior circulation for these three years. There were 52 males and 146 females. Their age ranged from 26 to 78 years. Newly developed cerebral infarction was identified using diffusion-weighted MRI or CT scan within two weeks after surgery. Multivariate analysis was employed to independent risk factors for postoperative cerebral infarction. **Results:** New cerebral infarction was found in 31 (15.7%) of 198 patients after surgery. Of these, 14 patients (7.1%) were asymptomatic. However, 15 (7.6%) and 2 (1.0%) patients developed transient and permanent neurological deficits, respectively. Cerebral infarction was located in the perforating artery territory in 24 patients and in the cortical branch territory in 7. The former was very small. The incidence of postoperative cerebral infarction was 47.1% in patients with anterior choroidal artery aneurysm, being significantly higher than those with other aneurysms. Multivariate analysis revealed that the location of aneurysm is an independent predictor for postoperative cerebral infarction ($P=0.0203$). In addition, intracranial atherosclerosis on MR angiography may predict it, although its statistical significance was in a borderline ($P=0.0606$). **Conclusions:** Cerebral infarction after clipping surgery for non-ruptured anterior circulation aneurysms is not rare. The location of aneurysm may be the most powerful predictor for it. Widespread application of intraoperaitve ICG videoangiography and motor evoked potential (MEP) may reduce its incidence in very near future.

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W P38

Blister-Like Aneurysms: Single Center Experience and Literature Review

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Introduction: Blood Blister-like aneurisms (BBAs) are still a controversial entity affecting intracranial vessels, a special type of aneurisms arising from the nonbranching sites of the supraclynoid Internal Carotid Artery (ICA), suspected to originate from a dissection and characterized by an extremely fragile wall, making its treatment very difficult. **Hypothesis: Our aim is to describe the BBAs cases in our center, as well as review the literature about this subject, trying to establish a clearer and more practical concept of BBA, with a special focus on the treatment. Methods:** We analyzed the 10 cases admitted to the University Hospital of Geneva, from 2004 to 2010, 9 of them presenting with Subarachnoid Hemorrhage in whom a BBA was considered to be the responsible of the bleeding, based on CT scan, arteriography or surgical findings. We assessed medical history, type of treatment (Neurointerventional +/- Neurosurgery), complications and clinical outcome. **Results:** The mean age was 48y; 6 women and 4 men; 6 aneurysms on the right supraclynoid ICA, and 4 on the left one; 7 patients immediately complicated with hydrocephalus, 6 of them were treated with an external ventricular drainage, and 1 was treated with lumbar punctures; the treatment of the BBA consisted of stenting and coiling in 5 patients, only stenting in 1 patient, coiling and clipping in 1 patient, only clipping in 1 patient, and conservative treatment in 2 patients; among the complications of these treatment, we found 2 thromboembolic events after stenting in the acute phase; final outcome was good (modified Rankin scale at 3 months less or equal to 2) in 7 patients. **Conclusions:** BBAs should be considered as a segmental vascular disease, more than an aneurysm itself. Regarding our data, stenting and coiling seems to be a safe and effective treatment for BBAs, assuring a good long term follow-up, in spite of possible acute thrombotic complications.

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W P39

Translational Stroke Research: Characterization of a New Embolism-Induced Intracerebral Hemorrhage Model to Assess Neuroprotection and Hemorrhage Reduction

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There has been some progress in the translational development of hemorrhage therapy that successfully reduces the escalating morbidity and mortality rate associated with brain bleeding. However, using an animal model representative of the human condition will be required for additional success. The rabbit large clot embolic stroke model (RLCEM) has previously been used to test drugs and devices for safety, because the model is particularly sensitive to embolism-induced intracerebral hemorrhage (ICH). This study refined the original embolization procedure using an automated, pump-assisted injection method to introduce large blood clots or macroscopic emboli into the middle cerebral artery (MCA) via an indwelling carotid artery catheter. ICH was classified into the following categories: (1) PH- parenchymal hemorrhage, (2) HIN- hemorrhagic infarction, (3) HPT- punctate hemorrhage and (4) SAH-subarachnoid hemorrhage. The study shows that rapid injection of blood clots (360ml/hr, 3 ml volume) produced a model where there is a high ICH incidence rate (79%) and a high stroke success rate (63%), compared to a low stroke success rate (19%) with no ICH when clots were injected at a slow rate (120ml/hr, 3 ml volume). Some of the animals had more than 1 type of ICH present in the brain. For quantitative purposes, we treated each individual hemorrhage observed as a separate entity. ICHs occurred throughout the brain and included the following structures: caudate putamen; thalamus; hippocampus; frontal, parietal, and occipital cortex; hypothalamus; suprachiasmatic area; cerebellum; pons; and midbrain. There were no apparent differences among the groups in the distribution of types or locations of hemorrhages. The rapid injection method, which produces a high ICH rate is particularly useful to study neuroprotective agents to attenuate embolism-induced ICH. In addition, we show that manual injection of blood clots, which produces a lower baseline ICH rate (41%) with a similar stroke success rate (65%), may allow investigators to study pharmacological agents to either up or down-regulate ICH incidence. Lastly, we show that in the rabbit embolic stroke model, hemorrhages are adjacent to areas of 2,3,5-triphenyltetrazolium (TTC)-negative tissue, normally associated with infarcted or ischemic tissue, suggesting that therapeutics that are neuroprotective may also be useful to limit the evolution of ischemic damage associated with a ICH, if not attenuate ICH itself. In conclusion, we have shown that we can modify ICH incidence in the RLCEM without directly affecting survival rate, by adjusting the rate at which an emboli is introduced into the brain vasculature, in particular the middle cerebral artery. In addition, we have provided evidence for distinct area of ischemic tissue (TTC-negative) adjacent to hemorrhages, areas that may be targets for neuroprotective agents to limit the extent of ICH damage.

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W P40

Translational Stroke Research I: Synthesis and In Vitro Optimization of a New Curcumin Hybrid Neurotrophic-Neuroprotective Compound

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The plant polyphenolic curcumin is a multifunctional molecule with upwards of 10 separate activities. However, there are some properties of curcumin that could be improved, including bioavailability and its lack of neurotrophic activity and the ability to inhibit excitotoxicity. To circumvent some of these problems, we synthesized a library of hybrid molecules between cyclohexyl bisphenol A (CBA), a molecule with neurotrophic activity and curcumin. A simple pyrazole derivative, called CNB-001, that eliminates the labile dicarbonyl group of curcumin and stabilizes the molecule, was identified and further characterized as follows. For the in vitro studies, we used (1) an in vitro ischemia assay with HT22 cells treated with 20 μM IAA iodoacetic acid (IAA), an irreversible inhibitor of glyceraldehyde 3-phosphate dehydrogenase (G3PDH), (2) an oxidative stress (Oxytosis) assay with HT22 cells treated with the excitotoxic amino acid glutamate (5 mM), which induces cell death mediated by the depletion of intracellular glutathione and (3) a trophic factor withdrawal (TFW) assay with primary cortical neurons from 18-day-old rat embryos cultured at a low cell density in DMEM/F12 with N2 supplement. For the IAA and oxytosis assays, cell survival was measured using an MTT colorimetric assay. For the TFW assay, viability was determined after 2 days using a fluorescent live-dead assay (and the data presented as the percentage of input cells surviving. First, there was a dose-dependent effect of CNB-001 on the survival of HT22 cells using both the in vitro ischemia (EC_{50} 0.3 μM) and oxidative stress (EC_{50} 0.7 μM) assays. CNB-001 promoted the survival of freshly plated, low-density cultured rat cortical neurons in a dose-dependent manner with an EC_{50} value of 0.7 μM. Thus, CNB-001 has neurotrophic activity in addition to neuroprotective activity. Second, we used the IAA assay to elucidate mechanisms underlying the neuroprotective effects of CNB-001. After IAA treatment, there were decreases in both ERK and Akt phosphorylation that were prevented by treatment with CNB-001. We also found that KN62, a CaMKII inhibitor, reduce CNB-001 neuroprotection and blocked the effects of CNB-001 on both ERK and Akt phosphorylation suggesting that CaMKII regulates the ERK and Akt pathways and is a more proximal target of CNB-001. Since CNB-001 rescues HT-22 cells from ischemia, and both ERK and Akt activation and CaMKII expression are downstream pathways activated by neurotrophic molecules such as BDNF, we determined if BDNF could rescue HT-22 cells expressing the BDNF receptor, TrkA using the in vitro ischemia model. We found that BDNF rescues cells transfected with wild type TrkA (TK4), but not cells containing a mutated nonfunctional receptor (TK1) and this rescue is blocked by KN62. The rescue is not, however, as complete as with CNB-001, suggesting that CNB-001 also functions by other mechanisms that remain to be defined.

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W P41

Translational Stroke Research II: In Vitro Cellular Toxicity Screening of an Optimized Curcumin Hybrid Neurotrophic-Neuroprotective Compound

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In the present study, we used a comprehensive cellular toxicity (CeeTox) analysis panel to determine the toxicity profile for CNB-001 [4-((1E)-2-(5-(4-hydroxy-3-methoxystyryl-)-1-phenyl-1H-pyrazoyl-3-yl)vinyl)-2-methoxy-phenol)], which is a hybrid molecule created by combining cyclohexyl bisphenol A, a molecule with neurotrophic activity and curcumin, a spice with neuroprotective activity. CNB-001 is a lead development compound, since we have recently shown that CNB-001 has significant preclinical efficacy in vitro in 3 separate assays. The industry standard CeeTox analysis assay allows investigators to determine the predicted C_{tox} value (an estimated concentration where toxicity would be expected to occur in a rat 14-day *in-vivo* repeat dose study) for a drug. For this, rat hepatoma derived H4IIE cells were used as the test system. The CeeTox assay measures of cellular toxicity including mitochondrial function, apoptosis, oxidative stress, protein binding, solubility and microsomal metabolic stability. CNB-001 was soluble up to 100 μM using the CeeTox assay system. The drug was not acutely toxic and no effect on membrane integrity or subcellular markers of acute toxicity, with the exception of a decrease in cell proliferation observed with a concentration that produced a half maximal response (TC_{50}) value of 88 μM, suggesting a cytostatic effect. CNB-001 did not affect measures of oxidative stress or apoptosis (i.e. Caspase 3 activity). We found that CNB-001 resulted in an inhibition of Ethoxyresorufin-0-deethylase activity, indicating that the drug may affect cytochrome P4501A activity and that CNB-001 was metabolically unstable using a rat microsome preparation assay system. CNB-001 was metabolized via phase 1 metabolism, since only 42% of parent remained after a 30 minute incubation with rat microsomes. The only 'toxicity' of CNB-001 was a cytostatic effect effect was only observed at 183-643 fold the EC_{50} for neuroprotective/neurotrophic activity using HT22 cell and primary cortical neuron *in vitro* assays. Based upon a proprietary CeeTox algorithm, the C_{tox} Ranking (μM) for CNB-001 was estimated to be 42 μM which places it in the CeeTox Inc. category of moderate to low probability of *in vivo* effects. However, it is important to realize that the C_{tox} ranking, a treatment regimen that may not be necessary for stroke patients. Taken together, the results indicate that there is a significant therapeutic safety window for CNB-001 and that it should be further developed as a novel neuroprotective agent to treat stroke.

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W P42

Translational Stroke Research III: In Vivo Activity and Mechanism of Action of a New Curcumin Hybrid Neurotrophic-Neuroprotective Compound

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We have shown that the curcumin analog CNB-001 has neuroprotective and neurotrophic properties in vitro and has a large safety margin using comparison studies done using HT22 and H4IIE cells. For in vivo characterization of CNB-001, we used the rabbit small clot embolic stroke model (RSCEM), which is a useful translational stroke model and predictor of clinical efficacy (Lapchak, TSR 1(2), 96-107, 2010). We tested the hypothesis that CNB-001 may be neuroprotective following cerebral ischemia using clinical rating scores as the endpoint. CNB-001 or DMSO were administered SC following the injection of small blood clots into the brain vasculature. Behavior was measured 24 hours following embolization in order to calculate the effective stroke dose (P50) that produces neurological deficits in 50% of the rabbits. A treatment is considered beneficial if it significantly increases the P50 compared to control. The initial study used a 5 min post-embolization treatment time, to ensure that the dose and route of administration of the drug can produce a neuroprotective or positive signal. There was a significant improvement in behavior and the P_{50} value for the CNB-001-treated group was increased by 157% compared with control. At this dose there was no overt behavioral response or toxicity within the time frame of the study. In addition, when tested 1 hour post-embolization, CNB-001 significantly ($P<0.05$) reduced stroke-induced behavioral deficits and increased the P_{50} value by 233% compared with the control group. To obtain insight into how CNB-001 functions in vivo, we examined a variety of signaling pathways previously implicated in stroke. Brain extracts were taken at 6 h post-embolism from control, stroked and CNB-001 embolized rabbits. Since the Ras-ERK cascade has been implicated in nerve cell survival in ischemia, we initially examined this pathway. A significant decrease in ERK phosphorylation in the stroked animals relative to control animals was observed, and this decrease was largely prevented in the presence of CNB-001 treatment. PI3K-Akt signaling, which is also implicated in neuronal cell survival following stroke was decreased in the stroked animals but was maintained in the presence of CNB-001. CNB-001 also has BDNF-like activity, and BDNF causes the activation of the ERK and Akt pathways. Since the expression of CaMKII is also increased by BDNF, we assayed CaMKII expression in CNB-001-treated animals. In this study, we found that CNB-001 increased CaMKII expression. Finally, the ER-associated chaperone ORP150 has been linked to the PI3K/Akt and BDNF signaling pathways. ORP150 expression was decreased in the stroked rabbit brains and this decrease was again prevented by CNB-001. In conclusion, CNB-001 promotes behavioral improvement following embolic strokes in rabbits, an effect that may be associated with the normalization of Ras-ERK and PI3K-Akt signaling pathways.

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W P43

12/15-Lipoxygenase Contributes To Brain Damage In Transient Global Cerebral Ischemia

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Background and Purpose: 12/15-lipoxygenase (12/15-LOX) is a major contributor to delayed neuronal cell death and vascular injury following transient focal cerebral ischemia. ALOX15(-/-) mice in which the gene encoding 12/15-lipoxygenase has been knocked out, are protected against transient focal cerebral ischemia. But it is unknown whether similar protection occurs in global cerebral ischemia. In this study, we hypothesized that increased vascular and neuronal 12/15-LOX exacerbates brain damage by causing oxidative stress and the death of neurons in a transient global ischemia model, implying that neurovascular injury should be reduced in ALOX15(-/-) mice after transient global cerebral ischemia. **Methods:** Wild type and ALOX15(-/-) mice were subjected to 20 minutes of transient occlusion of the bilateral common carotid arteries. To test the first part of our hypothesis, immunostaining was used to study 12/15-LOX expression at different times following global ischemia. In addition, a mouse model of 8 minutes of cardiac arrest followed by resuscitation, was employed to confirm the validity of the staining data. 12/15-LOX activity was determined by measurement of 12-HETE (12-hydroxyeicosatetraenoic acid), a 12/15-LOX metabolite in brain homogenates. Co-localization of 12/15-LOX with markers for oxidative stress and apoptosis was employed to study cell death processes. **Results:** 12/15-LOX was increased in a time-dependent manner in the vasculature and in neurons of cortex, striatum, and hippocampus following transient global ischemia. This was accompanied by a time-dependent increase in 12-HETE. Furthermore, 12/15-LOX co-localized with an oxidative stress marker, MDA2 (for proteins modified by oxidized lipids) and with FluoroJade-B (FJ-B), a marker for dying cells. 12/15-LOX expressing cells in the cortex also expressed high levels of apoptosis-inducing factor (AIF), a well-known mediator of non-caspase-related apoptosis. Very similar staining was found in the cardiac arrest model. Subjected to global ischemia, ALOX15(-/-) mice showed reduced FJ-B staining, compared to wild type mice. Likewise, ALOX15(-/-) mice showed reduced MDA2 and cleaved caspase-3 staining. Using a neurological severity score, ALOX15(-/-) mice were found to have less neurological impairment as compared to wild type. **Conclusion:** Taken together these data suggest that 12/15-LOX may contribute to neurovascular injury after global cerebral ischemia, in which activation of oxidative stress markers and both caspase-dependent and caspase-independent apoptotic pathways are involved.

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W P44

Interferon Gamma Contributes to Increased Neural Injury Following Ischemic Stroke

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Background: Immune cells enter the brain following ischemic stroke and initiate an inflammatory response resulting in delayed neural injury. Human umbilical cord blood (HUCB) cells administered 48 hrs following middle cerebral artery occlusion (MCAO) reduced inflammation resulting in decreased infarct volume. These cells migrate to the injured brain and spleen. The spleen contributes to increased neural injury following ischemia, as removal of the spleen prior to MCAO reduces infarct volume at 96 hrs. However, because labeled splenocytes were not found in the brain following MCAO the spleen likely contributes to increased injury through a humoral response. Hypothesis: Increases in splenic production of the pro-inflammatory cytokine interferon-gamma (IFNγ), which activates both microglia and peripheral macrophages in response to injury, is a mechanism by which the spleen contributes to increased neural injury following an ischemic stroke. **Methods:** Experiments were designed to establish a time course for IFNã expression at 3, 24, 48, 72, and 96 hrs post-MCAO (n=3). Immunohistochemistry and ELISA were performed on brain and spleen samples, respectively, from rats which received MCAO and HUCB cell or vehicle treatment 48 hrs post-MCAO (n≥3). To further examine whether IFNã is a mechanism by which the spleen increases neural injury, experiments were performed in which rats received either splenectomy or sham-splenectomy surgeries 2 weeks prior to MCAO, and were then administered recombinant IFNã or vehicle 48 and 72 hrs post-MCAO (n≥4). **Results:** IFNã was present in the brain and the spleen following MCAO and peaked 72 hrs post-MCAO ($p<0.01$). Systemic administration of HUCB cells reduced IFNã levels in both the brain ($p<0.01$) and the spleen ($p<0.01$) at 72 hrs post-MCAO. Mostly T cells, but also B cells and NK cells, were producing IFNã in the injured hemisphere. Splenectomized rats that received IFNã had infarct volumes significantly greater than vehicle treated rats ($p<0.001$), demonstrating recombinant IFNã abolishes the protective effect of splenectomy. **Conclusion:** These results indicate splenic derived IFNã production is a mechanism by which the spleen increases neural injury following ischemic stroke.

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W P45

Neuroprotective Effect Of Agmatine After Focal Cerebral Ischemia In Diabetic Rats

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Diabetes mellitus is a metabolic disorder associated with structural and functional alteration of various organ systems including the central nervous system. The aim of this present study was to investigate the progresses and pathogenesis of cerebral ischemia in diabetes. It is also aimed to determine the neuroprotective effect of agmatine administration during cerebral ischemic insult in diabetes. We established the streptozocine (STZ) induced diabetic model and middle cerebral artery occlusion (MCAO30) model in rat to demonstrate the difference in pathogenesis between simple cerebral ischemia and cerebral ischemia combined with diabetes. Diabetes was induced with streptozotocin (60 mg/kg, i.p.) in male adult rats. Diabetes rats underwent 30min suture-occlusion of the middle cerebral artery (MCAO30), and immediately injected with agmatine (100mg/kg, i.p.) following by reperfusion for 1 and 3 days. Moreover, different neurobehavioral tests were performed. The brain infarct volume was assessed with 2% solution of triphenyltetrazolium chloride (TTC). Western blot and immunohistochemical analysis were performed to determine neuronal nitric oxide synthase (nNOS) and inducible NOS (iNOS) expression in ischemic brain tissues. Caspase-3 activity and TUNEL staining were used to evaluate cellular apoptosis. Agmatine treatment decreased blood glucose in STZ-induced rats mildly. Agmatine treatment significantly improved neurobehavioral activity, and reduced infarct size and edema volume in diabetic MCAO30 rats at 1, 3 day reperfusion period compared with no treatment group ($p<0.01$). Western blotting and immunohistochemistry results depicted that agmatine treatment significantly decreased nNOS and iNOS expression in diabetic MCAO30 rats at 1,3 day reperfusion period ($p<0.01$). Moreover, Immunohistochemisty and TUNEL staining results showed that agmatine treatment significantly decreased number of caspase-3-positive and TUNEL-positive cells in diabetic MCAO30 rats at 1 and 3 day reperfusion period, respectively ($p<0.01$). In conclusion, these results suggest that agmatine may protect brain from focal cerebral ischemic damage in diabetic rats.

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W P46

Akt Isoforms Differentially Protect Against Stroke-induced Neuronal Injury in Vitro and in Vivo

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Background and Objective: Akt is implicated as a pro-survival signal in cerebral ischemic injury, as endogenous Akt phosphorylation transiently increases after cerebral ischemia and reperfusion, and PI3K/Akt inhibitors attenuate the effects of some neuroprotectants. Akt consists of 3 isoforms (Akt1, 2, 3), with predominance of Akt3 in the brain. How Akt isoforms affect stroke outcome, and whether exogenous Akt can protect neurons against ischemic injury is unclear. We examined whether Akt1 and Akt3 exert differential protective effects using in vivo focal ischemia and in vitro oxygen glucose deprivation (OGD) and serum deprivation (SD) models. **Methods:** We cloned constitutively active Akt1 and 3 (containing a src myristoylation signal and an HA-tag), and dominant negative Akt (AktDN) into a lentiviral vector that expresses eGFP via the IRES element, enabling co-expression of the Akt isoform and eGFP. To study exogenous Akt 1, Akt 3 and AktDN, we used an SD model in HT22 hippocampal neuronal cells, an OGD model in primary neuronal cultures, and a focal ischemia model in rats. Akt1, Akt3 and AktDN were expressed in HT22 cells by lipofectamine transfection, and lentivirus-expressing Akt1, Akt3 and AktDN were used to infect primary cortical cultures or stereotaxically injected into the brain cortex to be subjected to focal ischemia. We evaluated neuronal survival using a CCK8 kit in vitro, and measured brain infarction using TTC staining in vivo. **Results:** Western blot analysis showed that lentiviral expression of Akt1 and 3 increased Akt phosphorylation, and microscopy examination showed corresponding GFP expression and HA staining. Both Akt1 and 3 overexpression increased cell viability and decreased ROS production in HT22 cells induced by SD ($P<0.01$). However, Akt3, but not Akt1, increased the cell viability in primary cortical cultures after OGD ($P<0.01$). AktDN had no effect on cell survival in both HT22 cells and primary cortical cultures. Although gene transfer of both Akt1 and 3 reduced infarction size after stroke compared with the control group injected with lentiviral GFP vectors (n=6/group, $P<0.01$), Akt3 overexpression resulted in a smaller infarction than that of Akt1 (n=6, $P<0.05$), whereas AktDN overexpression had no effect. **Conclusion:** Both in vitro and in vivo studies showed that lentiviral-mediated overexpression of active Akt3 confers stronger protection than that of Akt1, suggesting that Akt isoforms have differential effects on neuronal survival after stroke. **Key Words:** cerebral ischemia, Akt1, Akt3, stroke

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W P47

Activation Of Phosphorylation Of The Signal Transducer And Activator Of Transcription-3 By Peroxisome Proliferator-activated Receptor Gamma Agonist Contributes To Neuroprotection In The Peri-infarct Region After Ischemia

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A previous study reported that the peroxisome proliferator-activated receptor gamma (PPARγ) agonist pioglitazone (PGZ) reduced cerebral ischemic damage by inhibiting phosphorylation of the signal transducer and activator of transcription-3 (p-STAT3). However, another study suggested that estradiol was neuroprotective after cerebral ischemia via an increase in p-STAT3 mediated by estrogen receptor α (ERα). Thus, the role of p-STAT3 after cerebral

ischemia remains controversial. To verify the role of p-STAT3 and PPARγ in neuroprotection, we did or did not subject 10-week-old female Wistar rats to bilateral oophorectomy (OVX^+, OVX^-). After 4 weeks we administered 1.0 or 2.5 mg/kg PGZ for 3 days and then performed 90-min middle cerebral artery occlusion-reperfusion (MCAO-R). We subsequently compared OVX^+ and OVX^- rats. Cortical- but not basal ganglia infarcts were significantly larger in OVX^+ than OVX^- rats; they were smaller in PGZ-treated rats. There was an inverse correlation between the infarct size and the expression of PPARγ and p-STAT in the peri-infarct region; PGZ increased their expression independent of estrogen and ERα. Each inhibitor of PPARγ and STAT3 abolished the induction of p-STAT3 and neuroprotection in PGZ-treated rats. Notably, p-STAT3 heterodimerized with PPARγ translocated to the nucleus to bind to specific DNA regions although PPARγ did not bind to DNA directly. The increase in p-STAT3 was associated with the transcriptional activation of anti-apoptotic- and survival genes and the reduction in caspase-3. Our findings suggest that the activation of p-STAT3 by PGZ is essential for penumbral neuroprotection and may be beneficial in elderly men and postmenopausal women with ischemia.

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W P48

Potential for Intravenous Oxygen-Carriers to Improve Oxygenation of Penumbra and Prolong its Lifespan

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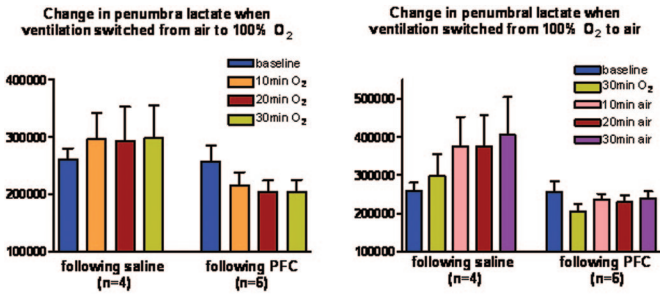
Background: Potentially salvageable penumbral tissue has a limited lifespan and, without intervention, becomes incorporated into irreversibly damaged ischaemic core in the first hours post-stroke. Perfluorocarbon molecules (PFCs, particle size $\sim 0.2\mu m$) are very efficient, non-toxic oxygen carriers that, when combined with oxygen ventilation, could improve oxygenation of penumbra and support its survival. Using a rodent stroke model and magnetic resonance imaging (MRI) we tested the hypothesis that increasing oxygen delivery to penumbra (100% oxygen ventilation with i.v. perfluorocarbon emulsion) would maintain aerobic metabolism and slow penumbral loss, thereby extending time available for therapeutic intervention. **Methods:** Following permanent middle cerebral artery occlusion in rats serial scanning (Bruker 7T Biospin) produced maps of ischaemic injury (from apparent diffusion coefficient, ADC maps) and cerebral blood flow (arterial spin labelling) to define penumbra from perfusion diffusion mismatch. Lactate data in penumbra were generated from MR spectroscopy. Intravenous perfluorocarbon (1.5mls) with 30mins 100% O_2 (n=6) was compared to saline with 100% O_2 (n=4). **Results:** In the control saline group (Figure), penumbra lactate increased by 15% during 30mins hyperoxia and by a further 36% following return to air (30mins). In the PFC group, penumbral lactate decreased by 21% during hyperoxia with a 17% increase on returning to air, thereby maintaining levels below the pre-hyperoxia baseline. ADC lesion expansion during 30mins O_2 + 30mins air, was $69\pm7mm^3$ in the saline group and 37 ± 10 mm^3in the PFC group (mean$\pm$SEM, P$<$0.05). **Conclusions:** Over the study time course, PFC with 100%O_2 inhibited the temporal increase in lactate levels and loss of penumbral tissue suggesting the potential to prolong penumbra survival and extend the time window for intervention and improved outcome.



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W P49

Xenon Echogenic Liposome's Neuroprotection Dose Response During Transient Middle Cerebral Artery Occlusion

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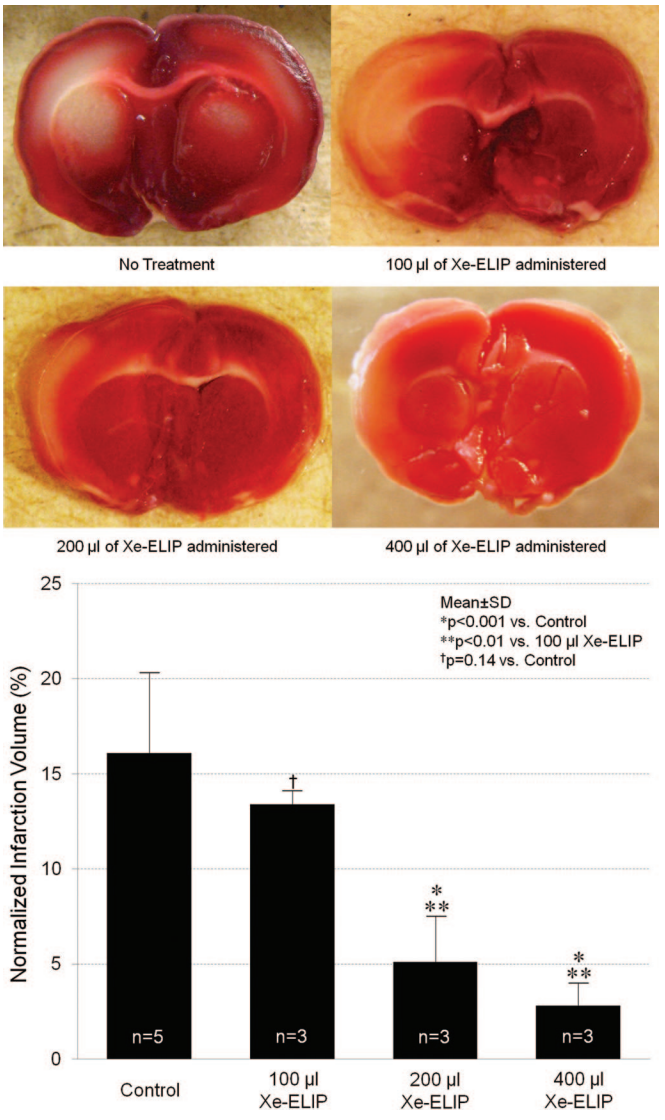
Dose Response of Xenon-Containing Liposomes on Neuroprotective Effects During Transient Middle Cerebral Artery Occlusion Background: Neurologic impairment following ischemic injury continues to complicate the quality of life for stroke survivors. Xenon (Xe) has favorable neuroprotective properties. We have developed a novel methodology for ultrasound-controlled Xe delivery using Xe-containing echogenic liposomes (ELIP), and demonstrated their neuroprotective effects. This study aims to evaluate the dose response of Xe-ELIP to improve neuroprotection at 3 hours after stroke onset. **Methods:** Xe-ELIP were created by a previously developed freeze-under-pressure method. Male Sprague-Dawley rats (n=14 total) underwent right middle cerebral artery occlusion for 2 hours. Rats were evenly divided into treatment groups received 100 il , 200 il and 400 il of Xe-ELIP through the ascending right common carotid artery 60 minutes after reperfusion. Ultrasound (0.26 MPa) was applied over the right internal carotid artery to trigger Xe release from the Xe-ELIP. Infarction size and behavioral outcomes were determined 3 days after intervention. **Results:** The freeze-under-pressure method encapsulated 10 il of Xe in 1 mg of ELIP. Treatment groups that received 200 l or 400 l of Xe-ELIP 3 hours after stroke onset (60 minutes after reperfusion) reduced the infarction size by 68% and 83%, respectively ($p<0.001$ vs. control). There was no improvement for animals with 100 l Xe-ELIP treatment ($p=0.14$) compared to the control group. All behavioral tests mirrored neurological results. **Conclusion:** This study demonstrates the dosage range of Xe-ELIP to provide best neuroprotection when administered within 3 hours, most effectively at 4 mg without toxic effect. This novel strategy for targeted therapeutic gas delivery may facilitate neuroprotection after cerebral ischemia-related injury with the potential to improve stroke treatment.



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W P50

Tissue Plasminogen Activator/Xenon Co-Encapsulation Provides Thrombolysis with Neuroprotection for Thrombotic Stroke Treatment

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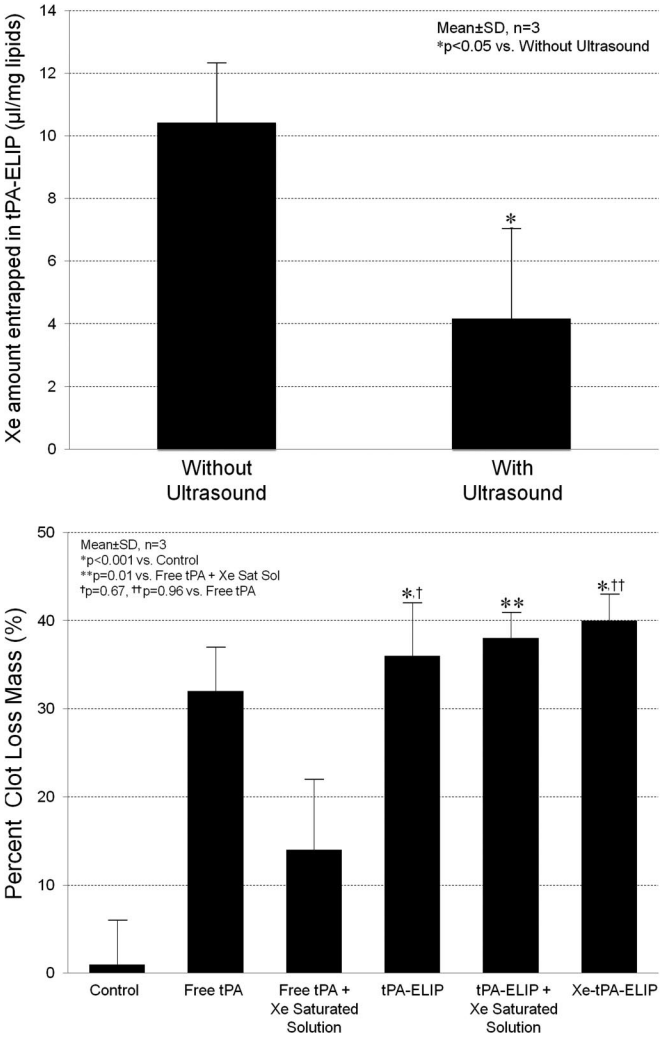
Background: Xenon (Xe) is a nontoxic neuroprotective gas, however its clinical application is limited by delivery methods issues. We have previously demonstrated tissue-plasminogen activator (tPA) encapsulation into echogenic liposomes (ELIP) for targeted ultrasound highlighting and lysis of thrombus. Co-delivery of Xe and tPA to the thrombus with ultrasound-triggered release of Xe and tPA into the cerebral circulation is an attractive strategy for stroke treatment. This study evaluates co-encapsulation of Xe into tPA-ELIP, with ultrasound-controlled site-specific Xe release. **Materials and Methods:** Xe-tPA-ELIP composed of phospholipids and

cholesterol were prepared by the pressurized-freeze method. Whole porcine clots were treated with plasma, free tPA, free tPA with Xe saturated solution, tPA-ELIP, tPA-ELIP with Xe saturated solution, and Xe-tPA-ELIP. Clots were weighed before and after 30 minutes of treatment, and percent clot mass loss was reported. Ultrasound (1 MHz, continuous wave, 2 W/cm^2, for 10 sec) was used to trigger the release of Xe from Xe-tPA-ELIP. Xe release from Xe-tPA-ELIP was evaluated by comparing the total Xe amount encapsulated before and after ultrasound application. **Results:** Ten il of Xe was entrapped into 1 mg of tPA-ELIP with retention of ultrasound reflectivity. Xe release of Xe-tPA-ELIP was enhanced with ultrasound activation (62±19% increase; P<0.05 vs. No ultrasound). Xe-tPA-ELIP (40±3%) and tPA-ELIP (36±6%) resulted in effective clot lysis (both P<0.001 vs. control) with an effect similar to treatment with free tPA (p=0.67 and p=0.96 vs. free tPA). Xe saturated solution inhibited free tPA activity (14±8%). This inhibitory effect by Xe was negated by encapsulation of tPA into ELIP (38±3%; p=0.01 vs. Xe saturated solution), suggesting a protective effect of the liposomes for tPA activity when delivered together with Xe. **Conclusions:** We have demonstrated co-encapsulation of a neuroprotective agent, Xe, and a thrombolytic agent, tPA, into ELIP with effective clot lysis and drug release using ultrasound. Xe-tPA-ELIP has an exciting potential with targeted thrombolytic delivery and ultrasound-facilitated neuroprotective agent release into the brain for thrombotic stroke treatment.



Author Disclosures: T. Peng: None. S.T. Laing: None. H. Kim: None. D.D. McPherson: None. S. Huang: None.

W P51

Neuroprotection of VELCADE is associated with Downregulation of Toll-like Receptor Signaling Pathway in Aged Rats after Stroke

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Background and Purpose: Activation of toll-like receptor (TLR) signaling pathway exacerbates ischemic neuronal damage. The present study tests the hypothesis that treatment of VELCADE, a selective proteasome inhibitor, modulates the TLR signaling pathway leading to neuroprotection in aged rats after stroke. **Methods:** Male Wistar rats at the age of 18 months were subjected to embolic middle cerebral artery occlusion (MCAo). VELCADE at a dose of 0.2mg/kg was intravenously administered 2h after stroke onset (n=12). Ischemic rats receiving the same volume of saline were used as a control group (n=15). Neurological functional outcome and infarct volume were measured. TLR2 and TLR4, and NF-êB expression were measured immunohistologically on brain tissue 6h and 24h after stroke onset. To examine the effects of VELCADE on neuronal TLRs and their downstream target gene expression, primary rat cortical neuronal cultures were challenged by oxygen and glucose deprivation (OGD) in the absence or presence different concentrations of VELCADE (0.1, 1, or10ng/ml). **Results:** In the normal brain, the immunoexpression of TLR 2 and TLR 4 was not detectable. Occlusion of the MCA for 6h substantially increased the density of TLR2 (137.2±27.2/mm^2, n=3) and TLR4 immunoreactive vessels (130±30.9/mm^2, n=3), which was co-localized to increased NF-kB positive vessels. However, 24 after MCAo, in addition to vessels, TLR2 and TLR4 immunoreactive neurons were also detected in the ischemic boundary region. Treatment with VELCADE significantly reduced density of vessels with TLR2 (44.4±4.2/mm^2 vs 73.4±4.3/mm^2), TLR4 (39.9±3.4/mm^2 vs 64.8 ±3.9mm^2), and NF-êB expression (16.9±2.2/mm^2 vs 29.2±3.1mm^2) compared with saline treated rats. Moreover, VELCADE significantly reduced infarct volume (20.9±2.0% vs 31.2±3.4%) and modified neurological severity score (7.3±0.3 vs 9.0±0.4) 7 days after stroke compared with saline treated rats. In vitro, Western blot analysis revealed that OGD for 3h robustly upregulated TLR2, TLR4, MyD88, an essential adaptor for TLR signaling, NF-êB, and Caspase 3 protein levels in neurons. VELCADE at doses of 1 and 10ng/ml led to a 50-100% reduction in OGD upregulated TLR2, TLR4, MyD88, NF-êB, and Caspase 3. **Conclusions:** The present study provides a novel mechanism by which VELCADE suppresses ischemia-activated TLR signaling pathway in cerebral endothelial and neuronal cells, leading to reduction of ischemic cell damage and improvement of neurological outcome.

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W P52

VELCADE Suppresses Tissue Plasminogen Activator-induced Genes That Promote Coagulation And Vascular Permeability In Cerebral Endothelial Cells Of Aged Rats After Stroke

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Background and Purpose: Treatment of experimental stroke with a proteasome inhibitor, VELCADE, neutralizes tissue plasminogen activator (tPA) aggravated BBB disruption, amplifies the thrombolytic effects of tPA, and exerts potent neuroprotection. The present study investigated the effect of VELCADE on expression of genes mediating coagulation and vascular permeability in single cerebral endothelial cells of the aged rat after stroke. **Methods:** Male Wistar rats at the age of 18-20 months were treated with VELCADE (0.2 mg/kg, n=4) alone, tPA (5 mg/kg, n=4) alone, VELCADE in combination with tPA (n=4), or saline (n=5) 2h after embolic middle cerebral artery occlusion (MCAo). All rats were sacrificed 24h after MCAo. Single cerebral endothelial cells were isolated by laser-capture microdissection from brain tissue immunostained with an antibody against von Willibrand factor (vWF), a marker of endothelial cells, and expression of matrix metaloproteinase 9 (MMP-9) intracellular adhesion molecule-1 (ICAM-1) and plasminogen activator inhibitor-1 (PAI-1) was assayed by real time RT-PCR. **Results:** Stroke significantly (P ± 1.3), ICAM-1 (2.4 ± 0.3), and PAI-1 (1.5 ± 0.8) of single endothelial cells in the ischemic boundary regions compared with the levels in homologous areas of the contralateral hemisphere. Treatment with tPA alone further increased MMP-9 (75 ± 2.2), ICAM-1 (133 ± 2.1), and PAI-1 (257 ± 22.7) in the ischemic boundary regions compared with levels in rats treated with saline. However, VELCADE monotherapy significantly (P<0.05) reduced mRNA levels of MMP-9 (7.9 ± 1.2), ICAM-1 (1.4 ± 0.1), and PAI-1 (1.1 ± 0.2) compared with saline treated rats. Moreover, in rats treated with VELCADE in combination with rtPA, VELCADE significantly reduced tPA-upregulated MMP-9 (8.0 ± 1.2), ICAM-1(1.4 ± 0.2) and PAI-1(2.2 ± 0.2) expression compared with levels in rats treated with saline. **Conclusion:** The present study suggests that downregulation of ischemia- and tPA-induced MMP9, ICAM-1 and PAI-1 in cerebral endothelial cells by VELCADE could contribute to beneficial effects of VELCADE on the neurovascular unit in the aged rat.

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W P53

Caspase Activation and MAPK Pathways are Important for Endogenous Neuroprotection in Suprachiasmatic Nucleus Neurons

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Background: Currently few strategies exist to protect brain cells from stroke. Suprachiasmatic nucleus (SCN) neurons are naturally resistant to excitotoxic challenges that are lethal for other brain regions. We are trying to understand the mechanisms behind this endogenous neuroprotection in order to exploit these processes to defend against stroke. **Methods:** Immortalized cultures derived from the SCN (SCN2.2) and from the neighboring hypothalamus (GT1-7) were treated with 10 mM glutamate (Glu) or media in the presence or absence of inhibitors to caspase 3,8, and 9 and ERK. Cell death was assessed by the live dead assay and TUNEL. Caspase activity was quantified with an activity assay. Members of the MAPK pathway were evaluated by immunoblot. A cardiac arrest model of global ischemia was also used to compare levels of activated caspases after ischemia or sham surgery. **Results:** In both our cell culture model and our in vivo global ischemia model, caspases 3, 8 and 9 were higher in the

SCN than in other neurons. Surprisingly, following either Glu or global ischemic insult, activity of all 3 caspases failed to increase in SCN, but did increase in other neurons. Inhibition of ERK allowed caspase activity levels to increase in the SCN following Glu challenge, and resulted in cell death in the previously resistant SCN. Exposure to Glu in the SCN2.2 cells caused a decrease in p38 levels and an increase in pERK levels. Just the opposite was seen in the GT1-7 cells, in which Glu exposure caused an increase in p38 and a decrease in pERK. **Conclusions:** SCN neurons are resistant to both Glu excitotoxicity and global ischemia through inhibition of caspase activation (associated with higher baseline levels) and facilitation of ERK activation. Further investigation into these endogenous pathways of neuroprotection is needed.

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W P55

Recombinant Expression Of Arginine Decarboxylase Rescues Mouse Cortical Neural Stem Cells From Oxidative Burden

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Ischemia/reperfusion injury ends up in the cascade of generating peroxinitrite and hydroxyl radical, which are capable of damaging lipids, proteins and DNA. Neural stem cells (NSCs) have attracted enormous attention for their potential applications in ischemic injury, but little is known about how the unique properties of NSCs are affected by oxidative stress prevails at the injury site. We have investigated the effects of stress induced by H_2O_2 on mouse NSCs. Agmatine, an endogenous primary amine and a novel neuromodulator synthesized from the decarboxylation of L-arginine catalysed by arginine decarboxylase (ADC) reported to possess neuroprotective properties. In this present study we determined whether the expression of ADC in NSCs can prevent the cells from stress injury. Retrovirus expressing human ADC (*v*hADC) was generated using a pLXSN vector. Cortical NSCs were infected with *v*hADC and subjected to H_2O_2 injury (200 μM for 15 hrs). Immunocytochemical staining results showed high expression of hADC protein in the *v*hADC infected NSCs (ADC-NSCs). HPLC analysis revealed high concentration of agmatine in the ADC-NSCs. H_2O_2 induced increase in lactate dehydrogenase leakage and intracellular ROS formation in NC and LXSN-NSCs but were prevented in ADC-NSCs ($p < 0.05$). DNA fragmentation and chromatin condensation following H_2O_2 injury was effectively abolished in ADC-NSCs. Apoptotic proteins p53, bax and caspase-3 cleavage showed significant ($p < 0.05$) decreased expression in ADC NSCs compared with contol and LXSN-NSCs suggesting the prevention from apoptotic cell death. The results of this study for the first time demonstrated that retroviral delivered hADC genes in NSCs synthesized agmatine endogenously and the ADC-NSCs were protected from oxidative injury which were evidenced by decrease in the LDH leakage by free radical scavenging, reduced chromatin and DNA fragmentation, prevented the apoptotic cell death. Our findings have opened up new avenues and more effective therapeutic approaches for improving the microenvironment/niche to which the stem cells homes and must resides during transplantation in ischemic and neurodegenerative diseases.

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W P56

Partial Ablation of Neuroprogenitor Cells in the Nestin-δ-HSV-TK-eGFP Transgenic Mice Did Not Affect Stroke Size

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Backgrounds: Emerging data suggests that there is a strong association between post-stroke functional recovery and neural regeneration. In order to assess the contribution of neurogenesis to post-stroke outcome, we adapted a causal approach to specifically ablate neuroprogenitors by gene targeting. In nestin-δ-HSV-TK-eGFP transgenic mice, the expression of a truncated viral thymidine kinase gene and an EGFP gene under the control of a nestin promoter is restricted to neural progenitor cells, enabling the conditional attenuation of neurogenesis by ganciclovir (gcv) and tagging of neural stem cells. The current study sought to investigate the degree to which ischemia-induced regeneration is dependent on the survival and differentiation of early progenitor cells and to determine whether ablation of neuroprogenitor cells affects stroke outcome. **Methods:** Gcv (200 mg/kg/day) or vehicle (saline) was administered via osmotic pumps in nestin-δ-HSV-TK-eGFP transgenic mice for 4 weeks beginning at six weeks of age. Stroke was induced by the distal MCAO method. In the gcv-treated group, both sham and stroke mice continued to receive gcv until 8 days following MCAO. All mice were euthanized at 8 days after MCAO or sham surgery and processed for immunohistochemistry. Double immunofluorescence staining for GFP/DCX was performed to quantify the type-1 (GFP immunoreactive) and the more differentiated type-2 progenitor cells (DCX immunoreactive) in the subventricular zone (SVZ) and the dentate gyrus (DG). Infarct volume was determined by unbiased stereology. **Results:** Following 4 weeks of gcv treatment, both type-1 and type-2 progenitor cells were reduced by 90% in the DG of the sham. Although MCAO increased the number of type-1 and type-2 progenitor cells, even in the continued presence of gcv, there was still a 60% reduction of dentate progenitor cells among the gcv-treated mice, compared to those treated with vehicle. The magnitudes of ablation by gcv and increase by MCAO were similar for both types of progenitor cells in the SVZ. Four weeks of gcv treatment did not impair stroke-induced gliogenesis. However, gcv reduced the dendritic arborization of DCX cells in the DG and SVZ. Although mice with conditional ablation of neuroprogentior cells had a tendency to have a larger infarct volume (gcv: 5.4 ± 1.6 mm^3; vehicle: 3.5 ± 1.8 mm^3; $p>0.5$), the difference was not statistically significant. **Conclusions:** Conditional partial attenuation of neuroprogenitor cells can be successfully achieved in nestin-δ-HSV-TK-eGFP transgenic mice with stroke, without affecting stroke-induced gliogenesis. The partial ablation of neuroprogenitor cells by 60% prior to stroke did not significantly worsen the stroke size. Ongoing investigation will determine whether the reduction in neurogenesis impairs post-stroke functional recovery and to what extent neurogenesis is restored following the removal of gcv.

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W P57

Therapeutic Time Window, Dose Response, and Biodistribution of Autologous Bone Marrow Mononuclear Cells for Ischemic Stroke

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Background: Mononuclear cells (MNCs) from the bone marrow are being investigated in phase I clinical trials in stroke patients. However, dose response, therapeutic time window and biodistribution have not been well-characterized in animal stroke models. **Methods:** 32 Long Evans male rats (3 months old) underwent common carotid artery/middle cerebral artery occlusion (CCA/MCAo) for 3 hrs and then 24 hrs later were randomized to receive saline IV or a bone marrow aspiration followed by an IV infusion of separated autologous MNCs. Animals that were assigned to MNCs received 1 million/kg, 10 million/kg or 30 million cells/kg and were evaluated on the cylinder and corner tests up to 28 days after stroke. In a separate experiment, 26 Long Evans rats underwent CCAo/MCAo, were randomized at 72 hrs or 7 days after stroke to receive a saline injection or autologous bone marrow MNCs (10 million/kg), and evaluated on the cylinder and corner tests up to 28 days after stroke. MNCs were tracked using Q-dot nanocrystals to monitor their migration and survival. **Results:** Animals treated with 10 million or 30 million cells/kg had significant reductions in neurological deficits compared to saline controls on both tests ($p<0.05$). There were no significant differences between 10 and 30 million cells/kg at 28 days. Animals treated with 1 million cells/kg had no significant differences in deficits on either test compared with saline treated controls. Animals treated with MNCs up to 72 hrs after stroke showed a significant reduction in neurological deficits by 28 days ($p<0.05$). Animals treated at 7 days did not show a difference in behavior on either test compared to saline controls throughout the study period. Labeled MNCs were found in the brain, spleen, lung, liver, and kidney at 1 hr and exponentially decreased to near undetectable levels over the ensuing week after injection. **Conclusion:** In the CCA/MCA model, we found a maximum reduction in neurological deficits at 10 and 30 million cells/kg and a therapeutic time window up to 72 hrs after stroke.

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W P58

Superiority Of Intra-arterial Delivery Of Auotologous Mononuclear Cells Compared With Intravenous Delivery In Ischemic Stroke

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Background: Bone marrow mononuclear cells (MNCs) is an investigational autologous cellular therapy for ischemic stroke. Both IV and intra-arterial (IA) routes of delivery are currently being explored in clinical trials but the optimal model of delivery is debatable. Recent studies from our laboratory suggest that rats treated with IA delivery of MNCs have better outcomes after stroke compared with rats treated with intravenously administered MNCs. One of the principal mechanisms of MNC-induced stroke recovery is immune-modulation and trophic factor up-regulation. **Purpose:** To investigate mechanisms that might partially explain the differences in outcome between IV and IA delivery of MNCs, we measured cytokines and cell death of peri-infarcted tissue as well as infarct size of rats treated either with IA or IV MNCs after stroke. **Methods:** Stroke was induced in middle-aged Long Evans rats by middle cerebral artery occlusion (MCAO). At 24 hrs after stroke, rats were randomized to receive an IV saline injection or an IV or IA (internal carotid artery) administration of 10 million autologous MNCs. Brain tissue from the ipsilateral cortex at 48 hrs after stroke was homogenized and the supernatant was analyzed for IL-1â using ELISA. In separate experiments, animals underwent the same protocol but brains were perfusion fixed and analyzed by TUNEL for cell death. In a third set of experiments, animals underwent the same protocol and at 7 days were sacrificed for infarct size analysis. Data are Mean $\pm$ SE of 5-7 animals in each experimental group and analyzed by ANOVA. **Results:** IL-1 â was significantly ($p<0.05$) decreased in the brains of IV or IA treated groups compared with saline controls (see table 1). There was significantly more reduction in IL-1â in the IA group as compared with the IV MNC group ($p<0.05$). TUNEL-positive cells were significantly reduced in the peri-infarcted regions of IV or IA-MNC-injected rats, respectively, compared with saline treated animals ($p<0.05$). IV and IA MNC-treated rats exhibited significantly reduced infarct size as compared with saline-treated rats. Greater protection was observed in the IA compared with the IV MNC administered groups ($p<0.05$). **Conclusion:** These findings suggest that MNCs promote cytoprotection in peri-infarct areas and reduce infarct size maturation after ischemic stroke. Intra-arterially administered MNCs led to better cytoprotection and decreased inflammatory cytokines at the site of ischemic injury as compared with intravenously delivered MNCs. The delivery approach might therefore influence the extent to which MNCs may promote recovery after stroke.

Table 1	Saline	Intravenous (IV)	Intra-arterial (IA)
IL-1 β (pg/ml)	1540 ± 40	1366 ± 50	640 ± 40
TUNEL + cells	74 ± 10	61 ± 4	36 ± 5
Infarct Volume (mm^3)	140 ± 10	120 ± 9	110 ± 8

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W P59

The Efficacy of Human Umbilical Tissue-Derived Cells in Restoring Neurological Function in a Rodent Transient Middle Cerebral Artery Occlusion (MCAo) Stroke Model: A Route of Administration Study

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Background: The main treatment for ischemic stroke - intravenous administration of tissue plasminogen activator - is only efficacious within 4.5 hours of the ischemic event. There is therefore a significant medical need to develop novel technologies for stroke patients. Human umbilical tissue-derived cells (hUTC) are currently evaluated. In this study, the optimal route of administration was analyzed, using a rodent transient middle cerebral artery occlusion (MCAo) model. **Method:** 120 male Wistar rats underwent transient middle cerebral artery occlusion (MCAo). All animal were then randomly assigned to one of 10 groups, for a total of 12 animals per group (8 animals for behavioral testing and 4 animals for serum evaluation and hUTC detection at 60 days), as defined below. Group 1: 3 million (MM) hUTC administered intravenously (IV); Group 2: 2 MM hUTC administered intraarterially (IA); Group 3: 1 MM hUTC administered via intracisterna magna (ICM); Group 4: 1 MM hUTC administered intrathecally (IT); Group 5: 1 MM hUTC administered intracerebrally (IC). Groups 6 to 10 were control groups treated with vehicle only (Group 6: IV; Group 7: IA; Group 8: ICM: Group 9: IT; Group 10: IC). Behavioral tests were performed at day 1 post-stroke and weekly thereafter. These tests included the modified neurological severity score (mNSS), the foot-fault test and the adhesive test. All animals were sacrificed at day 60. Histological assessments included infarct area measurement, immunohistochemical analyses to evaluate cell proliferation, cell death, and new vessels and synaptogenesis. **Results:** Significant functional improvements in behavioral test scores in hUTC-treated groups were observed as early as Day 14 post stroke. The IV route of administration exhibited the most consistent functional recovery across all 3 behavioral tests as compared to controls treated with vehicle only. The IC route was the second-most consistent. IA, ICM and IT routes of administration also demonstrated significant points of functional recovery but not with the consistency demonstrated with IV or IC administration. Histological evaluation showed that hUTC treatment increased cell proliferation, vessel number and microvessel diameters in the ipsilateral ischemic hemisphere. Apoptosis was decreased in animals receiving IC and IV delivery of hUTCs while synaptophysin expression was increased in all hUTC treatment groups except those receiving IT delivery. Antibodies generated against hUTC were detected in all cell treatment cohorts as was expected in this xenogenic model this however did not negatively impact the significant behavioral recovery that was observed. Efforts to detect hUTC via human genomic DNA detection methods proved inconclusive. **Conclusion:** Significant reduction in behavioral deficits was observed in all cell treatment cohorts with intravenous administration demonstrating the most robust effects.

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W P60

Bone Marrow Stromal Cells Promote Skilled Motor Functional Recovery and Enhance Contralesional Axonal Connections after Ischemic Stroke in Adult Mice

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To elucidate the neuroanatomical mechanisms underlying motor functional recovery after stroke treated with bone marrow stromal cells (BMSCs), we investigated axonal connections of the corticospinal tract (CST) between the contralesional cerebral cortex and the stroke-impaired side of the spinal cord in adult mice. Adult male mice, in which the CST was transgenicly labeled with yellow fluorescent protein (YFP), were subjected to right hemispheric pyramidotomy (PT) and right permanent middle cerebral artery occlusion (MCAo) or sham surgery. One day later, the mice were randomly selected to receive 0.4 ml of phosphate-buffered saline (PBS) or 1 x 10^6 BMSCs in PBS injected into a tail vein. Foot-fault test and single pellet reaching test were performed 3 days after MCAo and weekly thereafter to monitor skilled motor functional deficit and recovery. To retrogradely label axonal pathways between the impaired left forelimb and the cerebral cortices, 10 μl of trans-synaptic tracer pseudorabies virus (PRV)-614-m red fluorescent protein (RFP) were injected into the left forelimb flexor muscles 4 weeks after stroke (4 days before sacrifice). The brain and cervical cord were processed for vibratome sectioning to detect the RFP labeling in the cortical pyramidal neurons and the YFP labeling in the denervated side of the spinal cord with a confocal imaging system. Significant functional improvements were evident at 4 weeks compared with 3 days after PT and MCAo in mice treated with PBS ($n=8$, $P<0.01$) or BMSCs ($n=10$, $P<0.01$), but not in mice suffering PT and sham MCAo treated with either PBS ($n=8$) or BMSCs ($n=10$), while BMSC treatment significantly increased functional recovery compared with PBS treatment in the PT-MCAo mice ($p<0.05$). Furthermore, in the PT-MCAo mice, both CST axonal density in the denervated side of cervical gray matter and RFP-labeled pyramidal neurons in the left intact cortex were significantly increased compared with PT-sham MCAo mice ($p<0.01$). BMSCs significantly enhanced both CST density and RFP labeling in PT-MCAo mice ($p<0.05$), but not in PT-sham MCAo mice. Our data suggest that BMSCs amplify stroke-induced contralesional neuronal innervation, which may, at least in part, promote motor recovery after stroke.

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W P61

Combination Treatment with Low-dose Niaspan and Tissue Plasminogen Activator Provides Neuroprotection after Embolic Stroke in Rats

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Introduction: Niaspan, an extended-release formulation of Niacin (vitamin B3), has been widely used to increase high density lipoprotein (HDL) cholesterol and to prevent cardiovascular diseases and stroke. We have previously demonstrated that Niaspan (40mg/kg) administered at 2 hours after stroke induces neuroprotection. Tissue plasminogen activator (tPA) is an effective therapy for acute stroke, but its use remains limited by narrow therapeutic window. In this study, we tested whether combination treatment with low-dose Niaspan (20mg/kg) and tPA administered 4 hours after embolic stroke in a rat model provides neuroprotection. **Methods:** Adult male Wistar rats ($n=8$/group) were subjected to embolic middle cerebral artery occlusion (MCAo) and treated with low-dose Niaspan (20mg/kg) alone, tPA (10mg/kg) alone, combination of low-dose Niaspan and tPA, or Saline (control) 4 hours after stroke. A battery of functional outcome tests was performed. Rats were sacrificed at 7 days after MCAo and lesion volumes were measured. To investigate the underlying mechanism of combination treatment neuroprotective effect, deoxynucleotidyl transferase-mediated dUTP nick-end labeling (TUNEL), cleaved caspase-3, tumor necrosis factor alpha (TNF-alpha), matrix metalloproteinase-9 (MMP-9) and toll-like receptor 4 (TLR-4) immunostaining were performed. **Results:** Combination treatment with low-dose Niaspan and tPA decreased mortality rate and significantly improved functional outcome compared to saline control group ($p<0.05$), while treatment with Niaspan or tPA alone did not significantly decrease mortality or improve functional outcome compared to saline control group. Additionally, combination treatment significantly reduced infarct volume compared to saline control group ($p=0.006$) and infarct volume was significantly correlated with functional outcome ($p=0.0008$; $r=0.63$). Monotherapy with Niaspan or tPA did not significantly decrease infarct volume compared to saline control group. Combination treatment reduced apoptosis as measured by significant reduction in the number of TUNEL-positive cells and cleaved caspase-3 expression in the ischemic brain compared to saline control group ($p<0.05$). Combination treatment also significantly reduced the expression of TNF-alpha, MMP-9 and TLR-4 in the ischemic brain compared to Niaspan, tPA and saline treatment groups ($p<0.05$). **Conclusion:** Treatment of stroke with combination of low-dose Niaspan and tPA at 4 hours after embolic stroke reduces infarct volume, improves neurological outcome and provides neuroprotection. The neuroprotective effects of combination treatment were associated with reduction of apoptosis and attenuation of TNF-alpha, MMP-9 and TLR-4 expression.

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W P62

Niaspan Treatment Promotes Vascular Remodeling And Improves Functional Outcome After Stroke In Type 1 Diabetes Rats

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Diabetes mellitus is a risk factor for stroke. Niaspan (a prolonged release formulation of niacin) treatment of stroke increases vascular stabilization and improves functional outcome after stroke in wild type (WT) rats. In this study, we investigated the changes and the molecular mechanisms of cerebral vascular damage after stroke in type-1 diabetic (T1DM) and tested the therapeutic effect of Niaspan in T1DM-rats. T1DM was induced in adult male Wistar rats via injection of streptozotocin. At 14 days after induction of diabetes, rats were subjected to 2h transient middle cerebral artery occlusion (MCAo) and treated without or with Niaspan 40mg/kg starting 24h after MCAo daily for 14 days ($n=17$/group). WT-rats were also subjected to 2h MCAo. Compared to WT-MCAo rats, the ischemic lesion volume was not increased in T1DM-rats, however, T1DM-rats exhibited significantly increased brain hemorrhage and decreased functional outcome after stroke compared to WT-MCAo rats ($p<0.05$). T1DM-rats had significantly increased blood glucose level and blood-brain barrier (BBB) damage measured by endothelial barrier antigen (EBA), ZO1 (a tight junction protein), and desmine (a pericyte marker) compared to WT-MCAo rats. Niaspan treatment of stroke in T1DM-rats significantly decreased brain hemorrhage and BBB damage as well as promoted vascular remodeling measured by vWF, desmine and a-SMA immunostaining and improved functional outcome after stroke compared to non-treatment T1DM-control rats ($p<0.05$). To further investigate the mechanisms of Niaspan-induced vascular remodeling, Angiopoietin-1(Ang1), Ang2, matrix metaloproteinase-9(MMP9) and toll-like receptor-4 (TLR4) expression were measured in the ischemic border zone (IBZ). T1DM-rats exhibited significantly increased Ang2, MMP9 and TLR4 expression, but decreased Ang1 expression in the IBZ compared to WT-MCAo rats ($p<0.05$).

Niaspan treatment significantly decreased Ang2, MMP9 and TLR4 expression and increased Ang1 expression in the IBZ compared to T1DM-control rats. In vitro data show that arterial explant cell migration significantly decreased in arteries derived from T1DM compared to WT-rats. Niacin and Ang1 treatment increased artery cell migration compared to non-treatment T1DM-control ($p<0.05$). Anti-Ang1 significantly decreased Niacin-induced arterial cell migration. These data indicate that T1DM-increases brain hemorrhage and vascular damage as well as decreases functional outcome after stroke compared to WT-MCAo animals. Niaspan treatment attenuates the increased brain hemorrhage, vascular damage and improves functional outcome after stroke in T1DM animals. Niaspan may provide novel therapeutic effects for the treatment of T1DM-stroke and Ang1 contributes to Niaspan-induced vascular remodeling.

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W P63

Transplanted Adult Mouse Neural Stem/progenitor Cells Containing Arginine Decarboxylase Gene Promote Functional Repair And Plasticity After Experimental Stroke

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The transplantation of neural stem/progenitor cells (NPCs) is a promising therapeutic strategy for several ischemic models including stroke. However, transplanted NPCs have some limitations - low viability by deterioration of microenvironment, mal-differentiation and inflammation in ischemic region. Therefore, approaches towards enhancing NPCs therapeutic modality remain as an elusive goal. Here, we suggested that NPCs infected with retrovirus containing human arginine decarboxylase genes (hADC) which can synthesize agmatine endogenously ameliorated ischemic injury, regulated proliferation and differentiation of NPCs *in vivo*. Male Sprague-Dawely rats (280±15g) were subjected to 60min MCAO by well established method. Animals were divided into 4 different group; experimental control group, agmatine treatment group, mock vector (LXSN) infected-NPCs transplantation group, hADC infected-NPCs transplantation group. Animals were transplanted with BrdU-labeled NPCs ($1*10^6$ cells/10il, single dose) 7days after injury. To determine the functional recovery, rota-rod and limb placing test were excuted after MCAO. Immunohistochemistry was performed with anti-Ki67, anti-BrdU, anti-doublecortin (DCX), anti-nestin, anti-Tuj1, anti-GFAP and anti-Olig2 antibodies to verify whether hADC-NPCs transplantation could induce proliferation and differentiation at the injury site. Behavior experiments showed that rats transplanted with transgenic NPCs and agmatine treatment improved the score of both rota rod and limb placing tests depicting the neurological motor functional recovery compared with experimental control and LXSN-NPCs transplantation group. Reflex response was regained to 70% in hADC-NPCs transplantation and agmatine treatment group, but experimental control group recorded 50% reflex response for 4weeks after MCAO. Immunohistochemistry results showed numerous Ki67, BrdU and DCX-positive cells in hADC-NPCs transplantation and agmatine treatment group at 14days after MCAO representing the activation of proliferation at the injured site. Moreover, the hADC-NPCs transplanted group expressed more of nestin, Tuj-1, GFAP and Olig2 immunopositive cells compared with experimental control and LXSN-NPCs transplantation group showing that the transplanted NPCs were differentiated to mature neural cells at 28days after injury. Overall results demonstrate that combined treatment improves the microenvironment at the injury site and has a therapeutic clue for functional repair against CNS injuries.

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W P64

Essential Role Of Interleukin-6 For Post-stroke Angiogenesis

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Abstract Rationale: There is still a paucity of studies investigating longer-term endpoints after ischemic stroke. The pleiotropic cytokine interleukin (IL)-6 mediates multiple effects which may be both beneficial and detrimental to the injured brain but its impact on regeneration and chronic outcome after cerebral ischemia is not known. Objective - Here, we tested the hypothesis that IL-6 is an integral part of the regenerative long-term response of the brain to cerebral ischemia and is required for post-stroke angiogenesis. **Methods and Results:** We investigated the influence of IL-6 on long-term outcome in a well-characterized model of mild ischemic stroke. To do so, IL-6 knockout (IL6-/-) vs. wildtype littermate mice were subjected to 30 minutes of middle cerebral artery occlusion (MCAo) and reperfusion. As assessed by microarray analysis, there was a significant up regulation of angiogenesis-associated gene transcription at 2 but not at 10 days after MCAo in wildtype mice which was largely blunted in IL-6-/- mice. Similarly, circulating VEGF levels were elevated early after insult in wildtype, but not in IL-6-/- mice. Also, ischemia-induced STAT3 phosphorylation observed in wildtype mice was completely absent in IL-6 deficient mice. A 7-day series of daily bromodesocyuridine injections was begun on the day of MCAo. Histologic outcome at 28 days after MCAo/reperfusion revealed higher numbers of newly generated endothelial along with macrophage/microglial cells in wildtype compared to IL-6-/- mice. The density of perfused microvessels which was quantified using endovascular, auto-fluorescent Evans blue staining and tiled-field imaging was increased density of perfused microvessels in ischemic striatum of wild-type mice which was blunted in IL-6-/- mice. Moreover, while ischemic lesion sizes did not differ at early time points after MCAo, IL-6-/- mice showed increased lesion volumes and worse functional outcome at 4 weeks. **Conclusion:** These results identify IL-6 as an essential factor for post-stroke angiogenesis affording long-term histologic and functional protection.

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W P65

Roles of PDGF-PDGF-Rβ Signaling in Brain Pericytes in Ischemic Stroke

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Growing bodies of evidence suggest that brain pericytes play various important roles in brain functions, such as regulation of capillary blood flow, maintenance of blood-brain barrier, and angiogenesis. The platelet-derived growth factor (PDGF)-B and its receptor PDGF-Rβ signaling are requisite for recruitment of pericytes to capillary vessels and subsequent maturation and stabilization of the vessels during embryonic development. It has been reported that PDGF-B prevents neuronal cell death from ischemic insults in adult rodent models. However, the detailed mechanisms as to how the PDGF-PDGF-Rβ signaling protects neurons from ischemic damage are still unknown. In the present study, we investigated the mechanisms for protective roles of PDGF-PDGF-Rβ signaling in brain ischemia using a rodent middle cerebral artery occlusion model (MCAo) and cultured brain pericytes. Immunohistochemistry (IHC) demonstrated that PDGF-Rβ was upregulated gradually (peak at day 5) and specifically in capillary vessels of peri-infarct area, and was co-stained with NG-2 and Desmin, markers for pericytes, in MCAo. We confirmed that PDGF-Rβ was expressed highly in cultured brain pericytes, but not in cultured endothelial cells. Among various stimuli tested, basic fibroblast growth factor (bFGF) increased the expression of PDGF-Rβ significantly at both mRNA (3.5-fold at 6 hr, $P<0.01$) and protein (2-fold at 24 hr, $P<0.01$) levels in the cultured pericytes where FGF receptor 1 is specifically expressed. IHC demonstrated that bFGF was expressed in MAP2+ neurons and NG-2+ pericytes, but not in GFAP+ astrocytes, in peri-infarct area, suggesting that bFGF produced by neurons and pericytes in response to ischemia accounted for the upregulation of PDGF-Rβ. Immunoblot analyses demonstrated that PDGF-B activated markedly the Akt signaling in the pericytes, which was consistent with the finding that Akt was phosphorylated in the microvascular cells of peri-infarct area. PDGF-B attenuated the cell death induced by serum-depletion in the cultured pericytes, which was prevented by LY294002, an inhibitor of PI3K. PDGF-B significantly phosphorylated the pro-apoptotic factor Bad. Finally, we found that the brain pericytes produced potently a variety of neurotrophins, such as nerve growth factor and neurotrophin-3, at mRNA levels. In conclusion, the PDGF-PDGF-Râ signaling plays important roles not only in recruitment of pericytes into peri-infarct area during ischemic insults but also in mediating their survival in the pro-apoptotic environments, where the pericytes appear to play a protective role probably through the production of various neurotrophic factors.

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W P66

Trophic Effects In Brain Repair Of The Cdp- Choline Administration In The Cerebral Infarct. Experimental Study In Rats

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Introduction: Pharmacological agents that mimic trophic factors might promote one or more repair mechanisms following ischemic stroke. Animal experimental data have demonstrated that CDP-choline (Cit) administration is effective in recovery. **Aims:** To analyze the possible repair mechamism of CDP- choline through the functional evaluation in a model of focal cerebral ischemia in rats. **Material and Methods:** 28 Sprague Dawley male rats distribuited in 4 groups: 1- Healthy with ip CDP-choline (500 mg/kg); 2- Sham (surgery without infarct); 3- Control (surgery +infarct); 4- CDP-choline (surgery+infarct+ ip CDP-choline (500 mg/kg). We analyzed: Functional evaluation score (Rogers) and lesion volumen by Magnetic Resonance Imaging (MRI) at 24h and 14 days. At 14 days: Neuronal death by TUNEL and Endogenous Cellular Proliferation (BrdU) by inmunohistochemistry. In peri-infarct zone LRP, synaptophysin, GFAP and VEGF by Western Blot and inmunofluorescence. Rats were sacrificed at 14 days. **Results:** All treatment groups treated with CDP-choline showed less functional deficit (1.57±1.51; 0.71±0.75) than control group (3.4±0.89; 2.6±0.89) with significant differences at 24h and 14 days, respectively ($p<0,05$). CDP- choline group not decreased infarct size, but reduced significantly the number of TUNEL+ cells (Cit: 20.85±3.93; Control: 40.6±6.46), increase synaptophysin (Cit: 0.58±0.25; Control: 0.28±0.14) and VEGF (Cit: 1.06±0.14; Control: 0.41±0.1) and decrease LRP (Cit: 0.73±0.75; Control: 1.03±0.91) and GFAP (Cit: 0.79±0.29; Control: 1,12±0.3) respect to control group ($p<0,05$). **Conclusions:** CDP- choline trophic effect reduce cerebral damage (protective mechanism) and also by increase endogenous celular proliferation (repair mechanism), this might explain the observed benefit of CDP-choline on functional recovery.

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W P67

Concurrent Use of Granulocyte Colony-Stimulating Factor and Magnetic Stimulation Inhibits Angiogenesis and Functional Recovery in Stroke Rats

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Objective: To evaluate the effect of concurrent use of granulocyte colony-stimulating factor (G-CSF) and repetitive transcranial magnetic stimulation (rTMS) on the angiogenic mechanism and functional recovery after stroke. **Methods:** Seven-week-old male Sprague-Dawley rats were subjected to permanent middle cerebral artery occlusion and allocated into four groups (n=11 in each group): Saline with sham rTMS (group 1), G-CSF with sham rTMS (group 2), G-CSF with 1 Hz rTMS (group 3), and G-CSF with 20 Hz rTMS (group 4). Animals were received G-CSF or saline for 5 days and treated with 20-minute rTMS on their lesioned hemisphere for 2 weeks starting on the first day. Neurological function was evaluated on days 1, 7, 15, and 25. Western blot of Akt, phospho-Akt, endothelial nitric oxide synthase (eNOS) and phospho-eNOS (n=6 in each group) as well as immunofluorescence of BrdU/NeuN, BrdU/PECAM-1 and Iba-1 were conducted. **Results:** Group 4 showed worse function in the modified foot fault test than group 2 on day 7 (p=.009). Neurological functional score was poorer in group 3 and 4 than in group 2 on day 25 (p=.015). The level of Akt (p=.003) and phosphor-Akt (p=.047) in the ischemic core was lower in group 4 than in group 2. The level of phospho-Akt in ischemic border zone was lower in group 2, 3 and 4 than in group 1 (p=.043). Expression of eNOS in ischemic core was lower in group 3 than in group 2 (p=.047). In addition, expression of phospho-eNOS in ischemic core was lower in group 4 than in group 1 and 2 (p=.015), whereas lower in group 3 and 4 than in group 1 in ischemic border zone (p=.010). Iba-1 expression was greater in the G-CSF and rTMS-treated group than in the saline group. **Conclusion:** The concurrent G-CSF and rTMS, administered in the early subacute phase of ischemic stroke, may exert a hazardous effect on angiogeneic mechanism and functional recovery.

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W P68

A Role for Semaphorin 3A in Stroke Recovery

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Background and Purpose: Semaphorin 3A (Sema3A) is known for its role in axon guidance in the developing brain, but may also have detrimental effects after neural injury in the adult. We hypothesized that Sema3A may contribute to an inhibitory environment for neural regeneration after stroke by preventing axon extension and re-establishment of the neural network. **Methods:** We used immunohistochemistry to detect the expression of Sema3A and its receptor neuropilin-1 (NRP-1), in the post-ischemic cortex. To study the effect of increased levels of Sema3A in the recovery period following transient focal ischemia, we injected recombinant Sema3A into the striatum. To investigate the mechanisms of signalling through Sema3A, we treated cultured primary cortical neurons from either wild-type mice, or mice in which the downstream mediator 12/15-lipoxygenase had been knocked out, with recombinant Sema3A. Alternatively, Sema3A signaling was blocked by an inhibitory peptide, or by inhibition of 12/15-lipoxygenase. **Results:** Both Sema3A, and its receptor NRP-1 were increased in a time-dependent manner following transient focal ischemia. Injected recombinant Sema3A led to massive cortical damage, and this was prevented by co-administration of LOXBlock-1, a specific inhibitor of 12/15-lipoxygenase. Sema3A inhibited axon growth in wild-type neurons, but not in neurons derived from 12/15-lipoxygenase knockout mice. Similarly, Sema3A effects on axon extension were diminished in wild-type neurons in the presence of the inhibitory peptide, or an inhibitor of 12/15-lipoxygenase. The 12/15-lipoxygenase metabolites 12-HETE and 12-HPETE were able to replicate the effects of Sema3A, suggesting they may be downstream mediators of Sema3A signaling. **Conclusion:** Taken together, our results demonstrate Sema3A signalling through its receptor NRP-1 and 12/15-lipoxygenase contributes to a prohibitive environment for recovery after experimental stroke. Disruption of the Sema3A pathway may provide a therapeutic benefit during stroke recovery.

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W P69

Comparison Of Different Motor Behavioral Tests On Different Brain Injury In Rats

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Background and Purpose: Motor dysfunction, apart from cognitive impairment, is a common sequela in patients with moderate to severe brain injury, including stroke and traumatic brain injury. Currently there are a number of behavioral tests available for measuring motor dysfunction in rodents, such as Rotor-Rod, CatWalk, etc. However, it is still unclear which test best identifies motor impairment after different degrees of brain injury over time. The purpose of this study was to compare functional impairment after two levels of TBI in rat by two methods of automated test, CatWalk and Rotor-Rod. **Methods:** A linear motor impactor was used to generate the severe traumatic brain injury (sTBI) with 5.0 mm diameter tip, with 5mm depth, 1.5m/sec velocity and 120 ms contact time left of the mid-sagittal suture centering at (AP: 0.0 mm; ML: 3.0mm); while moderate traumatic brain injury (mTBI) was generated with 2.5 mm tip, with 2.5 mm depth, 1.5 m/sec velocity and 120 ms contact time at (AP: 0.0 mm; ML: 2.0mm). 18 rats were randomly divided into three groups: mTBI, sTBI and sham. Before TBI, rats were trained for two days on the Rotor-Rod and CatWalk equipments. **Results:** 1) Bederson's score was used to verify the motor deficits of injured rats, and sTBI and mTBI were significant different (2.83±0.1 vs 1.83±0.1, p< 0.01). 2) In Fig, Rotor-Rod analysis revealed a significant decrease in latency to fall of sTBI rats compared to sham in the 1st week after TBI; however, there was no significant change in mTBI rats. In the 2nd week, latencies were decreased to about 70% in sTBI and mTBI. From 3 week on, there was no significant decrease in injured animals relative to sham. 3) Quantitative CatWalk analysis at one week showed that sTBI caused significant decreases in Intensity in the contraleteral forepaw and both hind paws; while mTBI resulted in only contralateral hind paw deficit. Moreover, CatWalk analysis showed significant decreases in Intensity, Maxium areas, and Phase dispersion of contralateral right front and hind paws of mTBI rats 10 weeks after injury. **Conclusions:** For sTBI, CatWalk showed significant motor impairment in the first week after TBI as well as the differences between sTBI and mTBI; importantly, the CatWalk also showed significant motor abnormalities in mTBI rats 10 weeks after injury, while the Rotor-Rod was insensitive. Our data suggest that the CatWalk may be more sensitive to different degrees of brain injury over time. This is important for studies that employ pharmacological, physical or gene therapeutic interventions to improve regeneration and functional recovery after brain injury.

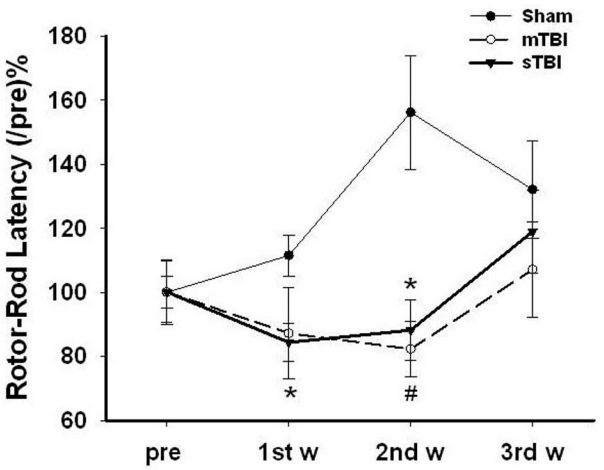

Fig. Rotor-Rod Latency three weeks after TBI. The curves show the percentage of the latency/pre-latency of each rat over time. *, p<0.05 sTBI vs Sham; #, p<0.05 mTBI vs Sham. N=6, student t test.

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W P70

Social Isolation Worsens Stroke Outcome, Role of Nuclear Factor KappaB and Sex

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Background: Social isolation (SI) is associated with dramatic long-term physiological and psychological consequences in both clinical and experimental studies. SI prior to an induced stroke increases injury, secondary to an enhanced inflammatory milieu. However, how SI worsens stroke outcome implied mechanisms and role of sex remains unknown. Identifying the involved mechanisms could dramatically change the treatment conditions for stroke patients and offer new therapeutic strategies. Nuclear Factor KappaB (NFkB) is an important transcription factor activated in stroke, and plays a critical role in initiating several inflammatory mechanisms. The aim of this study is to determine if SI activates NFkB translocation and leads to worsened stroke outcome. The role of sex in SI mediated NFkB translocation is also investigated. **Methods:** Stroke was induced by reversible middle cerebral artery occlusion (MCAO-60 minute) in mice (20-25g; C57BL/6N). Different group of animals for infarct analysis (n=8/group) and molecular analysis (n=4/group). Infarcts are analyzed by TTC at 24hrs after stroke and expressed as percentage of contralateral structure. Adrenal weights (mg/100g) and brains for protein analysis obtained from non-stroked mice cohorts. NFkB translocation was assessed using western blot analysis on fractionated nuclear samples from brain homogenates and levels were expressed as the ratio to the control band with densitometry analysis. Data expressed as mean±sem except for deficits (NDS), presented as Median (Interquartile-range). **Results:** SI for two weeks increased body-weights compared to pair-housed (PH) cohorts in both male (26.06±0.52 vs 23.02±0.71; P<0.05) and females (24.88±1.01 vs 19.06±1.26; P<0.05. n=8/group). SI has significantly worsened outcome in males (Total infarct: Males: 56.10±3.52; Females 59.05±4.31) compared to PH, NDS (Males: SI 3.0(1) vs. PH 2.0(0), P<0.05, n=8; Females SI 3.5(1) vs. PH 1.5(0.5) P<0.01). SI males had significant decrease in adrenal-weights compared to PH (14.21±0.38 vs 17.62±0.44; P<0.05), such changes were not significant in SI and PH females (21.4±0.27 vs 19.61±0.79). Interestingly striking sex differences in NFkB levels were observed with highest in SI males and PH females.

Conclusions: In this study, SI not only worsens stroke outcome in both sexes but also worsens NDS, this effect was more pronounced in females. We found that SI inversely influenced body and adrenal weights in males while increased body-weights in females without changes in adrenal weights. Western blot analysis indicates Isolation differentially influences NFkB translocation in males and females. Thus for the first time, our results highlights that NFkB could be an important mechanism involved in gender specific deleterious effects of SI.

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W P71

The Vermicelli Pasta Handling Task Reveals Different Patterns Of Adaptive Versus Maladaptive Forepaw Use Depending On Stroke Model

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Background: A novel measure of dexterous forepaw function has recently been described that is quantitative, easy to administer, and sensitive to the effects of damage to sensory and motor systems in the CNS of rats. We investigated differences in forepaw function following acute ischemic stroke caused by two different stroke models: reversible common carotid artery/middle cerebral artery occlusion (CCA/MCAo) and middle cerebral artery occlusion (MCAo). The CCA/MCAo is a model of selective cortical infarction whereas the MCAo produces cortical and subcortical damage. **Methods:** In this study, 17 Long Evans rats at 3mo of age underwent CCA/MCAo for 2hrs (n=9) or MCAo for 90min (n=8). Rats were given 7cm lengths of vermicelli pasta and the number of forepaw adjustments were counted as rats manipulated the pasta. Animals were fasted 18hrs prior to testing. Atypical movements, indicative of impaired forepaw use, were also quantified. Testing was administered pre-operatively and once a week for 4 weeks after stroke. **Results:** Rats with MCAo made significantly more adjustments (overall group mean=14.6, p=0.013) with the impaired limb compared to CCA/MCAo rats (overall group mean =7.11). Rats with MCAo also took on average nearly 3 times as long to eat the pasta at Weeks 1-4 compared to the CCA/MCAo group (all p's $<$0.010). In addition, atypical movements were significantly increased at Weeks 1-4 (p=0.007) compared to pre-stroke baseline but did not differ between the groups. **Conclusions:** Previous work from our lab has shown a persistent decrease in impaired limb forepaw adjustments and time to eat after CCA/MCAo, suggesting greater efficiency in pasta handling that does not rely on the unimpaired limb. Conversely, the present data suggest that while the MCAo group is making more adjustments than the CCA/MCAo group, these adjustments are ineffective in eating the pasta efficiently and may actually hinder the animals, causing them to eat more slowly. The MCAo model shows a different profile of more pronounced forepaw impairment compared with the CCA/MCAo model and may be more useful in evaluating whether new therapies can enhance hand function after stroke.

	CCA/MCAo		MCAo	
Time Point	**Impaired Forepaw Adjustments (Mean±SD)**	**Time to Eat Pasta (Mean sec±SD)**	**Impaired Forepaw Adjustments (Mean±SD)**	**Time to Eat Pasta (Mean sec±SD)**
Pre-Stroke	10.44±4.81	44.26±11.56	15.67±8.71	54.67±24.63
Week 1	8.57±4.62	56.57±16.35	14.31±9.71	254.22±154.86
Week 2	6.96±3.36	48.26±18.04	16.33±12.64	127.33±67.27
Week 3	5.52±2.31	41.22±9.39	12.95±8.46	121.36±82.87
Week 4	4.04±1.55	39.78±14.61	13.71±7.78	115.64±79.79

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W P72

A Selective TrkB Agonist, 7,8-dihydroxyflavone, Enhances Motor Performance and Promotes Motor Map Integrity Following Cortical Stroke

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Brain Derived Neurotrophic Factor (BDNF) has been associated with reducing infarct volume and enhancing cortical plasticity post stroke through activation of the Tyrosine Kinase Receptor (TrkB). Recent work has identified 7,8 Dihydroxyflavone (DHF) as a potent TrkB agonist and a potential therapeutic agent for treating several neurological disorders including stroke. We investigated the behavioral and neurophysiological effects of DHF treatment in a rodent model of cortical ischemia. DHF (5mg/kg, i.p.) was administered two hours prior to and once daily for three weeks post stroke. Stroke was induced by application of the vasoconstricting peptide ET 1 directly onto the distal branches of the middle cerebral artery. Animals were assessed on battery of forelimb motor tests including cylinder paw placement, sunflower seed opening, and pasta handling during a three week period post stroke. Intracortical microstimulation (ICMS) was then used to derive motor maps of forelimb movement representations in motor cortex three to four weeks post stroke. Results showed that rats receiving DHF had significantly reduced motor impairments and larger forelimb motor maps than vehicle treated animals. Histological analysis also revealed reduced infarct volume in DHF treated animals. These results suggest that DHF may be a viable compound for reducing loss of neural tissue and promoting physiological and behavioral improvement post stroke.

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W P73

The Practice of Carotid Endarterectomy in a Large Metropolitan Population

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Introduction: Carotid endarterectomy (CEA) reduces stroke risk when performed for appropriate indications and with an acceptable perioperative rate of morbidity and mortality. Studies from the 1980s in our population demonstrated that perioperative risk exceeded the recommended boundaries of 3.0% for asymptomatic stenosis and 6.0% for symptomatic stenosis. We investigated indications and outcomes for CEA in our population during 2005. **Methods:** We ascertained all CEAs performed at 16 hospitals within the Greater Cincinnati/Northern Kentucky (GCNK) region during 2005 as part of the GCNK Stroke Study. To allow 30-day follow-up, only CEAs performed before 12/01/05 were included in this analysis. Only residents of the core five-county GCNK region were included. Study nurses used an ICD-9 code of 433.1x with a DRG of 533 or 534 to identify cases. Patients were also included if they were identified as part of routine study surveillance for stroke and TIA. All identified TIAs or strokes which occurred before or after the CEA (during 2005) were abstracted by study nurses and reviewed by a study physician. The indication for CEA was categorized as asymptomatic or symptomatic stenosis. Stroke after CEA was ascertained if it occurred during the index hospitalization or if the patient returned to an emergency room or hospital after discharge with stroke symptoms. Death following CEA was tracked using study records, the Ohio and Kentucky Death Indices, and the Social Security Death Index. Events were analyzed using Kaplan-Meier statistics with censoring at the outcome of interest and the end of the study period. Perioperative complications other than stroke or death (such as myocardial infarction) were not routinely tracked. **Results:** Among approximately 1.3 million GCNK residents, 482 CEAs were performed between 1/1/05 and 12/1/05. There were 318 CEAs for asymptomatic stenosis (mean age 71, 56% male) and 164 CEAs for symptomatic stenosis (mean age 70, 59% male). For asymptomatic stenosis, 30-day perioperative risk of stroke or death was 3.5% (95% CI: 1.4-5.4%). For symptomatic stenosis, 30-day risk was 5.5% (1.9-8.9%). **Conclusions:** Carotid endarterectomy remains a common procedure in our population, with the majority of CEAs performed for asymptomatic stenosis. The point estimate for perioperative CEA risk for asymptomatic stenosis remains above the recommended benchmark and may reduce or eliminate benefit from this procedure. Population-based surveillance of outcomes following carotid revascularization remains important in the era of both carotid endarterectomy and carotid artery stenting.

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W P74

Collaterals and Venous Outflow Determine Outcome in Acute Internal Carotid Artery Occlusion

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Background: Acute internal carotid artery occlusion (ICAO) frequently causes devastating stroke. Arterial revascularization is often considered, yet hemodynamics may be important. Ipsilateral venous outflow has also recently been implicated in malignant middle cerebral artery infarct growth. We tested the hypothesis that hemodynamic features noted at angiography, including collateral circulation and the venous outflow pathways, may influence tissue fate and the clinical outcome in acute ICAO. **Methods:** Consecutive cases of acute ICAO evaluated with concurrent MRI and digital subtraction angiography (DSA) were studied. Serial diffusion-weighted imaging (DWI) was acquired immediately prior to angiography and at day 5, chronicling the evolution of infarct volume. DSA collaterals (ASITN/SIR), ipsilateral transverse sinus hypoplasia (TSH) and early venous drainage (EVD) were graded. These features were analyzed with respect to clinical variables, arterial revascularization and infarct growth. **Results:** 51 cases (mean age 66±16 years; 26 men, 25 women) of acute ICAO with DSA and DWI were analyzed. Initial NIHSS (median 19) was associated with baseline DWI lesions of mean 54±47 cc. Collateral grade was evenly distributed from 0-4 (median 2). Ipsilateral TSH was noted in 35% with no difference based on side of stroke (p=0.58) and EVD was seen in 22%. Collaterals and venous findings were unrelated to age or gender. More extensive collaterals were associated with smaller baseline DWI lesions ($p<0.01$) but not with initial NIHSS. With increasing collateral grade there was diminished infarct growth (p=0.02), less mass effect ($p<0.01$), and less frequent hemicraniectomy (p=0.02). Collaterals strongly influenced discharge mRS ($p<0.01$). TSH was associated with increased infarct growth (p=0.04) and hemicraniectomy (p=0.09). EVD, however, was unrelated to infarct evolution. Baseline hemodynamic status or higher collateral grade was associated with successful reperfusion after intervention (p=0.01) measured by thrombolysis in cerebral infarction (TICI) scoring. Arterial revascularization alone was not a predictor of infarct evolution or clinical outcome without consideration of collaterals. **Conclusions:** Collateral circulation is a strong determinant of infarct volume, lesion evolution and discharge clinical outcome in acute ICAO. Venous outflow features are also influential on infarct growth in this type of stroke. Arterial revascularization alone may be insufficient to offset the hemodynamic aspects of this condition that warrant further investigation.

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W P75

Carotid Atherosclerotic Plaque Neovascularization Identified by Contrast-Enhanced Magnetic Resonance Imaging

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Background: A large animal model of carotid atherosclerosis may greatly facilitate the identification of imaging characteristics of vulnerable plaques and the selection of patients for intervention. In this study, we assess the histological features associated with vulnerable plaques in a swine model of carotid atherosclerosis and evaluate the MRI patterns of neovascularity, which is a feature of vulnerable plaque. **Methods:** Carotid atherosclerosis models were created in the miniswines using the combination of partial ligation and high cholesterol diet as previously published, and a minimum 70% stenosis was confirmed by Doppler ultrasonography immediately post-ligation. All animals were imaged in a 1.5 Tesla MR scanner at three months, and carotid arteries were obtained and sectioned at 4 mm intervals for histopathological examination. Distal embolism was determined by the presence of atheroemboli in the ipsilateral rete mirabilis. The atherosclerotic changes of these carotid artery segments were classified as AHA/Stary type I to VI, and the instability feartures of carotid plaque were assessed. Neovascularity was assessed histologically and using immunohistochemisty with anti- matrix metalloproteinases-9 and vascular endothelium growth factor antibodies. TIWI pre- and post-contrast were used to match the histology findings. Signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) of the plaques were measured in the matching pre- and post-contrast T1WI. **Result:** 191 carotid segments from ten carotid atherosclerotic artery models were assessed histologically. 139 segments showed atherosclerotic changes, and 102 segments had the advanced plaque (Stary IV to VI). Advanced atherosclerotic plaques were found more frequently in the vessel wall proximal to the partial ligation than distal ($p<0.0001$). Distal embolism was found in all 10 rete mirabilis, and deemed to be from the ipsilateral vulnerable carotid plaques. A large lipid core, an abundance of foam cells, intra-plaque hemorrhage, any thrombus, marked plaque and cap inflammation, a thin fibrous cap, cap rupture and AHA/Stary VI were associated with vulnerable plaque (all $P<0.0001$). The matched contrast-enhanced MR imaging and histology slices showed moderate to good correlation for ratio of plaque size to lumen diameter ($r=0.80$, $P<0.001$). CNR was significantly higher in the group of plaques with marked neovascularization than in those without ($p<0.05$). **Conclusion:** Carotid atherosclerosis model with vulnerable plaque and distal embolism can be created by the combination of partial ligation and high cholesterol diet in the miniswines. Vulnerable plaques were associated with distinct markers. Increased plaque CNR is associated with neovasculization in the plaques and may be used to identify vulnerable plaques.

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W P76

Effects Of Carotid Endarterectomy On Brain Cognition, Metabolism And Perfusion

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Introduction: Carotid endarterectomy artery (CEA) decreases the risk of suffering a stroke. However, the effects of CEA on cognition, brain methabolism and perfussion continues to be controversial. **Hypothesis:** CEA may improve brain cognition and metabolism as measured by advanced neuroimaging and neuropsychology. **Methods:** We included 17 patients, 10 men and 7 women, mean age of 65 with severe unilateral carotid stenosis asymptomatic, or symptomatic which present with no acute lesion in MRI (TIA, amaurosis fugax) schedulded for CEA. We excluded patients with recent stroke or postoperative complications. We performed regular neurological studies, including 18-FDG PET, a HMPAO-SEPCT and neuropsychological studies before and three months after surgery. We performed a voxel-by-voxel analysis using SPM5 to analyse image studies. A comparison of the brain PET and SPECT images between basals and post-CEA images was performed using a paired t-test analysis. The SPM maps were obtained using a cluster and voxel level threshold of $P<0.05$ corrected by False Discovery Rate (FDR). Regions of interest (ROI) analysis were applied in cerebral lobes and subcortical structures regions using WFU-Pickatlas toolbox software for SPM version. We analysed neuropsychological studies by t-paired test ($p<0.05$, SPSS v.15.0). **Results:** 10 patients were operated on severe left carotid stenosis and 7, on right carotid stenosis. All patients presented with several vascular risk factors. A statisticallly significant improvement in 18FDG uptake was found on voxel-by-voxel and ROI analysis in occipital lobes, left cerebellum and right inferior temporal lobe of patients scheduled for left CEA in PET studies. A statistically significant improvement in cerebral perfussion was found on voxel-by-voxel and ROI analysis in contralateral occipital lobe in the same group. Neuropsychological studies show a significant improvement in verbal domains caused by the interference between newly learned tasks with old material, anatomically dependent on prefrontal cortex, so called proactive interference, in patients undergoing left CEA. Differences were maintained after excluding patients with recent TIA. **Conclusion:** There was an improvement in metabolism and perfusion in posterior regions, and in verbal domains after CEA.

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W P77

Serological Identification of Carotid Plaque Vulnerability

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Introduction: Assessment of embolization risk from carotid plaques and subsequent indication to revascularization is usually based on grade of stenosis; other morphological and serological determinants of plaque vulnerability are not broadly considered. Hypothesis. Plaque vulnerability may be associated with specific serological parameters. **Methods:** High sensitivity C-Reactive Protein (hsCRP) and Vascular Endothelial Growth Factor (VEGF) were assessed preoperatively in a group of consecutive patients with either symptomatic or asymptomatic carotid stenosis undergoing carotid revascularization procedures (endarterectomy - CEA, or stenting - CAS). Plaques from CEA were histologically divided into vulnerable and non-vulnerable (evaluating: microvessel density, fibrous cap thickness, inflammatory infiltrate and lipid core) in a blinded manner. In CAS, vulnerable plaques were defined by analyzing microscopically and ultrastructurally embolic debris captured by distal filters (filter surface involvement and occluded pores percentage). Results were correlated by Fisher's test, Student's t test and regression analysis. **Results:** A total of 48 patients were included in the study (22 CEA, 26 CAS). Mean hsCRP was 9.9 ± 17.1 mg/l, mean VEGF was 489.8 ± 248.6 pg/l; in symptomatic patients hsCRP levels were significantly higher compared to the asymptomatic ones (14.9 ± 22.3 vs. 4.7 ± 3.5 mg/l, $P<0.05$). In the CEA group, a vulnerable plaque was present in 9/19 samples (47%) and was significantly correlated with higher hsCRP levels (>5mg/l, OR 3; CI 95%1.2-7.5, $P<0.05$) and with VEGF levels (636.8 ± 304.7 vs. 356.0 ± 216.8 $P<0.05$; OR 3.6 when VEGF>500 pg/l CI 95%1.02-12.7, $P<0.05$). In CAS, all filters had microscopic debris (mean occluded pore percentage $29.2\%\pm10.3$, surface involvement $28.8\%\pm$ 8.1); the presence of more than 25% of occluded pore and surface involvement were correlated with higher hsCRP (>5mg/l) levels (OR 2.5 CI 95% 1.2-5.3 and OR 3.0 CI 95%1.2-7.5 respectively) and with a trend toward higher VEGF levels (775 ± 200 vs. 486 ± 17.6 pg/ml, $p=0.07$). **Conclusion:** High levels of hsCRP and VEGF are associated with plaque vulnerability. Although these data need to be confirmed by wider studies, this study suggests that serological determinants are useful in recognition of vulnerable plaques with higher risk of embolization.

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W P78

Predictors of One-Year Outcomes of Carotid Artery Stenting in Medicare Patients with Symptomatic and Asymptomatic Carotid Artery Stenosis

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Background: Carotid artery stenting (CAS) has been suggested as an alternative to surgical carotid endarterectomy (CEA) for patients with carotid stenosis, a major risk factor for stroke. We identified predictors of one-year outcomes after CAS in both symptomatic (S) and asymptomatic (A) patients using the Medicare database. **Methods:** All patients age $\geq$ 66 years with a discharge diagnosis of carotid revascularization for the years 2004-2006 were identified in a 5% nationwide random sample of Medicare patients based on ICD 9-CM codes. Outcome measures included in-hospital stroke and all-cause death rates in years 2004-2006 (CAS=1323) and one-year outcomes for 2004 and 2005 (CAS=737). **Results:** S Patients (n=168) comprised 12.7 % of CAS patients and did not differ from A group (n=1155) for age, gender, race and comorbidities except that S group had a lower prevalence of coronary artery, chronic obstructive pulmonary and peripheral vascular disease. In-hospital all-cause mortality (2.98% vs 0.61%, $p=0.0025$) and stroke rates (6.55% vs 1.2%, $P<0.0001$) were higher in the S group compared with the A group. By 1 year, significant differences persisted for stroke (18.3%, S vs 3.4%, A; $P<0.0001$) and stroke/death/MI (31.2%, S vs 14.6%, A; $P<0.0001$). Using multivariate Cox models, independent predictors of 1 -year stroke/death/MI after CAS in S patients were limited to age $\geq$ 80 years old (HR 2.87, 95% CI 1.15-7.12; $p=0.023$). In A patients only, predictors of 1-year stroke/death/MI after CAS were renal failure (HR 2.0, 95% CI 1.08-3.71; $p=0.028$), heart failure (HR 1.69, 1.01-2.80; $p=0.044$) and age $\geq$ 80 years old (HR 1.59, 1.04-2.43; $p=0.031$). **Conclusions:** Patients with symptomatic status have increased risk of adverse clinical outcomes compared with asymptomatic patients. Age $\geq$ 80 years is associated with increased risk of an adverse outcome within both S and A groups. In A patients, adverse outcomes relate to other serious comorbidities.

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W P79

Are Distal Protection Device '*Protective*' during Carotid Angioplasty and Stenting?

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Purpose: To evaluate the peri-procedural outcome after carotid artery stenting (CAS) with embolic brain protection (EBP+) versus without embolic brain protection (EBP-). **Methods:** We retrospectively reviewed data from a prospective non-randomized database of 357 patients who underwent CAS in the Neuroradiology Division of our Institution from 1999 - 2009. One hundred five patients underwent angioplasty and stenting without distal protection while 252 were treated with distal protection. Patients were analyzed according to their EBP status (+ or -) for the primary endpoints of perioperative stroke, death or myocardial infarction (MI). Secondary endpoints included postoperative serum creatinine increase, acute carotid artery

thrombosis/restenosis, intensive care unit (ICU) stay and length of in-hospital stay, as well as other minor adverse events. **Results:** Unprotected stenting was mostly performed in the early years of this study and this is reflected in significant baseline differences between the two groups as in our earlier experience CAS was utilized in patients with more significant co-morbidities. Diabetes mellitus ($p=0.04$), previous myocardial infarction (MI) ($p=0.037$), and symptomatic lesion ($p=0.013$) were significantly more common in the EBP- cohort. Despite these baseline differences, there were no significant differences in the primary endpoints (2% in the EBP+ group and 4.8% in the EBP-, $p=0.15$). The incidence of ipsilateral stroke in the EBP- and in the EBP+ group was 2.8% vs 1.2%, respectively ($p=0.27$). There were two perioperative deaths (one in each group) and four MIs (three in EBP+ arm and one in EBP- arm, all non-Q infarcts) ($p=$ NS) and the ICU stay was longer in the EBP- (1.6 ± 1.6 days) than in the EBP+ (1.3 ± 1.0 days) ($p=.051$). There were no differences in occurrence of serum creatinine elevation after procedure or in early in-stent occlusion between the two groups. **Conclusion:** Although the difference in occurrence of perioperative complications was not statistically significant between the two groups, the slightly higher incidence of ipsilateral stroke in unprotected CAS may be explained by the different distribution of risk factors, symptomatic status and experience of operator, unfavorable for the EBP- arm. In accordance with recent literature, this series cast doubts as to the real effectiveness of distal embolic protection devices in reducing peri-procedural complications.

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W P80

Angioplasty and Stenting in Common Carotid Artery Origin Stenosis: A Review of 16 Patients

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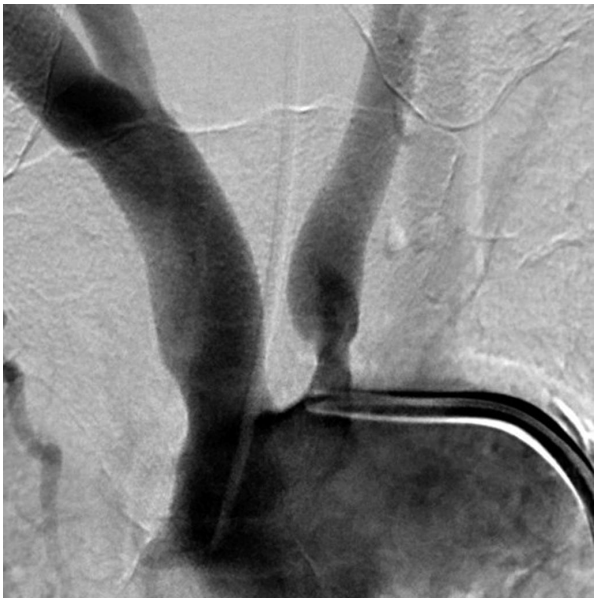
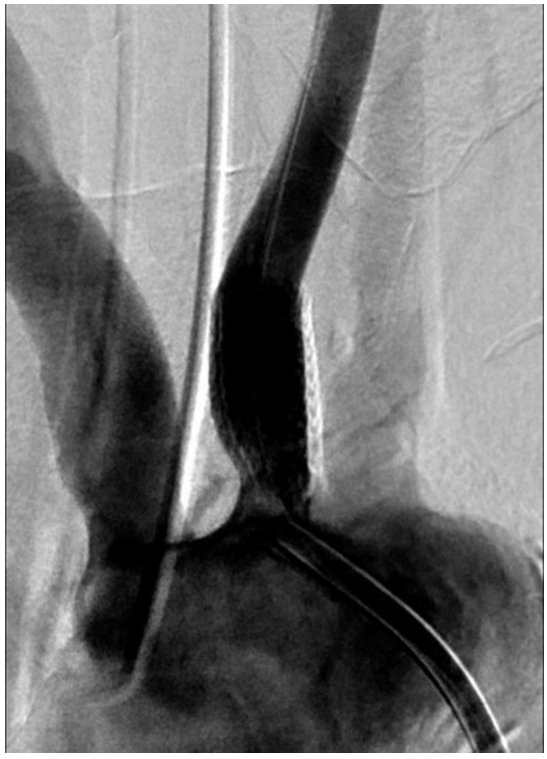
Introduction: Angioplasty and stenting of the common carotid artery (CCA) origin may be technically challenging due to the typical heavy calcification of these lesions, and the significant transition in vessel size necessitating precise placement of these stents. For these reasons, these lesions are excluded from analysis in most carotid stenting trials and registries. **Methods:** This was a retrospective study of a consecutive series of 16 patients with symptomatic CCA origin stenosis treated by angioplasty and stenting between July 2000 and July 2010. There were 9 males and 7 females in the series, with a mean age of 59 (range 14 to 88). Two of the patients had concomitant CCA bifurcation stenosis of 50% or greater which was treated with stenting at the time of the CCA angioplasty and stenting. All cases were performed with the use of a distal protection device, and all patients were pre-medicated with aspirin and clopidogrel prior to the procedure. The etiology of the CCA origin stenosis was primarily atherosclerotic disease in 11 patients, radiation therapy for malignancy related in 2 patients, William's disease in 1 patient, Takayasu's arteritis in 1 patient, and post vein bypass in 1 patient. Clinical follow up in 14 patients averaged 25 months, with 2 patient lost to follow up, and imaging follow up averaged 18 months. **Results:** The baseline stenosis in this series was 78% (range 50% to 95%), and the post angioplasty and stenting residual stenosis was 21%. There were no peri-procedural thromboembolic complications and one peri-procedure myocardial infarction, which was non-disabling. One patient died 5 months post-procedure from underlying malignancy, and one other patient was lost to follow up. With an average clinical follow up of 25 months in the remaining patients, two patients (14%) developed recurrent stenosis with ischemic symptoms that required repeat angioplasty and stenting. Both patients had isolated circulations. Two other patients (14%) have asymptomatic recurrent stenosis greater than 50% that is being managed with medical therapy. **Conclusions:** Angioplasty and stenting at the CCA origin can be performed with low morbidity. However, with an average imaging follow up of 18 months, there was a 28% re-stenosis rate of greater than 50%, with half of those presenting with recurrent symptoms.





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W P81

Validity of ^{18}F-fluorodeoxyglucose PET in Identifying Inflamed and Vulnerable Carotid Plaque - A Radiological and Pathological Study

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Objective: In this report, we assessed whether ^{18}F-fluorodeoxyglucose (FDG) PET can identify inflamed and vulnerable plaque at higher risk for subsequent ischemic stroke in patients with internal carotid artery (ICA) stenosis. **Methods:** This prospective study included 23 patients with ICA stenosis of more than 70%, including 18 males and 5 females. Their age ranged from 48 to 85 years. All 23 patients underwent ^{18}F-FDG PET, CT, MRI, and ultrasound to evaluate the plaque morphology and composition prior to carotid endarterectomy (CEA). Following surgery, the specimens were examined, using HE staining and immunohistochemistry. **Results:** Carotid plaque had a high uptake of ^{18}F-FDG in 9 (39%) of 23 patients. Intraoperative observations revealed that their carotid plaques were lipid-rich and vulnerable. Histological analysis detected a dense accumulation of lipid and activated macrophages in these plaques. On the other hands, such high uptake of ^{18}F-FDG was not observed in other 14 patients (61%). Of these, 12 were fibrous and were considered as "stable" plaques. Other two lesions had large subintimal hemorrhage associated with ulcer formation. **Conclusion:** The present results suggest that ^{18}F-FDG PET would be valuable to identify the inflamed, vulnerable plaque and predict the risk for subsequent ischemic stroke in patients with severe ICA stenosis.

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W P82

Pathology of Symptomatic and Asymptomatic Carotid Plaques. Are There Really Any Differences?

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Background and Purpose: Numerous authors have raised that, besides the degree of stenosis of the internal carotid artery, it is also important to identify the structural components of the atherosclerotic plaque. Moreover, the presence of markers of plaque vulnerability has been associated with an increased risk of ischemic stroke (IS) and transient ischemic attack (TIA). Our objective was to compare the histological features of atherosclerotic plaques of symptomatic and asymptomatic patients undergoing carotid endarterectomy (CEA). **Methods:** We assessed every patients undergoing CEA at our institution between 01/01/2006 and 12/31/2009. We analyzed the presence of the following pathologic findings in symptomatic and asymptomatic carotid plaques: 1) fibrosis, 2) myofibroblastic hyperplasia, 3) lipidic-necrotic core, 4) calcification, 5) hemorrhage, 6) inflammatory infiltrate, 7) mural thrombus, and 8) ulceration. We compared the frequency of these items between symptomatic and asymptomatic plaques. Finally we stratified each item into a 4-point semiquantitative severity scale (0 to 3) and we generated a score for every case by adding

the value of each item. We compared the mean and median scores for symptomatic and asymptomatic cases. Results We assessed 203 carotid plaques/patients: 164 (74.2%) males, aged 68±9 years. Twenty-eight (14.8%) were performed in symptomatic patients and 175 (86.2%) in asymptomatic individuals. The frequency of the presentation of the 8 carotid pathology items in symptomatic and asymptomatic patients was (values expressed in %): 1) fibrosis: 100.0 vs. 100.0, P = 1.00; 2) myofibroblastic hyperplasia 96.4 vs. 94.3, P = 0.64; 3) lipidic-necrotic core: 100.0 vs. 99.4, P = 0.69; 4) calcification: 89.3 vs. 92.6, P = 0.55; 5) hemorrhage: 50.0 vs. 40.0, P = 0.32; 6) inflammatory infiltrate: 42.9 vs. 56.0, P = 0.19; 7) mural thrombus 21.4 vs. 17.7, P = 0.64; 8) ulceration: 17.9 vs. 9.1, P = 0.16, respectively. The mean pathology score for symptomatic and asymptomatic cases was 4.5±2.0 vs. 4.4±2.1, P = 0.81. **Conclusions:** We found no differences in the carotid pathology of symptomatic and asymptomatic patients.

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W P83

Management of Acute Ischemic Stroke Associated with Acute Internal Carotid Artery Occlusion

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Introduction: Acute ischemic stroke resulting from cardioembolic or atherothrombotic occlusion of the internal carotid artery (ICA) results in high rates of morbidity and mortality. Endovascular therapy is traditionally not recommended; however some retrospective studies have shown endovascular therapy to be feasible and beneficial in select patients. We report our experience in endovascular recanalization of acute stroke patients with ICA occlusion. **Methods:** We performed a retrospective analysis of all ischemic strokes with ICA occlusion diagnosed by digital subtraction angiography (thrombolysis in cerebral ischemia (TICI) - 0) who underwent angioplasty, stenting, or mechanical embolectomy (Merci retrieval or penumbra) from February 2002 to April 2010. Adjunctive therapy with IV rt-PA within 4.5 hours and/or IA rt-PA within 8 hours of onset was used in appropriately selected patients. Post intervention outcome was assessed by TICI scores, head CT (secondary hemorrhages, classified using ECASS I criteria) and National Institutes of Health Stroke Scale (NIHSS) score at 24 hours. Good recannalization was defined as TICI score IIb-III. Clinical outcome was measured by discharge disposition. Discharge to home and in-patient rehabilitation was considered good outcome and nursing homes, hospice homes or death were considered poor outcome. Univariate analysis was done using t-test, Chi-square and Fisher exact test when appropriate. **Results:** 82 patients with internal carotid occlusion were identified out of 2976 ischemic strokes. Male to female ratio was 1.6:1. Mean age was 68.3±15 yrs (range 28-95 yrs). Left to right ICA occlusion ratio was 1.22:1. Mean baseline NIHSS was 19±7.3 (median=18; range= 1-41). Mean time to ET was 261±154 minutes (median= 230 minutes; range= 45-955 minutes). Mean duration of procedure was 138±59 minutes (range= 38-357 minutes). 79% patients had tandem MCA1 occlusion. Recanalization, outcome, and hemorrhage rates are shown in Table. Good outcome was achieved in 50% of cases. **Conclusion:** Revascularization of acute carotid occlusions in the stroke setting is technically feasible and potentially of great benefit. It may help to reduce stroke volume and increase good outcome in selected patients.

Table: Outcome in acute strokes with internal carotid occlusion who underwent mechanical intervention alongwith other interventions (N-81)

Type of intervention	Mechanical thrombectomy only	Mechanical thrombectomy and carotid stenting	Mechanical thrombectomy/ carotid stenting and rt-PA (IV)	Mechanical thrombectomy/ carotid stenting and rt-PA (IA)	Mechanical thrombectomy / carotid stenting and rt-PA (IV+IA)
Number of patients	59 (72.8%)	22 (27.2%)	22 (34.4%)	34 (42%)	17 (21%)
Good recannalization rate (TICI IIb-III)	36 (61%)	16 (72.7%)	15 (68.2%)	24 (70.6%)	11 (64.7%)*
Improvement in NIHSS more than 7 points	16/39 (41%)	04/17 (23.5%)	07/17 (41.2%)	08/20 (40%)	05/11 (45.5%)
Good outcome (Discharge to home/ in-patient rehabilitation)	26 (44.1%)	14 (63.6%)	14 (63.6%)	14 (41.2%)	07 (41.2%)
Asymptomatic hemorrhage (H1,H2,PH1)	15 (25.4%)*	06 (27.3%)*	07 (31.8%)	10 (29.4%)	05 (29.4%)
Symptomatic hemorrhage (PH2)	09 (15.3%)	02 (09.1%)	01 (04.5%)	06 (17.6%)	03 (17.6%)
Poor outcome (Death or discharge to Hospice/ Nursing home)	33 (55.9%)	08 (36.4%)	08 (36.4%)	20 (58.8%)	10 (58.8%)

* p<0.05

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W P84

The Risk of Carotid Endarterectomy in Patients with > 120 days since Qualifying Cerebrovascular Event

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Background and Purpose: The North American Symptomatic Carotid Endarterectomy Trial (NASCET) published in 1991 prompted the resurgence of endarterectomy for the treatment of symptomatic patients with severe stenosis (70-99%) of extracranial internal carotid artery. The concept of 'symptomatic stenosis' has led to misinterpretations, resulting in the prescription of carotid endarterectomy (CEA) in patients with dizziness, syncope, carotid bruits, etc. Another common misunderstanding is to consider patients as symptomatic when their qualifying cerebrovascular event did not occur within 120 days before surgery. Our objectives were: a) to evaluate the frequency of the diagnoses that prompt to CEA in asymptomatic patients, b) to determine how often CEA is prescribed in patients with cerebrovascular events not occurring within 120 days before surgery and c) to compare the outcome of this latter group with that of asymptomatic patients. **Methods:** We assessed every patient undergoing CEA at our institution between 01/01/2006 and 12/31/2009. We classified the diagnoses that prompted to CEA in: 1) Diagnosis of carotid stenosis during preoperative evaluation of coronary artery bypass grafting, valve replacement or coronary angioplasty [D1], 2) diagnosis during routine examination [D2], 3) Dizziness [D3], 4) Cerebrovascular events not occurring within 120 days before surgery [D4] 5) Diagnosis of carotid stenosis during assessment of a cerebrovascular event of contralateral carotid territory [D5], 6) Diagnosis during evaluation of peripheral vascular disease [D6], 7) Carotid bruit [D7], 8) Progression of previously diagnosed carotid stenosis [D8], 9) Syncope [D9] 10) Other causes [D10], and 11) Dizziness and syncope [D11]. We compared the combined outcome of ischemic stroke (IS), myocardial infarction (MI) and/or death between patients with D4 and the rest of the cohort ($\chi 2$ tests). Results Overall, 221 CEA were performed, 190 in asymptomatic individuals: 141 men (74.2%), mean age 69±8 years. The frequencies of diagnosis leading to CEA were: D1: 62 (32.6%), D2: 37 (19.5%), D3: 17 (8.9%), D4: 13 (6.8%), D5: 16 (8.4%), D6: 11 (5.8%), D7: 9 (4.7%) D8: 9 (4.7%), D9: 9 (4.7%), D10: 4 (2.1%) and D11: 3 (1.6%). The D4 group showed significant differences regarding the combined outcome of SI, MI and/or death when compared with the rest of the cohort: OR 5.8, 95%CI 1.3-25.1, P = 0.02. **Conclusions:** In our cohort, CEA performed in patients with cerebrovascular events not occurring within 120 days before surgery was associated with a fivefold risk of SI, MI and/or death.

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W P85

Correlation of Local Hemodynamics and Morphologic Changes in the Carotid Sinus

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Background: The morphology of adult carotid sinus and atherosclerosis are major risk factors for ischemic stroke. It has been investigated that the function of carotid sinus is pressure sensing and the regulation of heart rate, however, the development of the carotid sinus are not clearly understood yet. A recent study reported lifelong development of carotid sinus morphology from infancy to maturity. The most significant finding was the substantial development of the carotid sinus during late adolescence. For further investigation to understand correlation between hemodynamics and morphology in the sinus, a computational study was initiated using a finite-element-based Navier-Stokes equation solver. **Methods:** Three dimensional virtual models of the carotid bifurcations were created in four postnatal stages, infancy, childhood, adolescence, and young adulthood using 3D CAD design software (SolidWorks). The geometry of four age representative models was obtained from the previous investigation. A finite-element analysis computational fluid dynamics tool (ANSYS CFX) was employed to perform blood flow simulation. Physiological flow, time-averaged flow rate of 4.3 mL/s, was applied to common carotid artery in all models. The peak systolic Reynolds number and the Womersley number were set to 848 and 2.1. A constant viscosity and density of blood were assumed 3.5 cp and 1060 kg/m^3. **Results:** Velocity profiles at the mid-sinus area showed similar flow pattern during a cardiac cycle in all models. Mean and peak flow rates in the cross sectional area at mid-sinus did not show difference among all models. However, maximum values of wall shear stress at peak systole showed that infant model had the lowest value, which is 10 percent lower than those of other models. Kinetic energy (KE) was also measured at the mid-sinus and adjacent external carotid artery locations. When compared mean KE between two locations in each model, infant and pediatric models showed about 30 percent higher KE level at the sinus, however adolescence and young adult models did not show much difference. **Conclusions:** It is of both fundamental and clinical interest to understand the hemodynamics and developmental forces that play a role in maturation of the sinus. This understanding may lead to better prognostication and therapy of carotid disease.

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W P86

Atorvastatin and Psychomotor Agitation after Carotid Endarterectomy

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Background and Purpose: Psychomotor agitation has been described in up to 22% of patients undergoing vascular surgery. Its detection is important because it may be one of the first neurological manifestations of periprocedural stroke. Some authors have suggested that statins administered within the week before surgery reduces the risk of psychomotor agitation. Our goal was to conduct an exploratory analysis to assess the frequency of psychomotor agitation after carotid endarterectomy (CEA) and to evaluate the relationship between psychomotor agitation and atorvastatin administered before the procedure. **Methods:** We assessed the frequency of psychomotor agitation among every patient undergoing CEA at our institution between 01/01/2006 and 12/31/2009. We performed a univariate analysis to assess the association between atorvastatin and psychomotor agitation within the first 48 hours after CEA. An association was deemed significant if a two-tailed P value of ≤ 0.05 was reached ($\chi 2$, t-test and Mann Whitney). We compared age, gender, frequency of vascular risk factors, degree of stenosis of the operated and contralateral artery, history of dementia or depression, chronic obstructive pulmonary disease, chronic renal failure, and postoperative complications between patients treated and not treated with atorvastatin. Results Overall, 221 CEA were performed during the study period. We excluded 22 cases with simultaneous CEA a coronary artery bypass graft surgery, leaving 199 patients for the analysis: 145 (72.9%) were male, with a mean age of 69±8 years. Forty-four (22.1%, 95%CI 16.9-28.4) patients were previously treated with atorvastatin. We detected psychomotor agitation in 17 cases (8.5%, 95%CI 5.4-13.2). The proportion of patients who developed psychomotor agitation among patients previously treated with atorvastatin and among those not receiving this drug was (0.0 vs. 11.1%, P = 0.015). We found no differences regarding age, gender, frequency of vascular risk factors, degree of stenosis of the operated and contralateral artery, history of dementia or depression, chronic obstructive pulmonary disease, chronic renal failure, and postoperative complications between patients treated and not treated with atorvastatin. **Conclusions:** In our exploratory analysis of patients undergoing CEA, atorvastatin administered in the week before surgery was associated with a lower frequency of psychomotor agitation. Larger cohorts are needed to assess the relation between atorvastatin and psychomotor agitation.

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W P87

Variants at APOE Influence Risk of Deep and Lobar Intracerebral Hemorrhage

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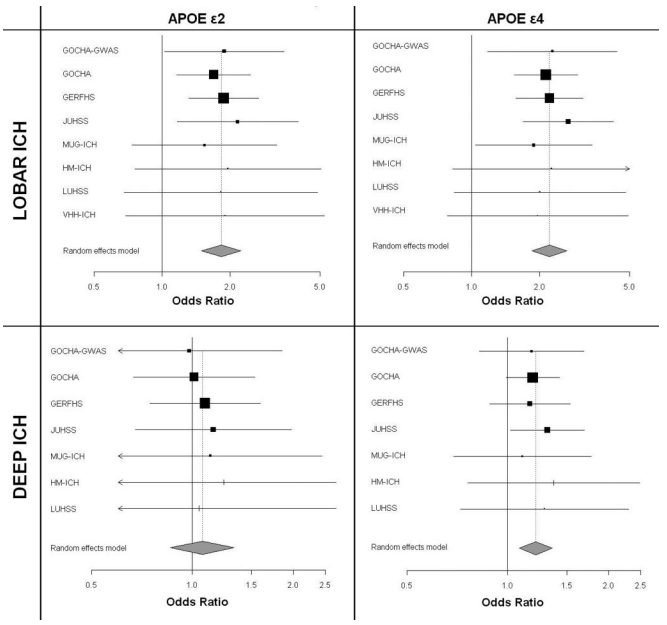
Introduction: Prior studies investigating the association between APOE alleles $\epsilon 2$ / $\epsilon 4$ and risk of Intracerebral Hemorrhage (ICH) have been inconsistent, limited to small sample sizes and did not account for confounding by population stratification or determine which genetic risk model was best applied. **Hypothesis:** we sought to determine whether APOE alleles $\epsilon 2$ / $\epsilon 4$ influence risk of ICH, whether confounding by population stratification might explain any observed association, and which genetic risk model best describes the effect of these alleles on disease risk. **Methods:** We performed a large-scale genetic association study of 2,189 ICH cases (1104 lobar and 1085 deep) and 4,041 controls from seven cohorts, which were analyzed using additive models for $\epsilon 2$ and $\epsilon 4$. Results were subsequently meta-analyzed using a random effects model. A proportion of the individuals (322 cases and 357 controls) had available genome-wide data to adjust for population stratification. We used the Likelihood Ratio (RT) test and Receiver Operator Characteristics (ROC) curves to determine which genetic model (dominant, recessive or additive) best predicts ICH presence in our large sample. **Results:** $\epsilon 2$ and $\epsilon 4$ were associated with lobar ICH (Figure) at genome-wide significance levels (Odds Ratio (OR) = 1.82, 95% Confidence Interval (CI) 1.50 - 2.23, $p = 6.6 \times 10^{-10}$ and OR = 2.20, 95%CI 1.85 - 2.63, $p = 2.4 \times 10^{-11}$ respectively). Restriction of analysis to definite / probable CAA ICH uncovered a stronger effect. $\epsilon 4$ was also associated with increased risk for deep ICH (OR = 1.21, 95% CI 1.08 - 1.36, $p = 2.6 \times 10^{-4}$). Risk prediction evaluation identified the additive model as best describing the effect of APOE genotypes on risk of both lobar and deep ICH (all p-values < 0.01). No evidence of confounding due to population stratification was identified. **Conclusion:** APOE $\epsilon 2$ and $\epsilon 4$ are independent risk factors for lobar ICH, consistent with their known associations with amyloid biology. In addition, we present preliminary findings on a novel association between APOE $\epsilon 4$ and deep ICH. Finally, we demonstrate that an additive model for these APOE variants is superior to other forms of genetic risk modeling previously applied.



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W P88

Variant for Atrial Fibrillation on Chromosome 4q25 Associates with Cardioembolic Stroke in Japan

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Introduction: Atrial fibrillation (AF) is a most common arrhythmia and an independent risk factor of ischemic stroke. Recently, advancing genome-wide association studies has showed that risk variants for AF are related to ischemic stroke in Caucasian patients. However, the association has not been replicated in Asian patients. The aim of this study is to demonstrate the association in Japanese stroke patients. **Method:** We enrolled consecutive ischemic stroke patients who admitted to Nagasaki university hospital within seven days of onset. Three single nucleotide polymorphisms (SNPs) of risk variants for AF, rs2200733 and rs10033464 on chromosome 4q25, and rs7193343 on chromosome 16q22 were tested using direct sequencing. The patients with acute ischemic stroke were classified into five subtypes according to the Trial Org 10172 in Acute Stroke Treatment classification, such as cardioembolism (CE), large-artery atherosclerosis, small-vessel disease, other determined etiology and stroke of undetermined etiology. We investigated the prevalence of three SNPs in the five groups. Furthermore, we divided patients into two groups, CE with AF and non-CE without AF, to determine odds ratios (ORs) with 95 % confidence intervals (CIs) for both dominant and recessive genetic models. **Result:** We included 60 patients of CE, 21 of large-artery atherosclerosis, 11 of small-vessel disease, 20 of other determined etiology and 37 of stroke of undetermined etiology. The prevalence of two copies of rs2200733T was significantly higher in CE than the other stroke groups ($p = 0.012$). The other SNPs had no association with any stroke subtypes. The ORs for the dominant rs2200733 model, TT and CT vs CC, and recessive model, TT vs CT and CC, were 3.72 (95 % CI 1.24 - 11.13; $p = 0.0145$) and 6.05 (95 % CI 2.28 - 16.05; $p = 0.0001$), respectively. **Conclusion:** Our result suggested that a variant SNP for AF, rs2200733 on chromosome 4q25, was associated with CE in Japanese stroke patients. The investigation of rs2200733 in acute stroke patients may be useful for diagnosis and treatment of CE.

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W P89

The Contribution of Cystatin C Gene Polymorphisms on Cerebral Ischemic White Matter Lesions

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Background and Purpose: Cystatin C (CSTC) is a 13k Da protein consisting of 120 amino acids, encoded by a 7.3-kb gene located on chromosome 20. CSTC functions as a major,

general extracellular cysteine protease inhibitor in mammals. *In vitro* experiments have indicated that it can inhibit several cysteine proteases, such as cathepsins B, H, K, L and S. The promoter polymorphism, -82G/C, and signal peptide polymorphism, +148G/A, were reported to account for reduced promoter activity and reduced CSTS secretion, respectively. The haplotype containing these SNPs was reported to be associated with low level of serum CSTS and coronary artery disease. These observations suggest that exaggerated protease activity due to the reduced production of an endogenous inhibitor, CSTC, could contribute to vascular remodeling. In healthy adults, the concentration of CSTC is 5 times higher in CSF than in plasma. Given the physiological function of CSTC described above, it might play an important role in cerebrovascular pathological changes. Accordingly, the effects of *CSTC* polymorphisms on ischemic white matter lesions were investigated under the case-control study design. **Methods:** Three *CSTC* polymorphisms were genotyped in 100 cases, identified by magnetic resonance imaging as having periventricular hyperintensity (PVH), grade 3 on Fazekas scale, and 200 controls with no PVH. Plasma CSTC levels in these subjects were also measured. Expression vectors containing wild type or +148A mutant type CSTC cDNAs were transfected into astrocytoma cells. Expression of CTSC mRNA was analyzed by quantitative RT-PCR. Intracellular and the secreted CSTC protein levels were determined by Western blot and ELISA, respectively. **Results:** A significant association was found between the *CSTC* haplotype and the ischemic white matter lesions (odds ratio=1.86; P=0.04). In a logistic regression model, the mutant haplotype was also associated with low plasma CSTC levels (odds ratio=0.38; P=0.02). The *in vitro* transfection study revealed that, in spite of no effects observed on the CSTC mRNA level, the +148A allele significantly increased intracellular but decreased the levels of secreted CSTC protein. **Conclusions:** Our study demonstrates the significance of *CSTC* polymorphisms in the generation of white matter lesions. The +148A allele of the *CSTC* decreased the extracellular level of CSTC protein probably by attenuating its secretion.

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W P90

Cumulative Association of Six Variants in the KCNK17, LRP, NOS3, SCNN1A and MMP12 Genes with Ischemic Stroke

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Background: We previously reported the association of single nucleotide polymorphisms (SNPs) in five chromosomal regions with ischemic stroke (IS). Each SNP alone showed a moderate association, with odds ratios (OR) ranging from 1.35 to 3.05, so we hypothesized that their combination could reveal a stronger association with IS. **Methods:** We evaluated the combined association with IS of 6 SNPs around the KCNK17 (rs10947803), LRP1 (rs7956957), MMP12 (rs2276109), NOS3 (rs10275136 and rs310585) and SCNN1A (rs5742912) genes in a Spanish population comprising 540 IS subjects and 540 control subjects. IS subjects were divided in cardioembolic (44.8%), atherothrombotic (20.9%) and undetermined (34.3%) etiologies. Statistical analysis and logistic regression were performed under an additive model. Predicted probabilities were calculated with receiver operating characteristic (ROC) curves and compared using the MedCalc software. **Results:** Each SNP was significantly associated with IS after adjustment for the other SNPs and established risk factors, including male gender, age over 55, diabetes mellitus, dislipidemia, hypertension and cigarette smoking. IS risk increased depending on the number of risk alleles carried. Additionally, the combination of 6 SNPs showed clear contribution to risk in comparison with conventional clinical stroke risk factors only, with predictive probabilities of 69.1% vs. 63.4% ($p<0.001$). In subjects who had any five or more of these SNPs, the predictive probability for IS was significantly higher compared with subjects carrying none or only one SNP (OR=26.06, P<0.001). Moreover the risk increased with the number of genetic plus clinical risk variable carried, although no subject in our population carried more than 9 markers. Finally, a risk score was assigned to each variable depending on the â value from the logistic regression and a risk scale from 1 to 45 was then used to classify subjects into three categories. 51.0% of IS cases were in the low risk category (score < 18) compared to 72.4% in the moderate (19 < score < 26, P<0.001 vs. low) and 92.3% in the high risk (35 < score, P<0.001 vs. low). This model permitted to reclassify 10% of the subjects with a moderate risk determined by classical risk factors into the high risk category considering both genetic and clinical data. **Conclusions:** Six SNPs plus classical stroke risk factors showed a cumulative and significant association with IS. These results open diagnostic and therapeutic expectations in stroke.

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W P91

Polymorphisms in the Thrombomodulin - Endothelial Cell Protein C Receptor System and the Risk of Cerebral Infarction in a Biracial Population: The Genetics of Early Onset Stroke Study

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Background and Purpose: The thrombomodulin–protein C system located on the endothelial surface plays a key role in both thrombosis regulation and inflammatory response. Thrombomodulin acts to decrease thrombin's pro-coagulant activity and to increase activated protein C, a natural anti-coagulant. The activation of protein C by the thrombin-thrombomodulin complex is enhanced when the substrate protein C is presented by the endothelial cell protein C receptor. These functions make the thrombomodulin (*THBD*) and endothelial cell protein C receptor (*PROCR*) genes promising candidate genes for stroke susceptibility and were predefined hypotheses for the Genetics of Early-Onset Stroke Study. **Methods:** Study subjects were drawn from a population-based case-control study of ischemic stroke among men (57%) and women (43%) aged 15-49 and included 832 cases of first ischemic stroke (41.4% African-American) and 883 age-comparable control subjects (49% African-American). Controls were identified by random digit dialing and frequency matched to the cases by age and geographical region of residence. Data on historical risk factors were collected by standardized interview. Analyses were performed on 17 single nucleotide polymorphisms (SNPs) in *THBD* and 19 SNPs in *PROCR*, which included the combined SNPs available from Illumina's Omni-1 QUAD GWAS and CVD SNP panels, providing thorough gene-specific coverage. Among Caucasians, SNPs in *PROCR* were among the top 5 risk-associated polymorphisms in our ongoing CVD and GWAS analyses. **Results:** Of the 17 *THBD* SNPs analyzed, 2 SNPs (rs1042579, rs3179123) were associated with stroke (OR~0.6, p=0.03) among African-Americans using an additive vascular model (adjusting for age, sex, race, hypertension, diabetes, smoking, MI). No *THBD* associations were found in Caucasians. Of the 19 *PROCR* SNPs analyzed, 10 SNPs were significant (OR~1.4 p=0.0008-0.02) among Caucasians using the same model; 9 of these SNPs were in strong linkage disequilibrium. No *PROCR* associations were found in African-Americans. Stroke subtype models showed no significant associations in either gene. **Conclusions:** *THBD* and *PROCR* polymorphisms may have race-specific associations with early-onset ischemic stroke. Replication studies are in progress to confirm these findings.

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W P92

The Effect of Survivorship Bias on Cross-Sectional Case-Control Genetic Studies of Highly Lethal Diseases

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Background: Survivorship bias is the phenomenon by which individuals are excluded from analysis of a trait because of mortality related to the expression of that trait. In genetic association studies, variants increasing risk for disease onset as well as risk of disease-related mortality (lethality) could be difficult to detect in cross-sectional case-control designs, possibly leading to underestimation of a variant's effect on disease risk. Hypothesis: We hypothesized that a simulation of longitudinal and case-control genetic association studies would allow quantification of the erosion in effect size estimates attributable to survivorship bias. **Methods:** We modeled cohorts for three diseases of high lethality (intracerebral hemorrhage, ischemic stroke, and myocardial infarction) using existing longitudinal data. Based on these models, we constructed an iterative simulation of case-control genetic association studies for genetic risk factors of varying effect sizes, lethality, and minor allele frequencies (MAF). **Results:** For each disease, erosion of detected effect size was larger for case-control studies of individuals of advanced age (age >75 years) and/or variants with very high event-associated lethality (Genetic-conferred Relative Risk for event-related death >2.0). We found that survivorship bias results in no more than 20% effect size erosion for cohorts with mean age <75 years, even for variants that double lethality risk. Ascertainment of at least 40% of lethal cases reduces this phenomenon, resulting in <20% effect size erosion even for cohorts of advanced age with extremely lethal phenotypes. Furthermore, we found that increasing effect size erosion was accompanied by depletion of MAF in the case population, yielding a "signature" of the presence of survivorship bias. Once again, ascertainment of 40% of lethal cases mitigated this MAF depletion. **Conclusion:** Our results demonstrate that failure to enroll lethal cases can distort the measured effect sizes for genetic variants affecting both disease incidence and lethality. However, this bias results in <20% erosion in effect size for commonly-encountered cohort conditions. Our simulation provides formulae to allow estimation of effect size erosion given a variant's odds-ratio (OR) of disease, OR of lethality, and MAF. These formulae will add precision to power calculation and replication efforts for case-control genetic studies. Our approach requires validation using prospective data.

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W P93

Sex Differences in Genetic Associations with Homocysteine in the Vitamin Intervention for Stroke Prevention (VISP) Trial

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Introduction: Elevated homocysteine (Hcy) is an independent risk factor for stroke and vascular disease. Genome-wide association studies have identified single nucleotide polymorphisms (SNPs) associated with Hcy levels and related diseases. For specific associated SNPs, the associations differed by sex. We sought to investigate the relationship of five previously associated SNPs in participants of VISP including potential sex differences. **Methods:** VISP was a double-blind, randomized clinical trial comparing low vs. high dose folic acid, vitamin B6, and vitamin B12 in patients with a non-disabling cerebral infarction and Hcy levels above the 25th percentile. Data were drawn from a genetic substudy including 2164 participants. Genotypic data were available for rs1801133, rs2274976, rs526934, and rs6586282 from an Ilumina GoldenGate assay. The fifth SNP, rs1047891, was genotyped using a Taqman assay. We studied the SNPs and log transformed plasma Hcy levels using unadjusted, minimally adjusted (sex, race, age), and fully adjusted (sex, race, age, body mass index, smoking status) linear regression models. We also used sex and race stratified analyses. RESULT: SNP rs1047891 in the carbamoyl phosphate synthase 1 (CPS1) gene was associated with Hcy in women (minimally adjusted, P = 0.03) (Table). For rs1801133 in the methylenetetrahydrofolate reductase (MTHFR) gene, the SNP was associated with Hcy in white men and women (minimally adjusted, P = 0.05) and white men (minimally adjusted, P = 0.05). None of the other three SNPs investigated were associated with Hcy. **Conclusion:** SNPs rs1047891 and rs1801133 demonstrate a sex effect regarding an association with plasma Hcy levels consistent with those reported in the literature; an effect in women for rs1047891 and an effect in men for rs1801133. Further studies should examine these SNPs in a larger, more diverse cohort and consider sex differences.

Table: Linear regression results

Chromosome	SNP	Gene	Sex	Race	Model	MAF	P^0	P^1	P^2
2	rs1047891	CPS1	Both	All	Additive	0.33	0.56	0.54	0.65
			F	**All**	**Dominant**	**0.32**	**0.04**	**0.03**	**0.04**
1	rs1801133	MTHFR	Both	White	Additive	0.33	0.13	0.31	0.26
			Both	**White**	**Dominant**	**0.36**	**0.03**	**0.05**	**0.04**
			M	**White**	**Dominant**	**0.35**	**0.01**	**0.05**	**0.05**
1	rs2274976	MTHFR	Both	All	Additive	0.04	0.70	0.84	0.98
11	rs526934	TCN1	Both	All	Additive	0.26	0.45	0.30	0.28
21	rs6586282	CBS	Both	All	Additive	0.16	0.12	0.12	0.05

P^0 = Unadjusted P-value for specified linear regression model
P^1 = Minimally adjusted (sex, race, age) P-value for specified linear regression model
P^2 = Fully adjusted (sex, race, age, body mass index, smoking status) P-value for specified linear regression model

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W P94

Gender Differences In Long-term Mortality After Ischemic Stroke

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Background: Women generally have worse stroke outcomes than men. Older age at stroke onset could be a determinant of this fact, but also differences in vascular anatomy, vascular risk factor control or hormonal profile could be implied in stroke outcome. We aimed to assess short-term outcomes and long-term mortality and recurrence by sex in patients hospitalized with ischemic stroke within a Latin American Healthcare system. **Methods:** Between 12/06 - 05/10, consecutive acute ischemic stroke patients admitted within a Buenos Aires healthcare system were prospectively enrolled in a secondary prevention program. We compared vascular risk factor prevalence and control between sexes, the independent effect of sex on functionality, cognitive status and depression one month post-discharge, as well as on long-term mortality. **Results:** Among 413 stroke patients, mean age 74.2±10 years (women 76±9; men 72±11; p=0.0005), 52% females. Large artery stroke subtype was more frequent in men (15% vs 10%) and cardioembolic events in women (20% vs 14%). Differences between both sexes are shown in the table below. After two years of follow-up Kaplan-Meier analysis shows higher all-cause mortality in women (82 % vs 89 %). Logrank test 0.01. **Conclusions:** women had worse short-term outcomes on functionality and cognition, as well as higher long-term mortality, despite vascular risk factor control at target levels in both sexes. These sex disparities were not explained only by age differences.

	Men (n=198)	Women (n=215)	P
DM	18% (35)	11% (23)	0.02
CHD	22% (44)	9% (19)	0.0001
CRF	17% (33)	7% (15)	0.002
Peripheral artery disease	15 % (29)	7 % (16)	0.01
Pre-stroke			
SBP (mmHg)	133±14	134±17	NS
DBP (mmHg)	79±10	77±10	0.04
Pulse pressure (mmHg)	53±11	56±15	0.01
Fasting glucose (mg/dL)	104±27	96±16	0.0007
Total colesterol (mg/dL)	187±37	201±37	0.0003
HDL-c (mg/dL)	42±10	52±13	0.00001
LDL-c (mg/dL)	114±34	121±33	0.05
Triglycerides (mg/dL)	116±55	117±47	NS
Post-stroke			
SBP (mmHg)	126±15	129±16	0.08
DBP (mmHg)	76±9	76±10	NS
Pulse pressure (mmHg)	50±11	53±13	0.005
Fasting glucose (mg/dL)	98±20	94±17	0.07
Total colesterol (mg/dL)	145±31	160±33	0.00001
HDL-c (mg/dL)	39±10	49±15	0.00001
LDL-c (mg/dL)	82±26	87±27	0.05
Triglycerides (mg/dL)	101±43	105±42	NS
Modified Rankin scale < 2	82% (162)	70 %(147)	0.003
Mean Barthel index	95±10	91±15	0.003
Cognitive impairment by Folstein MMSE	8%(16)	17%(34)	OR 2.4 (1,2-5); p 0.01
Abnormal clock-drawing test	20% (39)	36% (72)	OR 1.75 (1-2.9) p 0.03
Depression	20% (37)	37% (72)	OR 2.54 (1.5-4.2) p 0.0003

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W P95

Racial Differences in Blood Pressure Levels and Management Among Patients with TIA, Acute Ischemic Stroke and ICH

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Background & Purpose: Previous epidemiologic studies demonstrated that despite greater awareness of the diagnosis of arterial hypertension (HTN) and increasing HTN treatment rates, fewer Blacks achieve target blood pressure (BP) levels. **Subjects & Methods:** Consecutive patients with the diagnoses of transient ischemic attack (TIA), acute ischemic stroke (AIS), and intracerebral hemorrhage (ICH) were identified and a retrospective chart review was performed to obtain demographics, history of HTN, home antihypertensive medication use, admission BP, discharge BP, LOS, and antihypertensive medications at discharge. **Results:** A total of 393 consecutive patients admitted to a single tertiary care center from November 2008 thru June 2010 were included (Whites: TIA 31, AIS 93, and ICH 17; Blacks: TIA 38, AIS 176, ICH 38). Demographics and data elements are shown in the Table. Blacks were more likely to have a history of HTN (range 80%-90% vs. 63%-65% across all three diagnoses), to take antihypertensives at home, have higher BP values on admission (DBP and MAP among TIAs and ICH: range 90-110 vs. 83-90 and 112-133 vs. 96-114 mm Hg, respectively), and required twice as many medications at discharge to treat HTN in patients with AIS and ICH. Blacks were more likely to receive calcium channel blockers (all diagnoses) as well as ACE-inhibitors (TIA). Median LOS tended to be longer for Blacks in AIS patients (7d vs. 5d, p=0.053). **Conclusions:** Black patients with TIA, AIS and ICH had greater prevalence of pre-existing HTN and the use of antihypertensives prior to the event. Despite this, they had higher admission BP and required more vigorous antihypertensive treatment by discharge. Refractory hypertension may be one of the factors affecting the stroke rate as well as the increased LOS seen in our Black patients with AIS.

	TIA	AIS	ICH
Age, median (range)			
White	67 (42-97)	66 (26-97)	62 (28-85)
Black	59 (36-86)	65 (23-91)	57 (19-87)
	p=.005	p=.875	p=.085
Male, %			
White	58.1% (18/31)	60.2% (56/93)	64.7% (11/17)
Black	36.8% (14/38)	51.1% (90/176)	52.2% (20/38)
	p=.065	p=.098	p=.185
Admission SBP, median (range)			
White	138 (70-193)	158 (60-234)	169 (147-222)
Black	153 (107-201)	155 (89-260)	178 (107-284)
	p=.065	p=.752	p=.372
Admission DBP, median (range)			
White	83 (30-120)	89 (50-146)	90 (69-134)
Black	90 (49-123)	91 (54-178)	110 (13-168)
	p=.027	p=.426	p=.012
Patients with high BP on admission (SBP>140 or DBP>90), %			
White	51.6% (16/31)	76.3% (71/93)	100% (17/17)
Black	73.7% (28/38)	72.7% (128/176)	86.8% (33/38)
	p=.050	p=.312	p=.144
Patients with very high BP on admission (SBP>160 or DBP >100), %			
White	22.6% (7/31)	49.5% (46/93)	64.7% (11/17)
Black	50% (19/38)	51.1% (90/176)	73.7% (28/38)
	p=.018	p=.447	p=.356
Admission MAP, median (range)			
White	96 (43-140)	114 (66-167)	114 (101-163)
Black	112 (72-145)	112 (69-198)	133 (63-188)
	p=.035	p=.470	p=.051
History of HTN, %			
White	64.5% (20/31)	62.4% (58/93)	64.7% (11/17)
Black	81.6% (31/38)	79.5% (140/176)	89.5% (34/38)
	p=.092	p=.002	p=.037
Taking antihypertensive, %			
White	58.1% (18/31)	64.5% (60/93)	47.1% (8/17)
Black	76.3% (29/38)	74.4% (131/176)	70.3% (26/37)
	p=.087	p=.060	p=.091
NIHSS on admission, median (range)			
White	2 (0-10)	7 (0-29)	19 (3-26)
Black	1 (0-13)	7 (0-37)	15 (0-31)
	p=.357	p=.884	p=.171
LOS, median (range)			
White	2 (1-15)	5 (0-34)	11 (1-37)
Black	2 (0-7)	7 (1-52)	8 (1-86)
	p=.881	p=.053	p=.294
Discharge SBP, median (range)			
White	135 (109-165)	138 (86-184)	147 (113-173)
Black	135 (90-184)	143 (65-218)	147 (89-200)
	p=.686	p=.174	p=.785
Discharge DBP, median (range)			
White	78 (49-105)	75 (38-112)	76 (57-98)
Black	78 (42-112)	77 (38-129)	86 (50-116)
	p=.871	p=.515	p=.080
Discharge MAP, median (range)			
White	97 (70-122)	97 (67-135)	99 (81-119)
Black	95 (58-127)	98 (50-159)	104 (64-136)
	p=.981	p=.346	p=.255
# anti-HTN drugs prescribed on discharge, median (range)			
White	1 (0-3)	1 (0-4)	1 (0-4)
Black	1 (0-4)	2 (0-6)	2 (0-5)
ACE inhibitor, %			
White	45.2% (14/31)	58.1% (54/93)	64.7% (11/17)
Black	71.1% (27/38)	65.3% (115/176)	57.9% (22/38)
	p=.026	p=.149	p=.432
Beta blocker, %			
White	35.5% (11/31)	31.2% (29/93)	41.7% (8/17)
Black	15.8% (6/38)	42.0% (74/176)	50.0% (19/38)
	p=.054	p=.053	p=.536
Calcium channel blocker, %			
White	6.5% (2/31)	18.3% (17/93)	23.5% (4/17)
Black	23.7% (9/38)	32.4% (57/176)	57.9% (22/38)
	p=.050	p=.009	p=.018
ARB, %			
White	6.5% (2/31)	3.2% (3/93)	0% (0/17)
Black	10.5% (4/38)	7.4% (13/176)	5.3% (2/38)
	p=.439	p=.134	p=.473
Diuretic, %			
White	6.5% (2/31)	14.0% (13/93)	0% (0/17)
Black	18.4% (7/38)	18.2% (32/176)	13.2% (5/38)
	p=.133	p=.242	p=.144
Other, %			
White	6.5% (2/31)	6.5% (6/93)	17.6% (3/17)
Black	7.9% (3/38)	11.9% (21/176)	28.9% (11/38)
	p=.597	p=.111	p=.296
More than 1 BP med, %			
White	29.0% (9/31)	44.1% (41/93)	47.1% (8/17)
Black	44.7% (17/38)	58.0% (102/176)	60.5% (23/38)
	p=.138	p=.021	p=.262
Patients with high BP on discharge (SBP>140 or DBP>90), %			
White	41.1% (13/31)	46.2% (43/93)	70.6% (12/17)
Black	36.8% (14/38)	55.7% (98/176)	63.2% (24/38)
	p=.427	p=.089	p=.415
Patients with very high BP on discharge (SBP>160 or DBP >100), %			
White	16.1% (5/31)	17.2% (16/93)	17.6% (3/17)
Black	18.4 % (7/38)	19.9% (35/176)	23.7% (9/38)
	p=.530	p=.359	p=.452

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W P96

Dolichoectasia and Intracranial Arterial Characteristics In A Race-ethnically Diverse Community-based Sample: The Northern Manhattan Study

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Background: Dolichoectasia (DE) of cerebral vessels has been associated with adverse neurological outcomes, including stroke, but few population-based studies exist and normative data on vessel size are lacking. In addition, data are limited in Hispanic and black people who are at greater risk of stroke than whites. We investigated the prevalence of basilar artery (BA) DE and intracranial artery characteristics in a diverse urban community to establish population-based norms. **Methods:** The Northern Manhattan Study (NOMAS) is community-based and includes stroke-free participants who underwent head MRA. We used visual assessment and Smoker's criteria to assess basilar DE based on diameter (>2 SD cutoff of 4.6 mm in Smoker's clinical sample with mean age 48 years), transverse position compared to midline, and height of BA bifurcation. Using a semi-automated 3D tool, with automated tracking of vessel centerlines, we estimated anterior and posterior circulation artery diameters and BA length and volume. We used *t* or Chi Square tests, and multivariable linear regression to compare arterial measurements and participant characteristics. **Results:** There were 402 NOMAS participants with MRA data available (mean age 72±8, 62% women, 56% Hispanic, 23% black, 18% white). The mean±SD, IQR of vessel diameters were: BA=3.8±0.6 mm, 3.4-4.2 mm; left ICA=5.0±0.7 mm, 4.6-5.4 mm; right ICA=5.0±0.6 mm, 4.6-5.3 mm. The prevalence of BA DE was 20%. Eleven percent of our sample met Smoker's BA diameter cutoff of 4.6 mm (>2SD), but only 2% met our >2 SD cutoff of 5.1 mm, in this older population-based cohort. Transverse position was lateral to midline in 63%, and the BA bifurcated at or above the third ventricle floor in 48%. Adjusting for age and sex, DE prevalence was greater in blacks (22%) and Hispanics (23%), compared to whites (12%; black vs white P=0.04, Hispanic vs white P=0.03). In models adjusting for age and race/ethnicity, a larger BA volume/length ratio existed in men than women (P=0.002). Examining age, sex, and race/ethnicity, men had larger BA diameters (P=0.01), and both left and right ICA diameters (p<0.001), but correcting for total cranial volume (TCV) reversed the association (women greater than men; P<0.001 for all diameters). Adjusting for sex and race/ethnicity, ICA diameters were greater among those over 75 years (P=0.04), and correcting for TCV strengthened the association (compared to age <65: P<0.05 for age 65-74, P<0.01 for age 75+). **Conclusions:** Basilar DE was common in our stroke-free sample. Blacks and Hispanics were more affected than whites. Larger arterial diameters were seen in older participants, and sex differences were observed. Correction for head size appeared to be important and has generally not been done in prior studies. Our findings differ somewhat from the patient sample on which Smoker's criteria are based, and suggest brain artery architecture varies with age, sex and race.

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W P97

The Presence of Intracranial Artery Calcification is Associated with Mortality and Vascular Events in Ischemic Stroke Patients

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Introduction: Although intracranial artery calcification (IAC) is a known risk factor for ischemic stroke, its association with stroke outcome has not been assessed. The present study sought to evaluate the occurrence of all-cause death and vascular events in ischemic stroke patients with IAC. **Methods:** Three hundred and twelve patients with ischemic stroke were included by a single center. The seven main cerebral arteries were screened for IAC (defined as hyperdense foci with a peak density of more than 130 Hounsfield units). Complete follow-up datasets were available for 302 of the 312 patients. Major vascular events (included ischemic stroke, myocardial infarction, peripheral arterial disease (i.e. limb-threatening ischemia)) and all-cause deaths were noted. **Results:** IAC was present in 260 patients (83%). Over a median follow-up period of 26.8 months, 67 (22%) deaths or ischemic events occurred. Kaplan Meier analysis showed that the occurrence of all-cause mortality and cardiovascular events was significantly greater in patients with IAC than in IAC-free patients (p= 0.0012, log-rank test). A multivariate Cox proportional hazards analysis established that the IAC score (hazard ratio (HR): 1.25; 95% confidence interval (CI): 1.01-1.55; p=0.04) and glomerular filtration rate (HR: 0.89 for each increment of 10 ml/min/1.73m2; 95%CI: 0.98-1.0; p=0.045) were significantly associated with both all-cause mortality and vascular events. **Conclusions:** In ischemic stroke patients, the presence of IAC is significantly associated with both all-cause mortality and vascular events, suggesting that careful attention should be given to the presence of IAC as a prognostic indicator in a simple head CT scan.

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W P98

Relationship of Site of Vertebral Stenosis to Early Recurrent Stroke Risk in Posterior Circulation Stroke and TIA

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Background: In two recent studies, one Hospital based (St Georges Hospital: SGH) and the other population based (Oxford Vascular Observational Study: OXVASC) the presence of vertebro-basilar (VB) stenosis identified a group of patients with posterior circulation stroke who have a high early recurrent stroke risk. Pooled individual patient data from these two studies were analysed in order to confirm whether VB stenosis is a predictor of early stroke recurrence independently of other risk factors, and whether intracranial or extracranial stenosis confers a higher risk. Methods - 208 consecutive patients from the SGH study and 151 patients from the OXVASC study presenting with posterior circulation TIA or stroke were recruited and prospectively followed for 90 days. CE-MRA or CTA at presentation and 90 day follow up was available in 327. Any recorded posterior circulation TIA/stroke in the month prior to the presenting episode was referred as first event. **Results:** Taking the first event as the index case, the risk of recurrent stroke at 90 days was 24.6% in patients with any VB stenosis (>50%), compared to 8.9% in those without stenosis (OR = 4.2; $P < 0.0001$). The risk of stroke was higher in patients with intracranial stenosis 33.3% (OR = 6.5; $P < 0.0001$) and lower 16.2% in patients with extracranial stenosis (OR = 2.5; P = 0.06). Taking the presenting episode as the index event the risk of recurrent stroke was 9.6% in patients with stenosis compared with 2.8% in those without stenosis (OR = 3.7; P=0.012). The risk of recurrent stroke was higher in those with intracranial stenosis 13.8% (OR = 5.6; $P < 0.0001$); the risk was non significant in those with extracranial stenosis 5.4% (OR = 2.0; P=0.39). Cox regression analysis showed that VB stenosis confers a higher risk of early stroke recurrence independently of hypertension, hypercholesterolaemia, diabetes, smoking, previous stroke and gender. RR=3.5; P < 0.001 and RR=2.96; P = 0.05, taking the first and the presenting event as the index case respectively. **Conclusions:** VB stenosis is an independent predictor of stroke recurrence in patients presenting with posterior circulation stroke and TIA. Intracranial stenosis confers a higher risk. The high early recurrent risk provides a strong rationale for randomised trials, such as VIST, determining whether stenting can reduce recurrent stroke risk.

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W P99

Chlamydia Pneumoniae In Early Lesions Of Patients With Carotid Atherosclerosis

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Background and Purpose: Infectious agents, like *Chlamydia pneumoniae*, could play an important role in the development of atherosclerosis. Recent studies reported that *C. pneumoniae* directly interferes with infected host cells hypoxia-inducible factor-1á regulation during intracellular replication in hypoxia. Objectives were to study at what level of the lesion the infection appears and how this affects the development of the lesion. Furthermore, we studied a relationship between the presence of *C. pneumoniae* and an over-expression of the hypoxia-inducible factor-1á in carotid lesions. The study was performed in 38 carotids with stenosis <50%, 25 carotids with stenosis >70% and 10 middle cerebral arteries. **Results:** The presence of *C. pneumoniae* was detected with PCR. Sera from 22 patients who underwent carotid endarterectomy were subjected to a commercial micro-immunofluorescence test for measuring antibodies to *C. pneumoniae*. Immuno-histological analysis of carotid arteries was used to detect the presence of hypoxia-inducible factor-1á. 42.1% of carotids with stenosis <50% were negative whereas 57.9% were positive. 90.9% of the positive results came from preatheroma lesions whereas only 9.1% came from atheroma lesions. 32% of carotids with stenosis >70% were positive. All of the 10 middle cerebral arteries were negative. Of the 22 serum samples studied, 91% were positive and 9% were negative. There was a significant correlation between the over-expression of HIF-1á in the plaque area with the presence of *C. pneumoniae* in some parts of the artery ($p<0.05$). **Conclusions:** *C pneumoniae* might play an important role in activation and development of the initial stages of the carotid atherosclerotic lesions.

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W P100

Cervical Carotid Artery Dissection is Associated with Styloid Process Length

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Background: Cervical carotid artery dissection is a common cause of stroke in the young. The styloid process varies in length, angulation and proximity to the carotid artery, and there are rare reports of cervical carotid dissection in the presence of an elongated styloid. We hypothesized that styloid process anatomy may be a risk factor for dissection. **Methods:** We performed a retrospective case-control study comparing patients with carotid artery dissection to control patients without dissection. Cases were identified by searching our hospital radiology database from 2001-2009 for all patients with unilateral cervical carotid artery dissection on CT angiography (CTA). Controls were selected from patients who underwent CTA and were explicitly noted to lack carotid dissection, and were matched by sex and age. Two observers blinded to radiology reports measured bilateral styloid length, angulation relative to midline structures, and proximity to the carotid artery lumen by review of axial CTA images. The length of the styloid was calculated by three-dimensional linear approximation, and values were averaged between observers. **Results:** Fifty-one cases of dissection were identified and matched with 51 controls (53% male, mean age 55.2 ± 14.7 years for both). Interobserver correlation was high (r>0.86) for all measurements. In cases and controls combined, there was substantial variability in styloid process length (range 4.6 to 58.5 mm) and angulation relative to midline (range 14° to 104°), but styloid length (r=0.83) and angulation (r=0.77) were highly correlated when comparing the left and right sides. In cases, there was no difference comparing length ipsilateral to dissection to the contralateral side (mean length 30.1 vs. 29.1 mm, p=0.49) or angulation relative to midline between ipsilateral and contralateral processes (45° vs. 43°, p=0.57). The styloid process ipsilateral to the dissection was longer in cases than controls (mean length 30.1 vs. 27.0 mm, p=0.03). For every mm increased styloid length, there was an OR for dissection of 1.07 (95% CI 1.003 - 1.13, p=0.04). In the top quartile of styloid length (>30.7 mm) compared to the bottom three quartiles, the OR for dissection was 2.9 (95% CI 1.1 - 7.6, p=0.02). There was no difference in styloid angulation relative to midline between cases and controls (45° vs. 40°, p=0.21). In many cases, measurement of proximity of the styloid to the carotid artery ipsilateral to dissection was limited by pseudoaneurysm, stenosis, or occlusion. There was moderate correlation (r=0.33) in proximity measurements in controls between sides, allowing consideration of the contralateral side as a proxy for ipsilateral anatomy. The contralateral styloid of cases was not significantly closer to the artery than controls (4.4 vs. 5.2 mm, p=0.12). **Conclusion:** This study suggests that elongation of the styloid process is a risk factor for carotid dissection.

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W P101

Differential Association of Lipid Index in Extracranial and Intracranial Atherosclerosis

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Background: Intracranial and extracranial vascular beds had dissimilar histological characteristics. Atherosclerotic change would involve each of them in a different manner. Several studies to investigate the risk factors of intracranial large artery atherosclerosis(IC-LAA) revealed that hyperlipidemia did not have significant correlation with IC-LAA, in contrast to extracranial large artery Atherosclerosis (EC-LAA). The distinct effect of serum lipids on atherogenesis in the intracranial vascular bed from that in the extracranial vascular beds remained unclear. We assessed the hypothesis that serum lipid indices would be associated with the occurrence of EC-LAA but not with IC-LAA. **Methods:** We retrospectively analyzed 414 patients admitted with acute ischemic stroke from January, 2009 through November, 2009 to Seoul National University Hospital. Patient with incomplete workup or poorly qualified imaging were excluded (n=5). Baseline demographic and clinical information collected at admission. All patients had fasting lipid panels drawn the day after hospital admission. Low density lipoprotein (LDL) cholesterol was calculated. Non- high density lipoprotein (HDL) cholesterol, LDL:HDL,Total cholesterol (TC):HDL, Triglyceride(TG):HDL ratios were also investigated. Based on the clinical syndromes, the results of vascular studies, we divided patients into three groups: 1) those with occlusive lesion (≥50% stenosis or occlusion) of extracranial portion of carotid artery and vertebral artery (EC-LAA group, n=115). 2) Those with occlusive lesion of proximal portion of middle cerebral artery, basilar artery, intracranial portion of internal carotid artery and VA (IC-LAA group, n=127). 3) Those without significant occlusive lesion (non-LAA group, n=167). **Results:** The level of TC, LDL-cholesterol, non-HDL cholesterol, LDL/HDL ratio was higher in the EC-LAA group than IC-LAA and non-LAA group. Multi nominal logistic regression analysis was used to assess the association between the lipid indices and the EC-LAA, IC-LAA groups. Non- LAA group was as a reference. EC-LAA group was associated with TC (OR=1.434 per 1mmol/L increase, 95% CI 1.081-1.904), LDL-cholesterol (OR= 1.464 per 1mmol/L increase, 95% CI 1.074-1.996) and non-HDL cholesterol (OR=1.434 per 1mmol/L increase, 95% CI 1.072-1.918). IC-LAA group did not achieve significant association with lipid indices. **Conclusion:** The results of our study may be regarded as an evidence of differential effect of cholesterol in the pathophysiology of atherosclerosis of extracranial and intracranial vasculature.

Table 1. Multinomial Logistic Regression Analysis on Intra-Atherosclerosis and Extra-Atherosclerosis Group

Variables	OR for Intra-Atherosclerosis		OR for Extra-Atherosclerosis	
	OR	95% CI	OR	95% CI
Total Cholesterol	0.881	(0.670, 1.158)	1.434	(1.081,1.904)
LDL Cholesterol	0.952	(0.703,1.289)	1.464	(1.074,1.996)
HDL Cholesterol	0.590	(0.253,1.377)	1.290	(0.541,3.073)
Triglyceride	0.931	(0,796,1.089)	1.014	(0.873,1.177)
Non-HDL Cholesterol	0.922	(0.692, 1.229)	1.434	(1.072,1.918)
TC/LDL	1.161	(0,745,1.811)	0.663	(0.315,1.396)
TG/LDL	1.056	(0.931,1.198)	0.922	(0.720,1.182)
LDL/HDL	1.140	(0.891, 1.458)	1.181	(0.920,1.515)

* Non-LAA group as a reference group.
† Each lipid index was added individually to the model.
‡ Adjusted for gender, age, hypertension, diabetes, dyslipidemia, smoking, history of stroke, history of heart disease, hemoglobin, Hb A1C, Systolic blood pressure,
LDL = Low Density Lipoprotein, HDL = High Density Lipoprotein, TC = Total Cholesterol, TG = Triglyceride

Author Disclosures: M. Oh: None. B. Kim: None. W. Ryu: None. S. Lee: None. B. Yoon: None.

W P102

PFO Risk Factors and Onset Age of First-Ever Stroke in Young Adults

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Background: Several studies have documented the association between patent foramen ovale (PFO) and cryptogenic stroke, particularly in young adults. Certain anatomic features or coagulation profiles are believed to increase stroke risk. We investigated the relationship between PFO and the age at onset of first-ever PFO-associated stroke in consecutive young adult stroke patients. **Methods:** We reviewed our Get with the Guidelines-Stroke database from 2005-2010 (n=2643 cases) to identify 215 consecutive inpatients, age 18-45y. Additional clinical details were abstracted from the medical records by a stroke neurologist. The following characteristics of the PFO (diagnosed by trans-esophageal or trans-thoracic echo with contrast) were recorded: degree of right-to-left (R-L) shunt (small vs. large), presence of R-L shunt at rest, and presence of an ASA. We also recorded the presence of deep vein thrombus (DVT) and abnormal hypercoagulable panel results (protein C, protein S, or anti-thrombin III deficiency; factor V Leiden mutation; prothrombin gene mutation; elevated antiphospholipid IgG antibody level). The mean onset age of first-ever stroke was compared between patients with and without these factors, and between patients with different numbers of risk factors. **Results:** A total of 199 patients (93%) underwent echo evaluation; R-L shunt was detected in 97 (49%). Of these, 82 were considered to have a 'PFO-associated' stroke; the rest were excluded due to established etiologies such as cerebral artery dissection. The mean onset age of first-ever stroke was significantly lower in patients with large R-L shunts, R-L shunts at rest, with DVT, or abnormal hypercoagulable panel, as compared to patients with small R-L shunts, R-L shunt only with Valsalva, absence of DVT, or negative hypercoagulable lab abnormalities, respectively (Fig. 1). Patients with or without concomitant ASA had no significant difference in the mean age at onset (p=0.53). Patients with $\geq$2 risk factors had an earlier onset age as compared to patients with 0-1 risk factors (35$\pm$8 vs. 39$\pm$7 yr, p=0.02, Fig. 2). **Conclusion:** These data suggest that stroke risk in patients with PFO, as measured by onset age, may be increased in the presence of certain anatomic and lab profiles. Our results may have therapeutic implications. Further research is warranted.

Figure 1

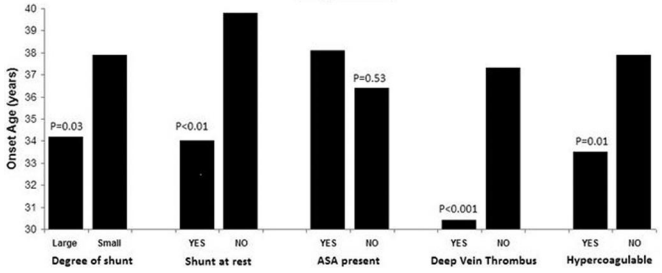
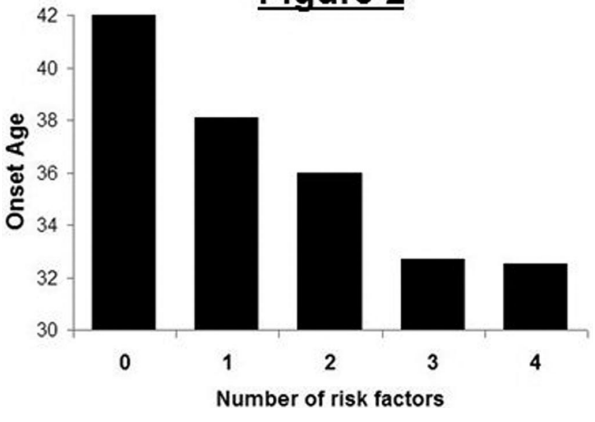


Figure 2



Author Disclosures: R. Ji: None. L.H. Schwamm: Consultant/Advisory Board; Modest; MA Dept of Public Health; Lundbeck Intl Steering Cmte DIAS-4. Other; Modest; Chair AHA GWTG. M. Pervez: None. A.B. Singhal: None.

W P103

Trends In Pregnancy Hospitalizations That Included A Stroke In The United States From 1994 To 2007: Reasons For Concerns?

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Background and Purpose: Despite the encouraging decline in overall stroke incidence and mortality among adults in the developed countries, recently concern that trends in young adults may be less favorable. Given a well documented increase on the prevalence of risk factors for stroke among pregnant women in the United States, we investigated the hypothesis of increasing trends among this group in a large nationwide dataset. **Methods:** Hospital discharge data were obtained from the Nationwide Inpatient Sample developed as part of the Healthcare Cost and Utilization Project sponsored by the Agency for Healthcare Research and Quality. Pregnancy-related hospitalizations with stroke were identified using the International Classification of Diseases, Ninth Revision (ICD-9-CM). All statistical analyses accounted for the complex sampling design of the data source. **Results:** Between 1994-1995 and 2006-2007, the rate (per 1,000 deliveries) of any stroke (hemorrhagic, ischemic, transient ischemic attack, cerebral venous thrombosis, or unspecified) among antenatal hospitalizations increased by 47% (from 0.15 to 0.22 per 1000 deliveries) and by 83% (from 0.12 to 0.22 per 1000 deliveries) among postpartum hospitalizations while remaining steady at 0.27 for delivery hospitalizations. In 2006-2007, about 32% and 53% of antenatal and postpartum hospitalizations with stroke, respectively, had indications for hypertensive disorders or chronic heart disease or heart disease. Changes in the prevalence of these problems from 1994-1995 to 2006-2007 explained almost all of the increase in postpartum hospitalizations with stroke during the same period. **Conclusions:** Our results have demonstrated an increasing trend in the rate of pregnancy-related hospitalizations with stroke in the United States, especially during the postpartum period, from 1994-1995 to 2006-2007.

Author Disclosures: E. Kuklina: None. X. Tong: None. P. Bansil: None. M.G. George: None. W.M. Callaghan: None.

W P104

Stroke and Major Adverse Cardiac Events and Mortality in Peripartum Lupus Patients: A Population-Based Study

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Objectives: To determine the incidence of stroke and the other major adverse cardiac events (MACE) and mortality in peripartum systemic lupus erythematosus (SLE) patients in Taiwan. Methods_ A population-based cohort study was performed on 1,132,089 parturients from 1999 to 2003 using a dataset linking birth. The Kaplan-Meier method was used to estimate the cumulated MACE-free rates and survival rates, and the log-rank test was used to examine the effect of SLE on the incidence of MACE and mortality. Cox-proportional hazard regression modeling incorporating sociodemographic factors and obstetric complications was used to determine the adjusted hazard ratios (HR) of SLE on the risk of MACE and mortality among peripartum women. **Results:** The incidence rate of any MACE and mortality among the peripartum women in the lupus group was 194.67 and 438.82 per 100,000 patient years respectively. Compared to women without SLE, peripartum women with SLE had higher MACE, including stroke (HR 8.02, CI 3.79-16.99, $P<0.0001$), myocardial infarction, (HR, 54.43, CI 16.04- 184.78, $P<0.0001$), heart failure (HR 11.10, CI 2.71-45.52, $P<0.0001$), percutaneous coronary intervention (HR 228.32, CI 43.34-1203.00, $P<0.0001$), thrombolysis therapy (HR 110.88, CI 23.66-519.65, $P<0.0001$), any MACE (HR 9.95, CI 5.60-17.67, $P<0.0001$), and maternal death (HR 11.68, CI 7.97-17.10, $P<0.0001$). Their greater risk remained significant at least 12 months postpartum. **Conclusions:** Although stroke, MACE and mortality are rare events in women of reproductive age, they are increased about ten-fold among peripartum women with lupus. Clinicians would be well advised to pay attention to the possibility of MACE in lupus patients even after successful delivery.

Author Disclosures: P. Chu: None. C. Tang: None.

W P105

Trends in Substance Abuse and Stroke: A Population-Based Study

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Introduction: Currently, the literature suggest that adults aged less than 45 years old represent about 5% of the stroke population. This figure has been rising over time in our region, where we have reported an increase from 4.5% in 1993-94 to 7.3% in 2005. Reasons for this increase are unclear, however increased use of recreational substances that have the potential to cause stroke is one possibility. We attempt to describe substance abuse trends in stroke patients within the Greater Cincinnati/Northern Kentucky Stroke Study (GCNKSS), a population-based study of stroke incidence. **Methods:** We used ICD-9 discharge codes 430-436 to ascertain potential stroke events during three one-year study periods (7/93-6/94, 1999, 2005) among residents of 5 counties that comprise the largely biracial study population of 1.3 million. All potential cases underwent medical record abstraction, and then physician review to determine case vs. not a case, and to further classify stroke subtype. Research nurses abstracted data from the medical record; substance abuse items included street drug, smoking, and alcohol use. Smoking was defined as current if present within the last 3 months. Alcohol abuse was present if there was consumption of 3 or more servings per day, or if heavy use was documented in the chart. Street drug use was defined as use of a substance reported in the chart or positive urine/blood test. **Results:** Over the 3 periods, there was a slight increase in current smoking (21%, 21%, and 24%, respectively), no change in alcohol abuse (5%-6% for all 3 periods), and an increase in street drug abuse (0.5% to 1.5% to 4.6%). In 2005, among 170 subjects with street drug abuse, 47% used marijuana, 35% used cocaine/crack, and 18% other; 76% had positive urine/blood testing. Smoking and alcohol consumption at time of stroke

peaked in the 35-65 year range, while street drug abuse was clearly more prevalent at youngest ages, falling off precipitously after age 55 (Table). Ischemic strokes (IS) accounted for 61% of events where substance abuse was reported. Current smoking was reported in 18-25% in subjects with intracerebral hemorrhage (ICH) and (IS), but in 40% of subarachnoid hemorrhages (SAH). Alcohol abuse was reported in 6-8% of all stroke types. Street drug abuse was reported in 10% of ICH, 5% of IS, and 14% of SAH. **Conclusions:** We found that even though smoking and alcohol use have remained relatively stable, street drug use showed an increase across study periods. The number of stroke subjects with street drug abuse is not trivial and this may contribute to the increased stroke incidence in younger age groups over time seen within our region.

Proportion of stroke subjects with reported substance abuse and age at time of stroke (2005 only)

Age (years)	Current smoker	Alcohol abuse	Street drug abuse
<35	27%	4%	21%
35-44	50%	8%	18%
45-54	47%	10%	15%
55-64	39%	11%	6%
65-74	23%	5%	2%
75-84	11%	2%	0%
85+	4%	1%	0%

Author Disclosures: F. De Los Rios La Rosa: None. J. Khoury: None. K. Alwell: None. C.J. Moomaw: None. D. Kleindorfer: None. J.P. Broderick: None. D. Woo: None. M.L. Flaherty: None. P. Khatri: None. O. Adeoye: None. S. Ferioli: None. J. Eilerman: None. B.M. Kissela: Research Grant; Significant; This work supported by NIH-NINDS R-01 NS30678.

W P106

Effect of Caffeine Consumption on Carotid Intimal Media Thickness and Risk of Stroke: The Framingham Offspring Study

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Background/Purpose: Recent studies support the hypothesis that caffeinated coffee consumption may reduce the risk of stroke. The association between caffeinated coffee consumption and reduction in cerebrovascular events remains unclear. Carotid intima media thickness (IMT) is a validated measure of atherosclerosis that predicts incident stroke and myocardial infarction. We sought to explore the association between caffeinated beverage use and carotid IMT with a goal of investigating one possible mechanism by which caffeinated beverages reduce the risk of stroke. **Methods:** We studied members of the Framingham Offspring Cohort (examination 6) who had carotid ultrasonography performed. Data regarding caffeine use, comorbidities predisposing to stroke and atherosclerotic disease, and factors influencing carotid IMT were obtained. Statistical analyses were done to evaluate the cross sectional relationship of caffeinated beverage use and carotid IMT and time to event analyses assessing the relationship of caffeinated beverage use and carotid IMT with the outcomes of death, stroke, and myocardial infarction (MI). **Results:** 3,380 patients were included. On multivariate analysis, after correcting for age, sex, body mass index, diabetes mellitus, hypertension, and smoking, higher mean of the maximum common carotid IMT values during diastole were noted among caffeine and coffee drinkers ($p = 0.037$ and 0.0088 respectively). The mean of the maximum common carotid IMT was significantly associated with a higher risk of MI (adjusted HR = 1.10, 95% CI 1.03-1.18, $p=0.0032$), stroke (adjusted HR = 1.12, 95% CI 1.02-1.24, $p=0.0234$) and death (adjusted HR =1.09, 95% CI 1.03-1.16, $p=0.0050$). Hazard ratios correspond to a 0.2 mm increase in carotid IMT. Increasing mean of the maximum internal carotid IMT measurements were also significantly associated with a greater risk for MI and death, but not stroke. **Conclusions:** Our results confirm previous findings that increasing carotid IMT is associated with stroke, death, and MI. These preliminary findings suggest that the mechanism by which caffeine and coffee consumption reduce the risk of stroke is not related to a beneficial effect on carotid IMT. Further investigations into the relationship between caffeine consumption and its role in the reduction of cerebrovascular events are necessary.

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W P107

Cerebral Venous Thrombosis in a Mexican Multicenter Registry of Cerebrovascular Disease: The RENAMEVASC Study

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Background: Cerebral venous thrombosis (CVT) is the rarest form of cerebrovascular disease. Few studies exist on all-type acute stroke addressing the relative frequency, characteristics and outcome of hospitalized patients with CVT. We aimed to describe a first-step stroke surveillance system on CVT. **Methods:** CVT cases were selected from the RENAMEVASC register, conducted during two years in 25 centers. Risk factors, neuroimaging and 30-day outcome as assessed by the modified Rankin scale (mRS) were analyzed. **Results:** From 2000 all-type acute cerebrovascular disease patients, 59 (3%; 95% CI: 2.3-3.8%) had CVT (50 women, female-to-men ratio 5.5/1, mean age 33 years). Puerperium (42%), contraceptive use (18%) and pregnancy (12%) were the main risk factors in women. In 67% men CVT was registered as idiopathic. No thrombophilia assessment was practiced. Longitudinal superior sinus was the most frequent CVT location (78%). Extensive (>5 cm) venous infarction occurred in 36% cases. Most patients (64%) were treated with heparin or heparinoids. Decompressive craniectomy occurred in 3%. Thrombolysis was not performed. Systemic venous thromboembolism (14%), endotracheal intubation (14%) and pneumonia (8%) were the main in-hospital complications. Thirty-day case fatality rate was 3% (95% CI: 0.23%-12.2%), inversely associated with Glasgow coma scale (GCS). Functional independency (mRS 0-2) was attained in 73%, being positively associated with increasing GCS, and negatively associated with age. **Conclusions:** Relative frequency of CVT in hospitalized Mexican patients is higher than in other registries. Thrombophilia assessment was suboptimal. In this primarily young cohort, acute case fatality rate is low, but at expense of more neurologic impairments.

Author Disclosures: J. Ruiz-Sandoval: None. E. Chiquete: None. L. Bañuelos-Becerra: None. C. Torres-Anguiano: None. C. González-Padilla: None. A. Arauz: None. C. Cantú: None. L.M. Murillo-Bonilla: None. J. Villarreal-Careaga: None. F. Barinagarrementeria: None.

W P108

Insufficient Platelet Inhibition Is Related With Acute Cerebral Infarction After Coronary Artery Angiography.

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Coronary artery angiography (CAG) occasionally causes cerebral infarction. The dislodgement of atheroma form the aortic arch during CAG has been raised as the most plausible mechanism, but the exact mechanisms of the infarction have not been clearly verified yet. We hypothesized that platelet aggregation would be one of the most important mechanisms of CAG related cerebral infarction. In phase 1 study, among the patients who were admitted to Asan Medical Center (AMC) due to acute coronary syndrome between Jan 2006 and July 2006, we retrospectively reviewed DWI and MR angiography, which was performed within 7 days after CAG, as a presurgical evaluation of coronary artery bypass graft (CABG) surgery. We analyzed the incidence and lesion patterns of acute ischemic lesions (AILs) defined by high signal intensity lesions on DWI, which represents acute cerebral infarction. In phase 2 study, we have prospectively recruited 102 patients who were scheduled for CABG after diagnostic CAG in AMC between July 2007 and June 2009. The extent of platelet inhibition by anti-platelet agents was measured using aspirin reaction unit (ARU), P_2Y_{12} reaction unit (PRU) and % inhibition within 6 hours after CAG. DWI and MR angiography were performed within 7 days after CAG. These parameters were compared between the two groups divided by the occurrence of AILs after CAG. AILs were observed in 45 patients (15.6%) in phase 1 study and 17 patients (16.7%) from phase 2 study. Majority of the AILs were located at the cortex (88.9%), and slightly more frequently observed in right carotid circulation (55.6%) than in left carotid (30.8%) or in vertebra-basilar circulation (13.7%). ARU and PRU were significantly higher in the patients with post-CAG acute cerebral infarction than those without (ARU: 489.5±71.5 vs 446.3±53.5; $p=0.02$, PRU: 351.7±65.2 vs 330.7±77.0; $p=0.002$). % inhibition, which represents the portion of inhibited platelets, was lower in the patients with post-CAG acute cerebral infarction (6.1±10.7 vs 15.3±17.8; $p=0.02$). WBC count (OR 1.354 95% CI 1.072-1.711; $p=0.01$) and ARU (OR 1.014 95% CI 1.004-1.024; $p=0.006$) were independently related to the occurrence of post-CAG acute cerebral infarction from the result of multivariate analysis. This study reveals that insufficient platelet inhibition by anti-platelet agents can cause acute cerebral infarction after CAG.

Author Disclosures: B. Kim: None. E. Lee: None. Y. Do: None. S. Lee: None. D. Kang: None. S. Kwon: Research Grant; Significant; This study was supported by a grant (A060171) of the Korea Health 21 R&D Project, Ministry of Health, Welfare and Family Affairs, Republic of Korea.

W P109

The Unchanging Risk of Stroke Following Cardiac Valve Replacement

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Objective: To determine if the incidence of stroke following cardiac valve replacement has changed over 20 years. Background: Heart valve replacement surgeries account for 20% of all

cardiac procedures and the number is expected to rise as the population ages. (Birkmeyer, NEJM 2002) Our previous work showed the rate of stroke after CABG was 1.4% (Dubinsky, Neurology 2007). **Methods:** Retrospective cohort analysis of the Nationwide Inpatient Sample (NIS, HCUP, AGRQ.gov), a 20% stratified sample of US hospital admissions, from 1988 - 2007. All adult admission records for cardiac valve surgery were analyzed. Records were divided into five-year cohorts to examine for trends over time. Logistic regression was used to control for confounders and the Charlson score for comorbidities. Because of multiple comparisons and the large number of records, p was set a priori at $< .0001$. **Results:** Of 311,945 records, 47.22% were women. The rate of post-operative stroke changed over time: 1988-92: 3.47%, 1993-7: 4.50%, 1998-02: 4.20%, 2003-7: 3.45%.; while the median age and comorbidities increased, length of stay and mortality decreased, and the proportion discharged to nursing homes increased. The rate of post-operative stroke was higher for women, those with $>$ median age, more comorbidities, and for the middle two cohorts. Logistic regression for post-operative stroke: male vs. female 0.94 (95% CI 0.90-0.97); age $>$ median 1.27 (1.22-1.32); Charlson score ≥ 4 compared to 0: 11.41 (10.56-12.3), 3 vs 0: 7.59(7.00-8.20), 2 vs 0: 5.08 (4.70-5.47), 1 vs 0: 3.22(3.00-3.47); 2003-7 vs 1988-1992:0.61(0.57-0.66), 1998-02:0.87(0.82-0.93), 1993-7: 1.01(0.95-1.08). **Conclusion:** Over the last 20 years, the incidence of stroke following valvular surgery has changed little and remains three times that seen after CABG. Advances in cardiac surgical techniques have resulted in older patients with more comorbidities undergoing valve replacement surgery.

Author Disclosures: C.G. Lechtenberg: None. R.M. Dubinsky: None.

W P110

Impact Of $CHADS_2$ Score On Severity And Outcome Of Ischemic Stroke

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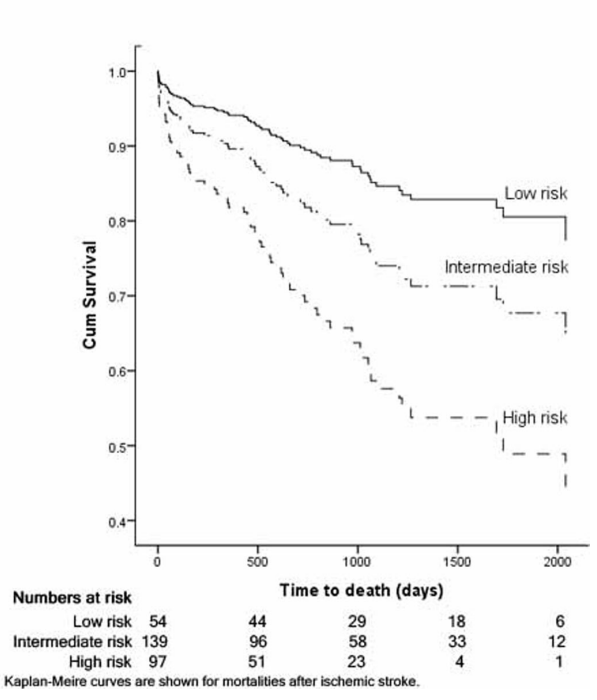
Background: $CHADS_2$ is a widely used system for estimating risks of incident stroke in patients with atrial fibrillation (AF). However, effects of $CHADS_2$ score on stroke severity and outcome in patients with stroke due to AF has not been elucidated yet. **Method:** We enrolled acute ischemic stroke patients with AF who visited the stroke unit within 7 days after onset between October 2002 and September 2008. The $CHADS_2$ scores were categorized into three groups: 0 point, low risk; 1-2, intermediate risk; 3-6 high risk. Poor neurological state was defined using the established systems: the National Institute of Health Stroke Scale (NIHSS) score$>$3 and the modified Rankin Scale (mRS) score$>$2 at discharge. Mortality information was obtained until the end of 2008. **Results:** A total of 298 patients with AF-related stroke were included in this study. The high risk $CHADS_2$ scores at admission were a powerful predictor of poor neurological outcome [for NIHSS: odds ratio (OR) 2.68, 95% confidence interval (CI) 1.11-6.44; for mRS: OR 2.97, 95% CI 1.23-7.16] after control of all possible confounders. In addition, the high risk $CHADS_2$ scores were an independent predictor of all-cause death during the follow-up (hazard ratio (HR) 3.01, 95% CI 1.18-7.65) and vascular death (HR, 12.25, 95% CI, 1.50-99.90). **Conclusion:** Although the $CHADS_2$ was originally designed in order to find patients with future risk of stroke, our study shows that this system may be used to predict poor neurological outcome after AF-related stroke.

Figure 1. Mortality curves of the study population according to $CHADS_2$ score



Kaplan-Meire curves are shown for mortalities after ischemic stroke.

Author Disclosures: D. Kim: None. J. Chung: None. C. Kim: None. W. Ryu: None. E. Park: None. S. Lee: None.

W P111

Predictive Value of The Essen Stroke Risk Score for the recurrence of non-cardioembolic stroke in Japanese patients. The Results from the EVEREST (Effective Vascular Event REduction after STroke) registry

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Background/Aim: The Essen Stroke Risk Score (ESRS) was derived from cerebrovascular patients in the CAPRIE (Clopidogrel versus Aspirin in Patients at Risk of Ischemic Events) trial. It was proved to be useful for secondary prevention strategies using the REACH (REduction of Atherothrombosis for Continued Health) registry data. However, it was still unknown whether the score is applicable in Japanese patients. We aimed to confirm clinical predictability of the ESRS in the EVEREST (Effective Vascular Event REduction after STroke) cohort that involved 3,452 Japanese outpatients with non-cardioembolic stroke (Ischemic Stroke; IS) of low to moderate disability from 2006 to 2008. Recurrent IS at one year follow-up was used as a primary outcome. **Methods:** To calculate annualized event rate, the total number of events was divided by total number of patient-year in each category of ESRS points. Cummulative event rate in each category of ESRS was compared by log-rank test. **Results:** Of the 3,452 the patients initially recruited, one year outcome data was available in 3,411 patients (follow-up rate 98.8%) Patient characteristics at baseline were as follows: mean age of 69 years, 67% of men, 75% of hypertension, 26% of diabetes mellitus, 2.2% of atrial fibrillation, and 23% of current smokers. ESRS distributed from 1 to 7 points, while 59% of them were with point 3 or less. There were 10 fatal strokes (5 from ischemic, 5 from hemorrhagic) and 5 cases of cardiovascular deaths, but no deaths from myocardial infarction. IS recurrence occurred in 157 cases (4.5%) and hemorrhagic stroke occurred in 15 (0.4%) during one-year follow-up. Annualized event rates were 3.27%, 3.15%, 3.85%, 5.49%, 6.14%, 5.28% for ESRS=1, 2, 3, 4, 5, 6/7, respectively (P=0.0051, for the difference among ESRS groups). Patients with ESRS of 4 or more exhibited significantly higher events rate of IS recurrence than others (P=0.0007). **Conclusions:** Similar to the result from the REACH registry, the ESRS may be used as a useful predictor for IS recurrence in Japanese stroke patients of the EVEREST registry.

Author Disclosures: Y. Okada: Research Grant; Significant; sanofi-aventis KK.

W P112

Albuminuria, Kidney Function and Risk of Stroke in the REGARDS Cohort

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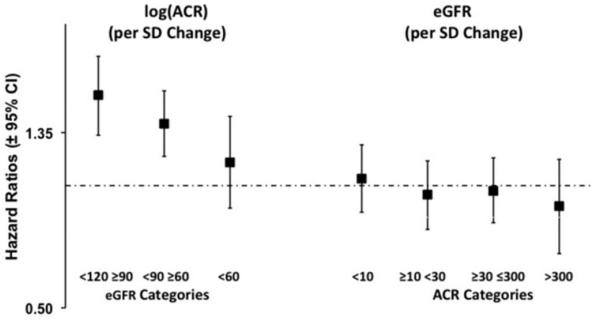
Background: Chronic kidney disease has been associated with increased stroke risk but previous studies have not evaluated the independent contributions of urinary albumin/creatinine ratio (ACR: mg/gm) and reduced estimated glomerular filtration rate (eGFR: ml/min/1.73 m^2) in the same cohort. **Methods:** The association between ACR and eGFR with incident stroke was evaluated among participants in the REasons for Geographic and Racial Differences in Stroke (REGARDS), a national population-based longitudinal cohort of 30,239 blacks and whites, aged $>=45$, enrolled 2003-2007. After excluding those with a history of stroke or end stage renal disease, the analysis population included 24636 participants. Blood, a spot morning urine, and physical measurements were collected during an in-home visit. Participants are followed every 6 months to identify incident strokes which were physician verified. The hazard ratio for incident stroke was calculated for eGFR and log-transformed ACR modeled as continuous variables normalized by standard deviation (SD). Adjustment was made for baseline age, sex, race, age-race interaction, anti-hypertensive medication use, systolic blood pressure, smoking, diabetes, history of heart disease, and body mass index. **Results:** Among REGARDS participants with eGFR $>=90$, higher ACR was associated with an increased multivariable adjusted hazard ratio for stroke (HR=1.67 (95% CI 1.33, 2.08) for each SD increase in log transformed ACR. This association was weaker for individuals with lower eGFR levels (p for interaction 0.02). In contrast, there was no association of eGFR and stroke across all strata of ACR (figure). Each SD change in eGFR was associated with stroke only in univariate models (HR=1.35, 95% CI 1.23, 1.47). After adjustment for age, race, and sex this association was no longer present (HR=1.08, 95% CI 0.97, 1.20). **Conslusions:** Among REGARDS participants ACR was associated with risk of incident stroke, independent of other factors, and only in those with normal eGFR. eGFR was not associated with stroke risk after accounting for ACR and other risk factors, in particular age, race and sex. Lack of association of ACR with stroke among those with eGFR <60 ml/min/1.73 m^2 may be due to competing risks of mortality, coronary events or incident ESRD. These findings suggest that measurement of ACR might be helpful to assess stroke risk in adults with normal kidney function.



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W P113

Impact of Chronic Kidney Disease on Outcome and Mortality in First-ever Ischemic Stroke: The Fukuoka Stroke Registry

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Background and Purpose: Chronic kidney disease (CKD) is recognized as an independent risk factor for cardiovascular disease including stroke. We examined the effect of CKD on the clinical characteristics, outcome and mortality in patients with acute first-ever ischemic stroke, and focused especially on subtypes of ischemic stroke. Methods-Fukuoka Stroke Registry is a multicenter epidemiological study database on acute stoke. From June 2007 to May 2009, 1,258 consecutive patients with acute first-ever ischemic stroke were enrolled. The patients were divided into 345 lacunar, 292 atherothrombotic, 287 cardioembolic and 334 undetermined subtypes of infarction. GFR was estimated using the equation proposed by the Japanese Society of Nephrology as follows: GFR (ml/min/1.73m^2) = 194 $\times$ Cr-1.094 $\times$ Age-0.287 $\times$ 0.739 (if female). An estimated GFR rate $<$ 60 mL/min/1.73 m^2 was defined CKD. We examined the association between CKD and 1-year outcomes and mortality in patients with acute ischemic stroke. **Results:** CKD was present in 30% of total stroke patients. The frequencies of CKD in cardioembolic, atherothrombotic, lacunar and undetermined subtypes of infarction were 43, 31, 20, and 26%, respectively. The frequency of CKD in cardioembolic brain infarction was significantly higher than those in the other types of brain infarction after adjustment for age. In total patients, the proportions of mild neurological deficit (the National Institutes of Health Stroke Scale score $</=$ 4) at admission and discharge were lower in the patients with CKD (56.2% and 75.0%) than those without CKD (66.7%; P$<$0.0005 and 81.8%; P$<$0.01). The proportions of favorable outcomes (modified Rankin scale $</=$ 1) at discharge, 3 months, 6 months and 1 year after onset of brain infarction were significantly lower in the patients with CKD (42.5%, 43.4%, 45.4%, 45.8%) than those without CKD (55.4%, 58.9%, 61.5%, 60.7%; P/= 2 points) during hospitalization tended to be higher in patients with CKD (P=0.09) than that in patients without CKD. The survival curves showed that one-year survival rate was lower in the patients with CKD (72.4% in cardioembolic, 87.9% in atherothrombotic) than those without CKD (86.7% and 96.0%). **Conclusions:** CKD is a strong independent predictor of poor outcome and mortality in patients with acute brain infarction.

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W P114

Type 1 Diabetes Mellitus and Ischemic Stroke: Clinical Features and Long-Term Prognosis

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Diabetes is a risk factor for both first and recurrent stroke. We previously showed that particularly type 1 diabetes (T1DM) is independently associated with 5-year risk of death and recurrent vascular events in young adults after ischemic stroke, while T2DM is not. We compared demographics and stroke type (TOAST) with outcome clinical features and prognosis between T1DM-, T2DM-, and nondiabetic patients using data of 1008 consecutive patients (age 15-49) with first-ever ischemic stroke (Helsinki Young Stroke Registry). Kaplan Meier statistics allowed risk estimations of (1) nonfatal or fatal recurrent ischemic stroke; (2) nonfatal or fatal myocardial infarction (MI), other arterial thrombotic event or revascularization procedure; (3) composite vascular endpoint (MI, any stroke, revascularization, or vascular death); and (4) death of any cause. Multivariate Cox proportional hazards function was used to investigate independent association of demographics and stroke type with outcomes 1 and 3 in T1DM-patients. Patients with T1DM (n=44) had more frequently hypertension and cardiovascular disease at baseline and their index stroke was more often related to small-vessel disease compared with nondiabetic patients (n=904). Compared with T2DM-patients (n=60), T1DM-patients were younger, less obese, but had more frequently cardiovascular disease and their index stroke was small-vessel stroke. After a mean follow-up of 9.0 ($\pm$3.8) years in survivors, patients with T1DM were at considerably higher risk of all studied outcomes (P<0.001 for all endpoints) compared with nondiabetic subjects, and at higher risk of MI/other arterial events and particularly composite vascular events (65.6% at 10 years) compared with T2DM-patients (46.9% at 10 years). In univariate comparison, female gender, longer diabetes duration, and retinopathy were associated with recurrent ischemic stroke. Female gender, dyslipidemia, hypertension, retinopathy, longer diabetes duration, and worse renal function were related to higher risk of a composite vascular event. In multivariate analysis, female gender (odds ratio 4.32; 95% confidence interval 1.48-12.58) and baseline retinopathy (6.33; 1.40-28.58) were associated with recurrent nonfatal or fatal ischemic stroke while dyslipidemia was associated with the composite vascular endpoint (3.28; 1.28-8.41). We conclude that young adults with first-ever ischemic stroke and T1DM had a distinct risk factor and etiologic profile compared with nondiabetic subjects and with T2DM-patients_and had strikingly high long-term risk of vascular events. Retinopathy had the strongest association with recurrent ischemic stroke and may reflect a generalized and active form of small-vessel disease.

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W P115

Effects Of Obesity On Clinical Outcome In Patients With Brain Infarction Fukuoka Stroke Registry

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Background: Although obesity is recognized as a cardiovascular risk factor, it is not fully understood whether obesity is associated with a worse clinical outcome. An obesity paradox, a decrease in mortality with increasing BMI, has been shown in patients with cardiovascular diseases; however, it is not reported in patients with cerebrovascular disease. The aim of this study is to determine if BMI influences the clinical outcome of the patients with acute brain infarction. **Methods:** The Fukuoka Stroke Registry is a multicenter epidemiological and observational study of acute stroke involved seven stroke centers in Fukuoka in south part of Japan, established on 2007. This study was approved of the local ethic committee of Kyushu University and each hospital. FSR is consisted of two database systems, i.e. prospective and retrospective databases. Prospective database recruited consecutive patients with acute stroke within seven days from the onset. At the hospitalization, written informed consent was obtained. The database collected data on patient demographics, medical history and outcomes. Moreover, long-term prognosis was collected. We analyzed the prospective data of these patients with first-ever brain infarction. BMI, subtype of brain infarction (athelotholombotic (ATBI), lacunar (Lac), cardioembolic (CE) and others), age and presence of risk factors (hypertension, diabetes mellitus and hyperlipidemia) were compared scores of modified Rankin scale (mRankin) at 1 year after onset. We defined good prognosis as mRankin 0 and 1 and poor prognosis as 2 to 6. **Results:** 1,432 patients with first-ever brain infarction were registered to FSR (from June 2007 to June 2009). BMI was significantly higher in the patients with good prognosis than those with poor prognosis (23.7$\pm$3.6 kg/m2 vs 22.2$\pm$4.0, P$<$0.01). Both younger age (66.9 years$\pm$11.5 vs. 76.0$\pm$11.2, P$<$0.01) and presence of hyperlipidemia (53.3% vs. 39.8%, P$<$0.01) were related with good prognosis. Neither hypertension nor diabetes influenced the prognosis. Distribution of the stroke subtype was significantly difference between good (18.6% in ATBI, 36.0% in Lac, 15.6% in CE and 29.9% in other) and poor prognosis (28.6%, 17.3%, 30.3%, 23.9%, respectively). Multivariable analysis showed that BMI, age, stroke subtype and presence of hyperlipidemia were independent predictors of one-year prognosis. **Conclusions:** In our stroke registry, high BMI is associated with good prognosis at one year after onset in patients with first-ever brain infarction. The relationship between BMI and outcome in patients with cerebrovascular disease is complex, and further study is important to elucidate the precise relationship.

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W P116

Influence of Body Mass Index (BMI) on Arterial Stiffness

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Hypothesis: Increased body weight (BMI) is an independent risk factor for stroke. We believe that BMI is associated with arterial stiffness. The aim of this study was to assess influence of growing BMI on arterial stiffness. **Patients and Methods:** Subjects were grouped into four BMI categories; normal weight (29 subjects, BMI=18.5-24.9), overweight (43 subjects, BMI=25.0-29.9), obese class I (23 subjects, BMI=30.0-34.9), and obese class II (10 subjects, BMI=35.0-39.9). There were no subjects in severely underweight (BMI40) categories. Arterial stiffness was measured in all subjects by Duplex sonography, e-Tracking mode on Aloka prosound â7, in both common carotid arteries, 3 cm proximal to carotid bifurcation. Logistic regression analysis was performed, adjusting for blood pressure, diabetes and age. Adjustment for cholesterol levels was not possible due to insufficient data. Level of significance in logistic regression for right ACC was P$<$0.028, and for left ACC was P$<$0.206. **Results:** There were 105 subjects, 54 females, and 51 males. Mean age was 58.4 years. Average BMI in four BMI categories was 22.6 in normal weight (BMI=18.5-24.9), 27.3 in overweight (BMI=25.0-29.9), 32.7 in obese class I (BMI=30.0-34.9), and 36.9 in obese class II (BMI=35.0-39.9). Average beta-stiffness measurements on common carotid arteries were for BMI normal weight group 7.96 (right ACC 7.81, left ACC 8.11), overweight group 8.77 (right ACC 8.85, left ACC 8.69), obese class I group 9.26 (right ACC 8.98, left ACC 9.47), and obese class II group 13.05 (right ACC 12.31, left ACC 13.5). In the regression analysis adjusted for confounding factors, the association of BMI and arterial stiffness remained significant (right ACC P$<$0.0055; left ACC P$<$0.0007). **Conclusion:** There is significant association of BMI with arterial stiffness. We speculate that arterial stiffness is a marker of stroke risk and that a decrease in stiffness may precede a decrease in stroke risk.

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W P117

Paradoxical Effect of Obesity on Hemorrhagic Transformation after Acute Ischemic Stroke

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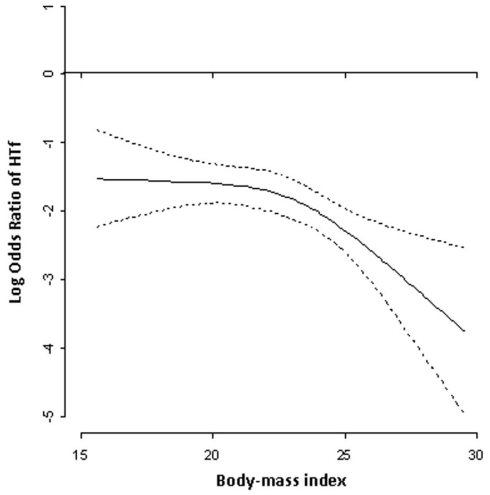
Introduction: Obesity has been implicated as one of the major risk factors of cardiovascular diseases, but obese patients with cardiovascular disease tend to have a more favorable prognosis which is known as "obesity paradox". Hemorrhagic transformation (HTf) frequently complicates ischemic stroke with or without thrombolytic treatment. HTf after acute ischemic stroke was determined to be one of the most important risk factors leading to poor outcome, but no previous clinical study has reported the effects of obesity on HTf. In this study, we investigated the relationship between obesity and HTf after acute ischemic stroke. **Methods:** Seven-hundred forty-three acute ischemic stroke patients who had been admitted to Seoul National University Hospital within 7 days after ictus between October 2002 and March 2006 were consecutively enrolled in this study after excluding patients with only transient ischemic attack. Demographic and clinical information was collected and HTf was evaluated through follow-up T2*-weighted gradient-echo MRI performed within 1 week after stroke. Body mass-index (BMI) and obesity status were examined in relation to HTf by logistic regression analyses. Obesity was defined using World Health Organization Western Pacific Regional Office criteria, which reflected different risk factor and body fat distribution in Asian population. **Results:** Among 743 included patients, HTf was noted in 90 patients (12.1%), mean BMI was 23.2±3.1 kg/m^2, and obesity was found in 27.5%. BMI was independently associated with decreased risk of HTf in acute ischemic stroke [odds ratio (OR), 0.91 per 1 kg/m^2; 95% confidence interval (CI), 0.84-0.99] after adjusted by age, gender, thrombolytic therapy, acute heparin treatment, stroke severity and subtype, and the history of stroke, hypertension, diabetes mellitus, hyperlipidemia and smoking. Compared to patients with normal weights, overweight patients showed a trend of decreased risk of HTf [adjusted OR, 0.58; 95% CI, 0.30-1.11], and obese patients had significantly lower risk of HTf [adjusted OR, 0.28; 95% CI, 0.14-0.63]. **Conclusions:** From our study, obesity status was associated with lower risk of HTf after acute ischemic stroke. This paradoxical effect of obesity on HTf may be considered in clinical stroke research and management.

Body-mass index by log odds ratio of hemorrhagic transformation using restricted cubic splines with 3 knots in patients with ischemic stroke



Author Disclosures: C. Kim: None. B. Kim: None. W. Ryu: None. S. Lee: None. B. Yoon: None.

W P118

Cerebral Microbleeds: Risk Factors And Relationship with Hematoma Volume And In-Hospital Mortality Following Intracerebral Hemorrhage

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Objective: To evaluate risk factors for cerebral microbleeds (CMB) and whether they influence acute hematoma volume or in-hospital mortality following intracerebral hemorrhage (ICH) **Introduction:** Presence of CMB on magnetic resonance imaging (MRI) is a known risk factor for future intracerebral hemorrhages. However, it is not clear if they 1) are markers for greater vascular fragility in the acute setting; 2) predispose to larger hematoma volume; or 3) alter outcomes following ICH. **Design/Methods:** We retrospectively reviewed the charts of consecutive patients diagnosed with spontaneous ICH at our institution between 2006 and 2010 and in whom brain MRI was performed within 30 days of admission. We collected data on patient demographics, medical history, admission creatinine, size and location of acute hemorrhage, and disposition at discharge. We also recorded the number of CMB evident on gradient echo sequencing (GRE) and presence of diffusion-weighted imaging (DWI) abnormalities on MRI. Univariable and correlational statistics were used to assess the relationship between 1) risk factors and CMB and 2) presence and number of CMB and ICH volume and discharge outcomes. We used logistic regression to identify independent risk factors for CMB. **Results:** Of 617 consecutive ICH patients, 276 (44.7%) underwent brain MRI and 245 (39.7%) had interpretable GRE imaging without artifact (mean age 59 years; 51.0% female; and 49.8% African-American). Hemorrhages were basal ganglionic in 39.2%, lobar in 40.2%, and infratentorial in 20.4% and median hematoma volume was 7.1 (IQR 1.9-20.2) mL. Microhemorrhages on GRE distant to the hematoma bed was noted in 59.6%; DWI abnormalities were noted in 23.7%. Presence of CMB was associated with advancing age (61.7 vs. 56.2 years, $p = 0.003$), GFR < 60 (79.0% vs. 50.0%, P<0.001), African-American race (67.2% vs. 52%, $p = 0.015$), and chronic hypertension (66.3% vs. 46.2%, $p = 0.003$). In multivariable analyses, GFR (adj. OR 3.78, 2.02-7.08) and African-American race (adj. OR 1.93, 1.12-3.33) were independently associated with presence of CMB. There was no correlation between number of CMB and size of hemorrhage (r_s = -0.037, $p = 0.565$), presence of CMB and ICH volume (median 6.25 mL vs. 7.30 mL, $p = 0.785$), or presence of CMB and in-hospital mortality (p=0.072). There was also no relationship between CMB burden and presence of DWI abnormalities (p=0.369), irrespective of hematoma location or ICH etiology. **Conclusions/Relevance:** Intracerebral hemorrhage patients with chronic microhemorrhages are more often African-American and have impaired kidney function. However, they are not more likely to have larger hematoma volumes, secondary DWI abnormalities, or increased in-hospital mortality. Further exploration into the clinical significance of microhemorrhage burden in acute ICH is warranted.

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W P119

The National Institutes of Health Stroke Scale Score (NIHSSS) Item Profiles: a More Sensitive Predictor of Patient Outcome

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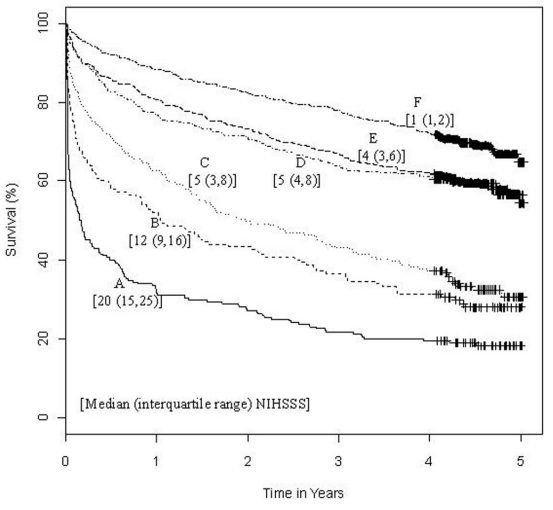
Background: Initial NIHSSS is highly predictive of outcome after ischemic stroke (IS). However after mild IS inconsistent prediction exists as well as some bias towards language symptoms. Objective Using latent profile analysis, we examined if grouping strokes by presence of individual NIHSSS symptoms could provide additional prognostic information beyond the total NIHSSS. Methods We identified all cases of clinically defined IS in 1999 and 2005 within a biracial population of 1.3 million. Research nurses extracted information from medical charts including retrospective NIHSSS. Latent profile analysis was used to form groups of 2005 IS patients with similar NIHSSS item responses; heterogeneity of NIHSSS responses is minimized within and maximized across profiles. Profile group was used as an independent predictor of patient outcome, 90 day and overall mortality and modified Rankin (mRS) at discharge ≤1, using Kaplan-Meier and logistic regression. IS cases occurring during 1999 were used for validation of the profiles. **Results:** A total of 2,251 clinically defined IS cases were identified in 2005, 2,468 in 1999. Fifteen cases in 2005 and 40 in 1999 were excluded due to missing NIHSSS. For patients with more than one IS occurrence during the year, the NIHSSS from the first IS was used. The 2005 IS patients had median age 72 years, and were 22% black, 56% female; 1999 patients were similar. Median NIHSSS for both study periods was 4 (IQR 2, 7). Six distinct profiles (A - F) were identified within the 2005 IS cases (Figure 1). Between the two most extreme profiles, 90 day mortality ranged from 55% in profile A to 5% in F, mRS at discharge ≤ 1 was 0% for A vs. 34% for F. Profiles falling between these two extremes, C and D, both had median NIHSSS of 5, but different outcome rates for 90 day survival (C 23% vs. D 11%, $p < 0.01$) and discharge mRS ≤1 (C 5% vs. D 10%, p=0.04). Difference in 90 day survival remained significant after adjusting for age, race, and gender. C patients were more likely to have decreased level of consciousness and abnormal language, whereas D were more likely to have abnormal right arm and right leg motor function. Characterization of 1999 cases using the profiles yielded similar associations with outcome. **Conclusions:** We describe a novel profile method of analyzing baseline symptoms and severity of IS patients that provides additional information regarding outcome beyond the baseline NIHSSS. In particular, we found two symptom profiles with identical median NIHSSS but with widely disparate outcomes. Such profiles might be clinically useful for prognosis, and could conceivably be used in future clinical trial design.

Figure 1. Survival by Profile



Author Disclosures: H. Sucharew: None. J. Khoury: None. C.J. Moomaw: None. K. Alwell: None. B.M. Kissela: None. S. Belagaje: None. O. Adeoye: None. P. Khatri: None. L. Heitsch: None. D. Woo: None. M.L. Flaherty: None. S. Ferioli: None. J.P. Broderick: None. D. Kleindorfer: None.

W P120

Changes in Ischemic Stroke Incidence in the United States Between 1996 and 2006

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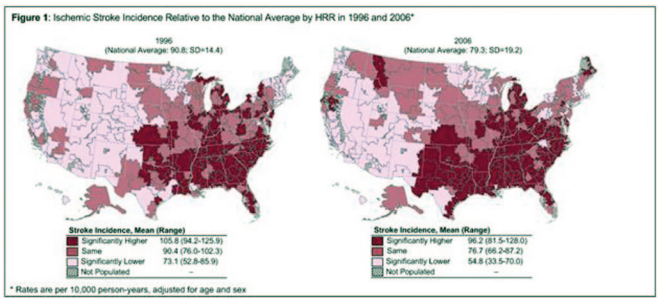
Background: Death due to ischemic stroke has declined in the US over the past 50 years, although to varying degrees in different regions of the country. Because there is no national surveillance system, less is known about patterns of stroke incidence. **Purpose:** To estimate national and regional ischemic stroke incidence rates among the elderly in the US in 1996 and 2006 using administrative data. **Methods:** The study cohort included all fee-for-service Medicare beneficiaries $>=$age 68 years discharged with an incident ischemic stroke (ICD-9 primary codes 433, 434, 436, without a discharge diagnosis of ischemic stroke for 3 years prior to index event). A hierarchical Poisson model was constructed to estimate age-, sex-, and race-adjusted incidence rates nationally for the country's 306 hospital referral regions (HRRs) in 1996 and 2006. National maps were created to show HRR-specific rates categorized as being higher, no different, or lower than the national average using a significance level of 0.05. **Results:** We identified 244,232 incident ischemic stroke cases in 1996 and 245,882 in 2006. The mean age, sex-, and race-adjusted ischemic stroke incidence rates declined from 90.8$\pm$14.4 cases per 10,000 person-years in 1996 to 79.3$\pm$19.2 in 2006 (Figure). Incidence varied by HRR during both periods, with higher rates in the Southeastern US. More HRRs had incidence rates higher than the national average in 2006 as compared with 1996 (44.1% in 2006, 34.6% in 1996). Similar proportions of HRRs had lower than average rates during each period (27.5% in 2006, 28.4% in 1996). **Conclusions:** Ischemic stroke incidence among the elderly declined in the US over the past decade suggesting improvements in primordial and primary prevention. Rates were not geographically uniform and were consistently higher in the Southeast. Understanding the reasons for this geographic disparity in stroke incidence might help to better target preventive interventions.



Author Disclosures: J.H. Lichtman: None. S.B. Jones: None. Y. Wang: None. E. Watanabe: None. E.C. Leifheit-Limson: None. L.B. Goldstein: None.

W P122

Risk Of Stroke Following Self-report Of Stroke, Tia Or Stroke Symptoms In The Regards Study

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Introduction: It is well known stroke and TIA are risk factors for subsequent stroke. However, no population studies have compared stroke risk in persons with previous stroke vs TIA, vs presence of stroke symptoms not diagnosed by a physician. We studied the risk of future stroke with increasing progression of symptom/diagnosis status: 1) asymptomatic (Asx), 2) those reporting stroke symptoms only (SS), 3) TIA, 4) stroke in the distant past (DS), and 5) recent stroke (RS). **Methods:** In 2003-2007 the REasons for Geographic And Racial Differences in Stroke (REGARDS) cohort enrolled 30,239 black and white Americans age 45 and older. Stroke status groups were self-reported during the baseline interview; DS and RS were defined as strokes occurring >5 or <5 years before baseline, respectively. SS were a history any of six sudden onset stroke symptoms. Stroke status categories were mutually exclusive using the hierarchy of Asx, SS, TIA, DS, RS (e.g. a participant reporting RS and TIA was classified as RS). Incident stroke was ascertained and validated during follow up. We derived Kaplan-Meier estimates of stroke risk, and used Cox proportional hazards models to obtain hazard ratios. Additional data were collected using a combination of in home assessment with a health professional and telephone interview. **Results:** With 4.4 $\pm$ 1.6 years follow up and including 557 validated strokes, compared to Asx persons, SS, TIA, DS and RS all had increased risk of future stroke, with increasing magnitude of risk in each hierarchical group (see figure). Adjusting for age, race, sex, region, income, education, hypertension, diabetes, smoking status, dyslipidemia, atrial fibrillation, and history of cardiovascular disease, stroke risk was 1.3-fold increased for SS (95% CI 1.0, 1.7), 1.7-fold for TIA (95% CI 1.2, 2.5), 2.2-fold for DS (95% CI 1.5, 3.2) and 3.0-fold for RS (95% CI 2.2, 4.1). **Discussion:** Results suggest a spectrum of risk from stroke symptoms to TIA, distant stroke, and recent strokes, and imply a need for establishing these categories in patients in order to prevent stroke. This paradigm could be tested in controlled clinical trials. Figure: Kaplan Meier Curves examining risk of stroke in the REGARDS study by history of stroke, TIA or stroke symptoms.

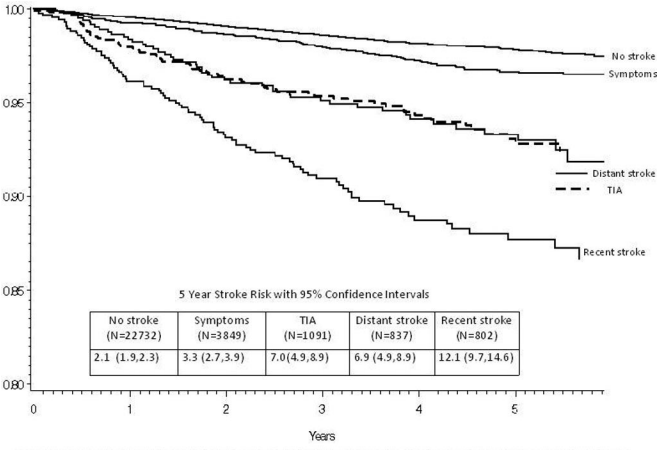

Figure: Kaplan Meier Curves examining risk of stroke in the REGARDS study by history of stroke, TIA or stroke symptoms.

Author Disclosures: S.E. Judd: None. D.O. Kleindorfer: Speakers; Modest; Genetech. L.A. McClure: None. J.D. Rhodes: None. M. Cushman: None. V. Howard: None. G. Howard: None.

W P123

Mitral-Doppler Measurements are Weakly Correlated with the Risk of New-Onset Atrial Fibrillation in Patients with Cryptogenic Stroke

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Introduction: Paroxysmal atrial fibrillation is a frequent under-diagnosed etiology for cryptogenic stroke. While electrical manifestations of atrial fibrillation (AF) can easily be missed given the transient nature of this arrhythmia, recovery of the mechanical function of the atria has been shown to be a slower phenomenon. We hypothesized that, in patients in sinus rhythm following cryptogenic stroke, abnormal mitral-Doppler findings, such as small A-wave velocity and large E/A ratio, could predict the risk for stroke recurrence and new-onset AF. **Method:** A retrospective analysis of all subjects admitted at the Centre Hospitalier Universitaire de Sherbrooke with a diagnosis of cryptogenic ischemic stroke from January 1993 to August 2009 was conducted using the hospital database. Data from early echocardiography performed during initial stroke workup were recorded. Data collected included mitral-Doppler A-wave velocity, E-wave velocity and E/A ratio, and were correlated with the incidence of recurrent stroke and new-onset AF in the study population. **Results:** Out of 698 subjects meeting the inclusion criteria, 68 (9.7 %) had recurrent stroke and 98 (14 %) had new-onset AF detected after the index hospitalization. No statistically significant correlation was found between the risk of stroke recurrence and A-wave velocity ($p=0.859$) or E/A ratio ($p=0.880$). Moreover, new-onset AF did not correlate with either A-wave velocity ($p=0.143$) or E/A ratio ($p=0.368$). However, a multivariate logistic regression model showed that E/A ratio (OR=2.4), presence of high blood pressure (OR=1.7) and age over 60 years old (OR=1.1) were independent predictors of a new onset AF in the study population. Meanwhile, A-wave and E-wave velocity were not predictors of stroke recurrence. **Conclusions:** Mitral-Doppler E/A ratio is a weak clinical predictor of new-onset AF among patients with cryptogenic ischemic stroke. This observation suggests that unrecognized paroxysmal AF may be a less common cause of cryptogenic stroke than we think. It is also possible that atrial mechanical dysfunction is a poor indicator of recently converted AF. Also, the time to recovery of effective atrial mechanical after a newly converted AF may be shorter than that required to obtain the echocardiography. Finally, many of new onset AF episodes could be silent and were not recorded. However, Mitral-Doppler E/A ratio could be used in more complex models for predicting new onset AF and stroke recurrence.

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W P124

Iphone and iPad Display of Acute Stroke CT Scans: Discrimination of Hemorrhage and Early Ischemic Changes

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Background: Telestroke systems have recently expanded potential access to subspecialty stroke expertise around the clock at remote locations. Advances in technology now permit rapid transfer of medical images to portable devices for critical decisions about emergent stroke therapies, yet the quality of such interpretations remains unaddressed. We tested the diagnostic accuracy of remote image interpretation via two distinct handheld devices compared with in-hospital readings in a setting that simulated routine clinical practice. **Methods:** Noncontrast CT scans obtained on hospital arrival in 60 consecutive acute stroke patients within 3 hours of stroke symptom onset were analyzed. Scans were divided into 3 groups and loaded on different interpretation platforms: iPhone, iPad, and desktop computer. Three readers, including a neuroradiologist, a stroke neurologist imaging expert, and a general neurologist, separately rated the CT scans without knowledge of clinical history. Every reader utilized each of the interpretation platforms for 20 cases, limited to a duration of 5 minutes per scan. Images were evaluated for early ischemic changes (EIC) and hemorrhagic findings, including ASPECTS rating and detection of potential contraindications to thrombolysis. **Results:** 60 noncontrast CT scans were rated by 3 readers across 3 interpretation platforms. The average patient age was 69.4 years. The cross-platform accordance rates for diagnoses were: iPad vs desktop PC, SAH - 100%, ICH - 96.7%, EIC - 88.3%; iPhone vs desktop PC, SAH - 100%, ICH - 95%, EIC - 90; iPad vs iPhone, SAH - 100%, ICH - 98.3%, EIC - 86.7%. **Conclusion:** Subarachnoid and intracerebral hemorrhages on noncontrast CT are sensitively detected when imaging interpretation is performed by readers with various skill levels on portable devices such as the iPhone or iPad. Early ischemic changes are also detected well, considering the subtle nature of these findings in hyper-early images. Further studies should prospectively test the performance of remote image interpretation in thrombolytic decisions.

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W P125

SPOTRIAS: Hyperacute C-Reactive Protein Levels Predict Stroke Outcome in Mild Stroke

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Objectives: Subacute levels of high sensitivity CRP (hsCRP) after stroke have previously been associated with poor outcome, however earlier studies were confounded by stroke severity, and their impact diminished by the extended window for blood draws. This study was designed to determine if hsCRP measured in the hyperacute phase of stroke could predict outcome, particularly in mild strokes where outcome is difficult to predict. **Methods:** We prospectively measured hsCRP and NIHSS scores on consecutive acute stroke patients (< 9 hours from symptom onset) in a multicenter acute ischemic stroke biomarker study. Patients with acute infection, active malignancy, or systemic inflammatory disorder were excluded. Pearson's correlation was used to quantify the association between continuous variables. Multivariate linear and logistic regression models were used to adjust for the effects of potential confounding variables. Continuous NIHSS scores were dichotomized at the median (NIHSS score 5) as "mild" (1-5) and "moderate-severe" (6-33). The outcome measure was the 90-day mRS, dichotomized as good (mRS 0-2) or poor (mRS 3-6). **Results:** We included 309 patients, 44% female, mean age 69.2 (range 23- 97 years), with baseline NIHSS, baseline hsCRP and 3 month mRS in this analysis. There were 167 (54%) mild strokes and 142 (46%) moderate-severe strokes. Thirty seven percent (114 patients) had a poor outcome. The mean hsCRP was 6.4 mg/L (s.d. 9.6 mg/L) in mild strokes, compared to 14.0 mg/L (s.d. 37.1 mg/L) in moderate-severe stroke. In univariate analyses, hsCRP correlated with NIHSS ($r = 0.24$, $P<0.01$), systolic and diastolic BP ($r=-0.17$ and -0.16, respectively, $P<0.01$), and WBC ($r=0.16$, $P<0.01$), but was not associated with demographic characteristics, medical conditions, or medications. In unadjusted univariate models, poor outcome was correlated with baseline NIHSS, age, and level of hsCRP. However, in a multivariate model, the effect of hsCRP was attenuated after adjustment for baseline NIHSS score. In a stratified analysis, after adjustment for age, sex, and tPA use, hsCRP predicted poor outcome in mild stroke (OR1.05, 95% CI 1.01-1.10, $p=0.03$) but not moderate-severe stroke (OR1.0, 95% CI 0.99-1.01, $p=0.43$). The logistic regression models yielded an AUC of 0.84 for mild stroke and 0.69 for moderate-severe stroke. **Conclusions:** hsCRP is a better predictor of outcome in patients with mild, rather than moderate-severe, stroke. In mild strokes, each 1 mg/L increase in hsCRP, increases the risk of poor outcome by 5%.

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W P126

Effect of Age and Circle of Willis Anatomy on Blood Flow in Major Cerebral Vessels

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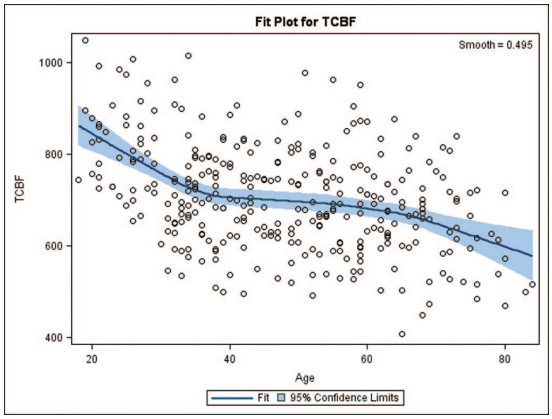
Objective: We sought to examine the effect of age and anatomic variations in the Circle of Willis on flow rates in individual major cerebral vessels, using quantitative magnetic resonance angiography (QMRA) to assess both vascular anatomy and flow. **Methods:** 326 healthy adult volunteers with no history of cerebrovascular disease underwent QMRA of head and neck vessels using commercially available software, NOVA (Vasol, Inc.). Individual vessel and combined territory flows were reviewed in relationship to patient variables and Circle of Willis anatomy. **Results:** The volunteers ranged from 18 to 84 (mean 48) years old, with 58 (48%) females. Mean blood pressure (MBP) ranged from 66-127 mmHg (mean 93). Total cerebral blood flow (CBF), defined as the sum of bilateral internal carotid artery (ICA) flows and vertebral artery flows, was not altered through the MBP range ($p=0.20$) when adjusting for age, consistent with cerebral autoregulation. Total CBF declined with age ($p<0.001$), from 768 $\pm$ 115 ml/min in the youngest decades (age 18-35), to 645 $\pm$ 103 ml/min in the oldest decades (age 65-84). This represents a 2.7 ml/min/year drop in a linear regression model, although a local regression model suggests a relative plateau in flows in the mid-decades (age 40-60) (see Figure). In paired intracranial vessels, the left middle cerebral artery and left posterior cerebral artery demonstrated higher flows ($p<0.01$) than the right. Vessels proximal to the circle of Willis, the ICA and basilar artery (BA), were examined relative to cerebrovascular anatomic variants. The BA flow in the overall cohort averaged 138 $\pm$ 40 ml/min, but was significantly lower in individuals with one or both fetal PCAs (84 $\pm$ 28 ml/min, $n=39$) compared to those with no posterior communicating arteries (PcoAs) (155 $\pm$ 31 ml/min, $n=115$) ($p<0.001$). Similarly ICA flows were affected by PcoA and PCA anatomy, but also by the anterior cerebral artery (ACA) A1 segment anatomy. ICA flows were significantly higher on the side of a fetal PCA (277 $\pm$ 55 ml/min) compared to those with absent PcoAs (250 $\pm$ 56 ml/min) ($p<0.01$). Furthermore, flow was significantly lower in the setting of absent or hypoplastic A1 segment (defined as flow < 15 ml/min) at 194 $\pm$ 49 cc/min compared to 259 $\pm$ 54 ml/min ($p<0.01$). **Conclusions:** Cerebral vessel flows are affected predominantaly by age and, for proximal intracranial vessels, also by the patient's specific cerebrovascular anatomy. Understanding of these variations carry important implications for interpretation of vessel flows in the setting of cerebrovascular disease.



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W P128

Gene Expression Signatures Of Large Vessel And Cardioembolic Stroke

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Background and Purpose: The cause of stroke remains unknown or cryptogenic in many patients. We sought to determine whether gene expression signatures in blood can distinguish between cardioembolic and large vessel causes of stroke, and whether these profiles can predict stroke etiology in the cryptogenic group. **Methods:** A total of 194 samples from 76 acute ischemic stroke patients were analyzed. RNA was isolated from blood and run on Affymetrix U133 Plus2.0 microarrays. Genes that distinguish large vessel from cardioembolic stroke were determined at 3, 5, and 24 hours following strokeonset. Predictors were evaluated using cross-validation and a separate set of patients with known stroke subtype. The cause of

cryptogenic stroke was predicted based on a model developed from strokes of known cause and identified predictors. **Results:** A 40 gene profile differentiated cardioembolic stroke from large vessel stroke with >95% sensitivity and specificity. A separate 37 gene profile differentiated cardioembolic stroke due to atrial fibrillation from non-atrial fibrillation causes with >90% sensitivity and specificity. The identified genes elucidate differences in inflammation between stroke subtypes. When applied to patients with cryptogenic stroke, 17% are predicted to be large vessel and 41% to be cardioembolic stroke. Of the cryptogenic strokes predicted to be cardioembolic, 27% were predicted to have atrial fibrillation. **Conclusions:** Gene expression signatures distinguish cardioembolic from large vessel causes of ischemic stroke. These gene profiles may add valuable diagnostic information in the management of patients with stroke of unknown etiology though they need to be validated in future independent, large studies.

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W P129

Characteristics of Ophthalmic Artery Flow in Moyamoya Disease

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Background: The clinical value of ophthalmic artery (OA) color Doppler flow imaging (CDFI) in the evaluation of moyamoya disease has not been fully investigated. The aim of the study was to clarify typical sonographic features and to define sensitivity for clinical symptoms with regard to the intracranial hemorrhage. **Methods:** Fifty-one moyamoya disease patients (mean age: 38 years) confirmed by angiography or magnetic resonance angiography (MRA) were examined. Their initial symptoms were an ischemic attack in 36 patients and an intracranial hemorrhage in 15 patients. Using the CDFI, the peak systolic flow velocity (Vs) and pulsatility index (PI) were evaluated on the symptomatic side OA in each patient. In 36 age-matched healthy volunteers, the average Vs was 0.36 ± 0.07 m/sec (mean±SD) and the average PI was 1.54 ± 0.37. These values were used as normal controls in this study. Based the above control values, the authors defined the high hemodynamic stress stage as follows: Vs more than or equal to 0.43 m/sec (this value corresponds to the mean Vs plus 1SD of normal control values) and PI less than or equal to 1.17 (this value corresponds to the mean Vs minus 1SD of normal control values). **Results:** 1) The average Vs was 0.43 m/sec, which was significantly ($P<0.05$) high compared to the normal controls. The average PI was 1.09, which was significantly low compared to the controls. 2) In the patients presenting with intracranial hemorrhage, the average Vs was 0.64 m/sec and the average PI was 0.82. In the patients presenting with ischemic event, the average Vs was 0.35 m/sec and the average PI was 1.20. These Vs values and PI values were statistically significantly different between these two groups 3) Twenty patients showed the high hemodynamic stress stage. Among them,13 patients (65%) presented with intracranial hemorrhage. In the other 31 patients those were not in the high hemodynamic stress stage, only 2 patients (6.5%) presented with intracranial hemorrhage. Intracranial hemorrhage was statistically significantly ($P<0.05$) seen in the high hemodynamic stage. **Conclusion:** The OA CDFI findings in moyamoya disease were characteristic and valuable noninvasive examination for the intracranial hemodynamic stage. The patients with OA high hemodynamic stage according using CDFI showed the high incidence of the intracranial hemorrhagic episode.

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W P130

Ultrasonography and Pathology in Symptomatic and Asymptomatic Carotid Plaques

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Background: Atherosclerotic disease is a process in which stability conditions may change to produce an ischemic event. Carotid plaques provide a unique opportunity for the study of atherosclerosis in living subjects. Differences in the characteristics of carotid plaques between symptomatic and asymptomatic patients would identify genuinely unstable plaques. We analyzed ultrasound and pathology findings of carotid plaques obtained during surgery. **Methods:** Data was obtained from the FLENI Stroke Data Bank. We analyzed demographics, clinical features, and ultrasonography and pathology findings in carotid plaques of patients who had carotid endarterectomy (CEA) between July 2005 and June 2010. We used standardized criteria for ultrasonographic and pathological classifications. The ultrasonographist and the pathologist provided a "stable/unstable" assessment for each plaque. We considered symptomatic those patients who met NASCET criteria. We excluded patients who were not studied within the one week prior to surgery in the institutional Doppler laboratory and those in whom substantial fragmentation of the plate occurred during surgery. **Results:** We evaluated 164 carotid plaques (54% asymptomatic, 46% symptomatic) from 161 patients undergoing CEA. There were no differences in age, gender distribution, vascular risk factors, degree of carotid stenosis, and statin use between symptomatic and asymptomatic sunjects. Use of aspirin and antihypertensive drugs were more frequent in asymptomatic patients ($p<0.02$). Prevalence of ultrasonography findings consistent with unstability was similar in symptomatic and asymptomatic plaques. Pathology findings determined unstability in 61 of 75 (81%) symptomatic plaques and in 32 of 89 (36%) asymptomatic plaques ($p<0.001$). **Conclusions:** Presence of symptoms prior to CEA and pathology findings are reliable methods for identifying unstable plaques. A potential role of aspirin and antihypertensive drugs in plaque stabilization deserves further study. Non invasive diagnostic methods that identify unstability are needed during the presymptomatic and preoperative periods.

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W P131

Can iPhones Be Used For The Evaluation Of Acute Stroke?

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Objectives: Recent technological advances allow for rapid transfer of medical images to portable viewing devices for critical decisions about acute stroke management, yet the diagnostic utility of interpretations needs to be systematically evaluated. We tested the intra-observer accuracy (IOA) and confidence of a stroke diagnosis on non-contrast head CT scan at presentation utilizing a portable viewing device (iPhone, by Apple). **Methods:** Three neurologists (R1, R2, R3) retrospectively reviewed 33 non-contrast head CT scans of patients presenting to the emergency department with symptoms of acute stroke. CT scans selected for inclusion into the study had a range of findings including hemorrhage (8), subtle infarct (9), obvious infarct (8), and normal (8). Cases were initially reviewed using the mobile hand-held device utilizing a mobile display technology with a web-based thin client application system followed by review on a standard PC display system. Data on the presence of infarct and/or hemorrhage and level of confidence 1 (lowest) to 4 (highest) was collected using a standardized form. Simple IOA between the iPhone and standard PC workstation interpretations, as well as average confidence levels was calculated. **Results:** Simple IOA for acute ischemic infarcts between the portable viewing device and standard PC was good for all readers (R1=82%, R2= 79%, R3=79%). Differences in simple agreement were primarily secondary to chronic infarcts being mistaken for subtle infarcts on the iPhone. IOA for hemorrhages between the iPhone and PC were 100% for all 3 readers. Average confidence levels of interpretations on the iPhone vs. the PC were as follows: R1=3.63 vs. 3.72 ($p=0.41$), R2=3.93 vs. 3.90 ($p=0.32$), R3=3.33 vs. 3.27 ($p=0.70$), respectively. None were statistically significant. **Conclusions:** Overall confidence when interpreting acute stroke imaging on a portable viewing device was good. The simple IOA of acute stroke imaging interpretation using an iPhone compared to a PC workstation was good. Chronic infarcts being mistaken for subtle infarcts on the iPhone accounted for the small percentage of intra-observer discordance. With the continued development of mobile technology, it is very likely that mobile devices will play a significant role in patient care in the future.

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W P132

A Tissue-Based Definition of Transient Ischemic Attack: a Lose-Lose Situation for US Healthcare Dollars

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Objectives: The AHA/ASA recently endorsed a tissue-based definition of transient ischemic attack (TIA), requiring absence of infarction on imaging. MRI/DWI was recommended as the preferred imaging modality. In a bi-racial population of 1.3 million, we determined the proportion of TIA patients who would be reclassified as ischemic stroke (IS) by the new definition and estimated the impact of changing discharge diagnosis from TIA to IS on Medicare expenditure and hospital reimbursement. **Methods:** All clinical TIA cases (focal neurologic symptoms lasting < 24 hours) that presented to every local emergency department in our region in 2005 were identified by screening ICD-9 codes 430-436. Medical records were reviewed by study physicians who adjudicated TIA cases. Ischemic lesions on MRI/DWI were redefined as IS. A model, incorporating risk factors previously identified for a + DWI, was built to determine how many additional TIAs from 2005 would be reclassified as IS if all had received MRI/DWI. Medicare reimbursement rates for DRG code 69 ($4618, uncomplicated TIA), for DRG code 66 ($5421, uncomplicated IS), and for a brain MRI/DWI ($544) were used to estimate Medicare expenditures and net hospital reimbursement, ie the sum of DRG payment minus the cost of MRI. Incremental changes in Medicare expenditure and net hospital reimbursement were estimated and then

extrapolated to US healthcare expenditures. **Results:** In 2005, 834 clinically defined TIA patients were identified in the Cincinnati region. In total, 323 had MRI/DWI, of which 51 with +DWI were redefined as IS. Our model estimated that if all subjects had received MRI, 175 (21%) of the TIA cases would have a +DWI, resulting in an additional 124 cases reclassified as IS. The incremental DRG payments for the 124 reclassified DWI+ strokes would result in increased Medicare expenditures of $99,572 for 2005. However, this would require an additional 511 MRIs to be performed, at a cost of $277,984. Subtracting this cost from DRG payments would result in a decreased net hospital reimbursement of $178,412. Extrapolating these results to the entire US population with 200,000 clinically defined TIA cases/year presenting to emergency departments, we estimated 40,600 cases would be reclassified as IS, with increased Medicare expenditures of $21 million while net hospital reimbursements would decrease by $41 million. **Conclusions:** While performing MRI/DWI on all clinically defined TIA cases in our population would identify additional cases of infarction, it would result in increased overall healthcare expenditures and decreased hospital reimbursements. Given the current economic environment and given the fact that a DWI+ MRI may not change the clinical management of these patients, further research is warranted to determine which TIA patients would benefit from an MRI/DWI.

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W P133

Expanded Operational Classification of Early Neurological Deterioration (END)

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Background&Purpose: A novel hypothetical classification (Stroke 2009; 40:e443-50) describes 3 types of diffusion weighted imaging (DWI) appearance of ischemic brain lesions and proposes likely mechanisms leading to early neurological deterioration (END). We applied this classification to consecutive stroke patients to evaluate if all early deteriorations fall under the original imaging classification. Subjects&Methods: Consecutive ischemic stroke patients were evaluated for subsequent neurological deterioration (NIHSS>=4 points) within the first 72 hours from symptom onset. Etiologies leading to deterioration were classified as systemic causes and neurological causes. Intracranial hemodynamic steal was diagnosed according to previously published criteria using transcranial Doppler. DWI lesions detected at the first MRI scan were classified as END-A, B, C, or other, and the latter DWI patterns were analyzed. Outcomes included discharge NIHSS, mortality and modified Rankin Scores at 3 months. **Results:** Among 600 consecutive patients (51% male, age 62±15yrs, baseline median NIHSS=11, range 0-42), 44 patients (7%) had experienced END including 26 without cardio-pulmonary decompensation or other systemic causes. We identified five additional DWI imaging patterns termed END-Watershed, END-Subcortical, END-Posterior, END-Lacunar and END-Zero that describe patient initial imaging prior to deterioration. Baseline NIHSS, DWI findings and stroke outcomes are summarized in Figure. Among patients with END, 65% had documented hemodynamic steal vs. 3% of those without END ($p<0.0001$). Proximal occlusions were common: END- A, B, and C 57% vs. other END 50% ($p=1.00$) with re-occlusion/re-embolization detected in 40% END-W and 20% END-C ($p=0.16$). Outcomes tended to be better with END-0, L, P, S, W types compared to END-A, B, C ($p=0.068$). **Conclusions:** We have identified 5 additional DWI patterns on initial imaging prior to END. Certain patterns- END-0, L, P, S and W have lesser stroke severity and show a trend toward better clinical outcomes than previously proposed END-A, B and C. Of particular interest, most early END events occurred in the presence of intracranial hemodynamic steal and re-occlusion.

DWI								
TYPE	END-A	END-B	END-C	END-W	END-S	END-P	END-L	END-0
NIHSS	15	19	17	7	6	8	4	1
Steal	33%	83%	80%	67%	50%	0%	0%	100%
Mortality	33%	0%	40%	0%	0%	0%	0%	0%
mRS 0-1	0%	0%	0%	33%	0%	0%	0%	100%

DWI- Diffusion Weighted Imaging, END- Early Neurological Deterioration, W-Watershed, S-Subcortical, P-Posterior, L-Lacunar, 0-DWI -ve, NIHSS- National Institutes of Health Stroke Scale, mRS- Modified Rankin Scale.

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W P134

Wall Shear Stress in the Internal Carotid Siphon In Healthy Volunteers Assessed Using High Speed Phase Contrast 3D-Radial Velocimetry

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Introduction: Cardiovascular disease is the leading cause of death in industrialized countries. Abnormal wall shear stress (WSS) is prevalent at sites prone to atherosclerosis and aneurysm formation. Therefore, WSS analysis may have prognostic value in finding areas vulnerable to both atherosclerosis and aneurysms. A limitation of prior investigations of WSS using magnetic resonance angiography (MRA) is insufficient resolution to visualize the boundary zone (BZ) within clinically-useful scan times. We have developed PC HYPRFlow, an advanced 3D radial imaging modality capable of acquiring whole brain angiograms with scan times of ~5 minutes and spatial resolution more than 40 times higher than conventional techniques, allowing better BZ visualization. The internal carotid siphon (ICS) is of interest because aneurysms and atherosclerotic plaques are commonly found in the siphon; We examine WSS in four segments (C2, C3, C4, and C5) of the ICS in 10 healthy volunteers. **Materials & Methods:** 10 healthy volunteers (6 female, 4 male) were scanned using a GE Discovery 750 3.0T MR Scanner using PC-VIPR. The images were imported into Ensight where cutplanes axial to the vessels of interest were made. The velocity data was then imported into a custom Matlab runtime environment developed at the University of Freiburg, Germany, which used B-spline interpolation with Green's Theorem to calculate time-average WSS from velocity measurements from PC-VIPR. **Results:** The time average WSS for all subjects in the C2 segment of the ICS was 1.19 ± 0.32 Pa. The WSS in C3 was 1.11 ± 0.33 Pa, the WSS in C4 was 1.03 ± 0.34 Pa, and the WSS in C5 was 0.86 ± 0.30 Pa. These values are consistent with values found in the literature for WSS measured with PC-MRA. A WSS map of the left ICS is shown in Figure 1. Streamlines derived from velocity information from PC-VIPR are shown in Figure 2. **Conclusion:** The combination of PC-VIPR and automated spline interpolation allows calculation of velocity, volume flow rate, and WSS in vessels of interest with total processing time of 15 minutes per vessel. We anticipate that by combining WSS, velocity measurements, and morphology acquired using PC HYPRFlow, we can better evaluate patients at risk of atherosclerosis, aneurysms, transient ischemic attacks, and hemorrhagic or ischemic stroke due to pathology in the carotid siphon.

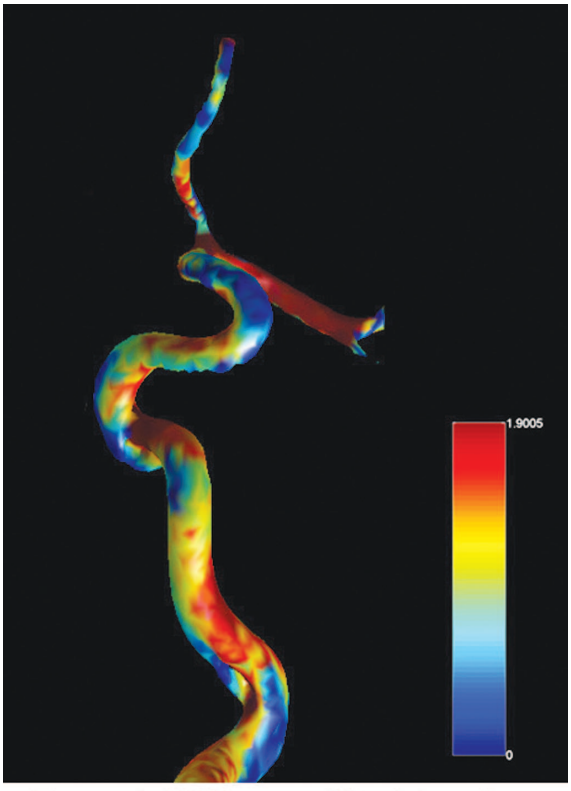

Figure 1: WSS map of the internal carotid siphon generated from velocity data acquired using PC-VIPR.

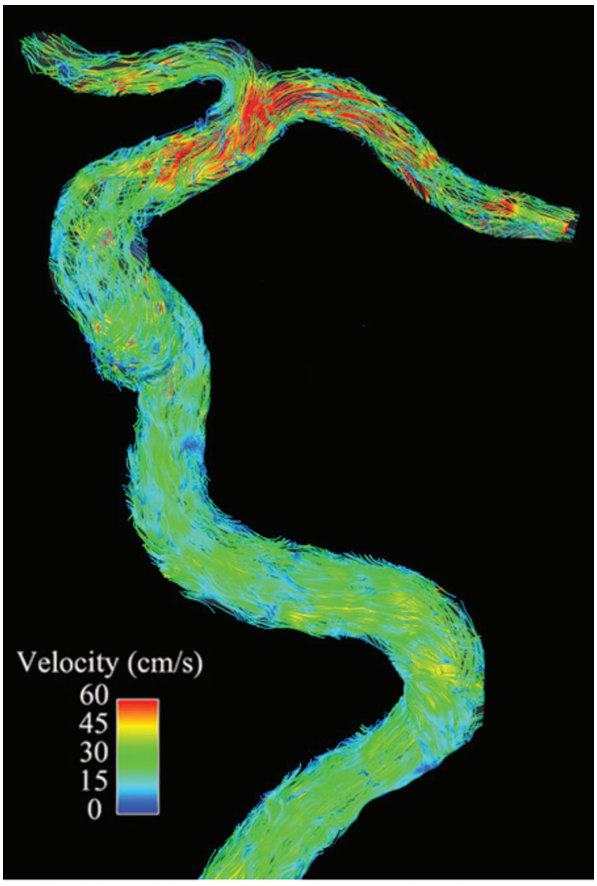

Figure 2: Streamlines from PC-VIPR velocity data in the internal carotid siphon.

Author Disclosures: W. Chang: None. B. Landgraf: None. S. Kecskemeti: None. Y. Wu: None. K. Johnson: None. O. Wieben: None. C. Mistretta: None. P. Turski: None.

W P135

Pilot Study of Cardiac Magnetic Resonance Imaging for Detection of Embolic Source after Ischemic Stroke

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Background: Transesophageal echocardiogram (TEE) is the current standard for evaluating cardioembolic source of stroke. However, TEE is semi-invasive and many strokes remain cryptogenic even after TEE. Cardiac magnetic resonance imaging (CMRI) may have advantages over TEE for detection of cardioembolic source, as prior studies have suggested that CMRI may be superior to TEE for detection of intracardiac thrombus in patients with cardiac disease. We performed a pilot study comparing CMRI to TEE after stroke to assist in planning future definitive studies. **Methods:** Individuals with non-lacunar stroke within 90 days of enrollment undergoing TEE for clinical purposes were prospectively identified and underwent a research CMRI on a 1.5T scanner. Exclusion criteria included relevant carotid or vertebrobasilar stenosis of $>=$50% and inability to undergo non-sedated CMRI with intravenous gadolinium (for example claustrophobia, implanted metallic devices, or contrast dye allergy). A descriptive comparison of detection of a cardioembolic source (intracardiac thrombus/mass, aortic atheroma $>=$4mm, or patent foramen ovale (PFO)) by study type was performed. Patient preference for study type was assessed by interview. **Results:** Twenty patients underwent both CMRI and TEE a median of 6 days apart (inter-quartile range (IQR): 3, 8.5). Median patient age was 51 (IQR: 40, 63.5), 40% had hypertension, 15% had diabetes, 25% had prior stroke/TIA, 5% had atrial fibrillation, and none had coronary disease or heart failure. Two patients had incomplete CMRI scans (claustrophobia (n=1) and arrhythmia affecting image quality (n=1)). No patient had intracardiac thrombus or mass detected on either study. There were no cases where CMRI detected a cardioembolic source not identified on TEE. Aortic atheroma $>=$4mm thick was identified by TEE in one patient. CMRI identified aortic atheroma as $<$4mm in this patient (3mm on CMRI compared with 5mm on TEE). PFO was identified in 6/20 patients on TEE; CMRI found only 1 of these. Patient preference at 24 hours after the second test was definitely/somewhat preferred CMRI: 45%; definitely/somewhat preferred TEE: 25%; no preference: 20%; missing response: 10%. **Conclusions:** Few cardiac sources of embolism were identified on CMRI or TEE in this relatively young population of stroke patients. Future studies of CMRI after stroke should consider specifically targeting populations at the highest risk of cardioembolic source. CMRI was insensitive for detection of PFO, consistent with prior research. Patients tended to prefer CMRI over TEE, though selection bias may have played a role due to exclusion of patients with claustrophobia.

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W P136

Oxygen Challenge MRI May Detect Crossed Cerebellar Diaschsis

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Background: We have recently presented pilot results for the Oxygen Challenge MRI Technique in acute ischemic stroke(Santosh et al, JCBFM, 2008; Dani et al, Annals of Neurology, 2010). This deoxyhaemoglobin sensitive technique involves the transient application of hyperoxia during continuous T2*-weighted MRI. We have demonstrated that in 'healthy' tissue, T2*-weighted signal increases after hyperoxia. In operationally defined infarct core such increases are attenuated, and signal increases in regions likely to be penumbra are generally exaggerated. These findings support the concept that this technique is sensitive to underlying metabolic activity. In this study we investigated if Crossed Cerebellar Diaschisis (CCD; hypometabolism in the contra-lesional cerebellar hemisphere following stroke) could be detected by Oxygen Challenge MRI. **Methods:** Inclusion criteria were 1) ischemic anterior circulation stroke, 2) scanned $<$24h, and 3) DWI lesion $>$ 50ml. Regions of interest were manually delineated in the ipsi- and contra-lesional cerebellar hemisphere and the magnitude of T2*-weighted signal increases was measured by 'percentage signal change' and the 'area under the T2*-weighted signal intensity-time curve'. Results were compared between hemispheres using the Wilcoxon signed ranks test. **Results:** The magnitude of signal change was greater in the ipsilateral cerebellar hemisphere compared to the contralateral cerebellar hemisphere in 6/12 (50%) of subjects (Figure 1). In no case was the change greater in the contra-lateral hemisphere compared to the ipsilateral hemisphere. For the 12 subjects, the mean percentage signal change in the ipsilateral cerebellar hemisphere (5.1%, standard deviation = 2.7%) was significantly greater ($p=0.03$) than the corresponding value in the contralateral cerebellar hemisphere (3.8%, standard deviation = 3.1%). Analyses of 'area under the curve' also showed this difference ($p=0.002$). No difference between hemispheres was detected using standard perfusion MRI 'time to peak ' maps. **Conclusion:** Oxygen Challenge showed an attenuated response in the contra-lesional cerebellar hemisphere, consistent with CCD. The failure to observe changes on perfusion maps is consistent with the observation that metabolic changes are significantly more pronounced than perfusion changes in CCD (Gold and Lauritzen, PNAS, 2002). These results further validate the Oxygen Challenge technique, and further evaluation is warranted.

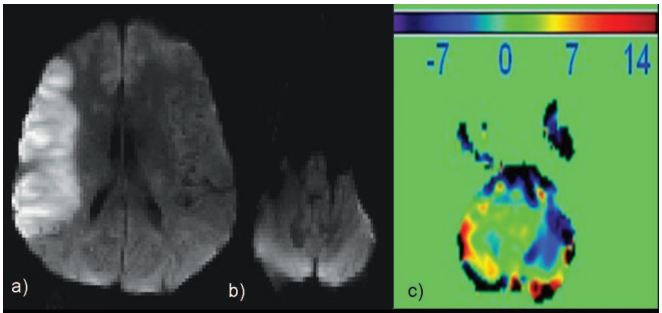

Figure 1. Attenuated Oxygen Challenge Response in the Contra-lesional Cerebellar Hemisphere. Images are from a representative subject. a) Diffusion weighted imaging of the stroke lesion, b) normal diffusion weighted imaging in the cerebellum and c) attenuated response in the contra-lesional cerebellar hemisphere on Oxygen Challenge Scan. The colour scale is in units of percentage signal change.

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W P137

Characteristics of Stroke Subtype in a Stroke Registry in Da Nang, Vietnam

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Background: Developing countries are currently experiencing a health transition from infectious to chronic conditions in which cardiovascular diseases are having a devastating impact on the population. Data on stroke subtypes in Vietnam are not available in the literature. Objectives: We sought to learn more about patient characteristics of hospitalized stroke by

developing a stroke registry in Da Nang, Vietnam. **Methods:** Data on all potential strokes admitted to Da Nang Hospital for three months (April-June 2010) were entered into a system based on the WHO Stroke STEPS instrument. Data were collected by physicians and nurses in the Ministry of Health who treated these patients. **Results:** During these three months, a total of 212 strokes presented to the Emergency room and were treated in the intensive care unit (33%), cardiology (51%) or general internal medicine (16%) wards. Of these, 205 were classified as definite strokes in adults 18 years of age or older. This was a first (incident) stroke for 86% of the patients. Age ranged from 18 to 90 years with a mean of 49.5 (SD 16.1) years. Over 40% of the strokes occurred in women. Utilizing CT scans to classify subtype, 94 (46%) were diagnosed as ischemic, 88 (43%) were hemorrhagic, and 23 (11%) were unspecified. There were no differences in age or gender by stroke subtype. Neurological signs present at admission differed significantly by stroke subtype ($p < .001$): 65% of patients with hemorrhagic strokes were found to have disturbed consciousness compared to 28% of those with ischemic stroke; 75% with haemorrhages had speech disturbances compared to 60% with ischemic stroke and 95% of patients with ischemic stroke presented with weakness compared to 76% of those with hemorrhagic stroke. While a high rate of hypertension was identified at admission (84%), there was no difference by stroke subtype. Eleven patients (5.6%) died while in hospital after an average length of stay of 17 days, 5 with ischemic and 6 with hemorrhagic subtype. Of those discharged from the hospital alive, many were seriously disabled: 18% were discharged with severe disability as assessed by the modified Rankin scale, 30% had moderate disability/were unable to walk, 18% had moderate disability but were able to walk, and 35% had no or slight disability. **Conclusions:** Stroke in Vietnam is a serious cause of morbidity presumably due to untreated hypertension occurring at relatively young ages and presenting in a much higher percentage of women than in developed countries. Specific risk factors for this population need to be investigated and verified. Culturally appropriate interventions for treatment and prevention will be critical to help ease the burden of this disease.

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W P138

Proposed Angiographic Criteria for Measurement of Vertebral Artery Origin Stenosis, the Vertebral Origin Treatment with Endovascular therapy (VOTE) method

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Introduction: Vertebral artery origin (VAO) stenosis is a treatable cause of stroke, however no standard measurement criteria have been established. The tortuous VAO anatomy presents challenge in interpretation of stenosis severity. We assessed the hypothesis that inter-rater agreement of VAO stenosis measurement could be improved with exclusion of the tortuous V1 segment in measuring normal artery diameter. **Methods:** A retrospective database of patients referred for endovascular therapy of VAO stenosis was accessed and a consecutive series of ten patients was identified. Magnified cerebral angiograms were reviewed independently by three experienced angiography raters on a picture archiving and communications system and stenosis was measured using a submillimeter digital caliper. Two measurement methods were compared differing only by the location used for measurement of the normal diameter: 1. within the V1 segment, or 2. at the beginning of the V2 segment. The equation for measurement of VAO stenosis was [1 - (Dstenosis/Dnormal)] x 100, where Dstenosis was the diameter of the most stenotic portion of the lesion. The first method used the V1 segment for measurement of Dnormal. In the second method, Dnormal was the diameter of the first disease-free portion of the V2 segment with exclusion of any region of post-stenotic dilatation. Average interobserver agreement for stenosis variance of 10% and 5%, intraclass correlation coefficient (ICC), and kappa were calculated for each of the two measurement methods. **Results:** Ten consecutive patients with VAO stenosis were reviewed. No tandem lesions were present. All stenoses were greater than 50%, and mean stenosis was 71.9% (SD 10.7) with the first method and 66.9% (SD 10.6) with the second method. Average interobserver agreements were 80% with the first method and 87% with the second method. Intraclass correlation coefficient showed higher inter-rater agreement when the V2 segment was used to measure normal diameter (ICC = 0.7750), when compared to the use of the V1 segment for measurement of normal diameter (ICC = 0.7256). Kappa statistics were the best between the 3 raters with 10% variance with the use of the V2 segment at 0.73 (overall agreement 87%). **Conclusions:** Exclusion of the tortuous V1 portion in measurement of the normal diameter shows improved inter-rater agreement and allows a simple method for measurement of high-grade vertebral artery origin stenosis. If validated in larger series, these criteria can be a consistent method of vertebral artery origin stenosis measurement in future studies.

Author Disclosures: M.A. Lazzaro: None. A. Badruddin: None. M. Abraham: None. O.O. Zaidat: None.

W P139

NIHSS Thresholds for Prediction of Perfusion Deficits in Acute Cerebrovascular Syndromes

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Background and Purpose: Perfusion-weighted imaging (PWI) in acute ischemic stroke patients provides useful diagnostic and prognostic information. Due to increased costs and resource allocation, PWI is not routine in many centers and is used on an ad hoc basis, without clear selection criteria. The severity of clinical deficits is often part of the decision making process in selecting patients for PWI. We aimed to identify a threshold for clinical severity, based on the National Institutes of Health Stroke Scale (NIHSS) score, that would predict perfusion deficits as well as PWI-diffusion-weighted imaging (DWI) mismatch in patients presenting with acute focal neurological symptoms. **Methods:** Patients with acute ischemic cerebrovascular syndromes were imaged with PWI-DWI acutely and an NIHSS score was assessed prior to MRI. An arterial input function selected from the contralateral middle cerebral artery and deconvolution algorithm were used to generate Tmax maps from raw PWI data. Tmax maps were thresholded to a 4 second delay (Tmax+4s) and manual planimetric measurements of Tmax+4s and DWI lesion volume were made. Patients were considered to have significant PWI deficits if the Tmax+4s volume was >10 ml. A PWI-DWI mismatch was considered to be Tmax+4svol/DWIvol>1.2. We conducted an ROC analysis of the sensitivity and specificity of the NIHSS for prediction of PWI deficits and mismatch paterns. **Results:** A total of 76 patients were included; 33 (43.4%) of whom had no perfusion deficits and 43 (56.6%) of whom had perfusion deficits. The median time from onset to MRI was 7.50 hours (IQR=4.00,15.48) in patients with PWI deficits and 13.00 hours (IQR=6.48,19.67) in those without PWI changes ($p=0.091$). The median NIHSS of patients with PWI deficits (13, IQR=7,18) was higher than that of patients without PWI deficits (4, IQR=3,5); ($p<0.001$). Patients with perfusion deficits had minimum and maximum NIHSS scores of 1 and 23 respectively. Patients without perfusion deficits had minimum and maximum NIHSS scores of 0 and 18 respectively. Logistic regression indicated that NIHSS score was a significant predictor of perfusion deficits (OR=1.4 per 1 NIHSS point, $P<0.001$). ROC analyses indicated good to moderate sensitivity and specificity of NIHSS score as a predictor of PWI deficits (AUC=0.86) and mismatch (AUC=0.68). An NIHSS ≥10 had a PPV and specificity for PWI deficits of 92.6% and 93.9% respectively but only 58.1% sensitivity. In our study, an NIHSS cutpoint of >=1 would have been required to capture all patients with significant PWI deficits. **Conclusions:** Higher NIHSS scores do predict the presence of focal hypoperfusion, but even patients with mild clinical deficits often have blood flow changes. Penumbral imaging should be considered in all patients with neurological deficits, even when NIHSS scores suggest a mild clinical syndrome.

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W P140

Temporal Evolution of Imaging Findings of Extracranial CranioCervical Arterial Dissection with Clinical Correlation: Mid-term Follow-Up

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Background and Objective: Extracranial craniocervical arterial dissection is believed to have a relatively benign natural history and generally is managed with anticoagulation or antiplatelet therapy. The clinical decision on the duration of anticoagulation is often based on follow up imaging findings. The purpose of this study is to analyze the temporal evolution of vascular imaging findings in extracranial craniocervical arterial dissection patients. **Methods:** Thirty two patients (M:F=23:9, mean age=49) with clinical evidence of craniocervical arterial dissection and at least one of the following suggestive imaging findings on either CT Angiography or MR angiography were included. Suggestive imaging findings include: 1) arterial stenosis, 2) arterial occlusion, 3) ectatic change of lumen, 4) pseudoaneurysm, and 5) dissection flap. The temporal evolution of imaging findings were analyzed by 2 neuroradiologists. **Results:** Twenty five patients had spontaneous dissection (25/32, 78%), and 7 patients had a history of trauma (21.8%). Fourteen patients presented with TIA/stroke (14/32, 43.7%), 9 patients had neck pain (28.1%), and 5 patients presented with Horner's syndrome (15.6%). There were 19 internal carotid artery dissections (59.3%), 9 vertebral artery dissections (28.1%), 2 common carotid artery dissections (6.3%) and 2 bilateral carotid dissections (6.3%). In 27 patients (84%), at least one follow up vascular imaging study was available (mean=1.5 years). On presentation, arterial stenosis, arterial occlusion, ectatic change of the lumen, pseudoaneurysm, and dissection flap were identified in 29 (91%), 6 (19%), 6 (19%), 12 (38%) and 16 (50%) respectively. On follow up, arterial stenosis improved in 58% (14/24), worse in 8.3% (2/24) and showed no interval change in 33.3% (8/24). The mean follow up period which demonstrated luminal narrowing improvement was 77 days (median=87.5 days). Regarding pseudoaneurysms, there was no change in shape and size of the lesion in 58% (7/12), larger in size in 25% (3/12), smaller in size in 8% (1/12). Two patients developed a new pseudoaneurysm at the dissection site on follow up imaging. All patients were managed with anticoagulation or antiplatelet therapy since the diagnosis. During the follow up period, all patients were stable, without any additional neurological episode except one patient who developed a TIA (3.7%, n=1/27). **Conclusion:** Post-dissection vascular imaging findings are dynamic. With medical management, more than half of the arterial stenoses after craniocervical dissection improved within a relatively short period of time (about 2.5 months) and the risk of repeated neurological event appears to be very low.

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W P141

New Auto-Freeze, Operator-Independent, Carotid Intima-Media Thickness Measurement for Atherosclerosis Screening

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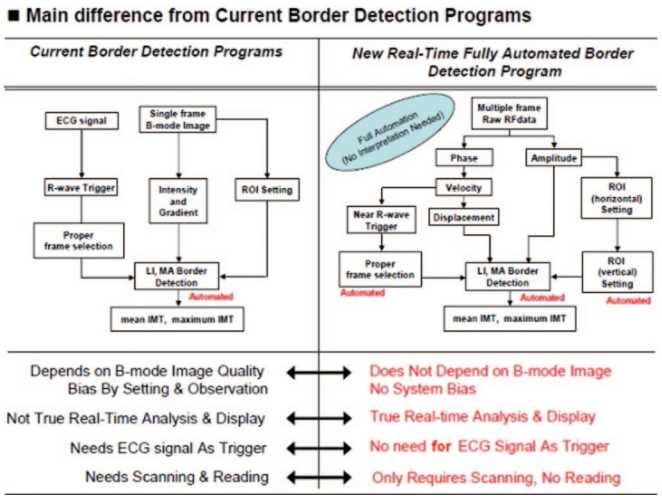
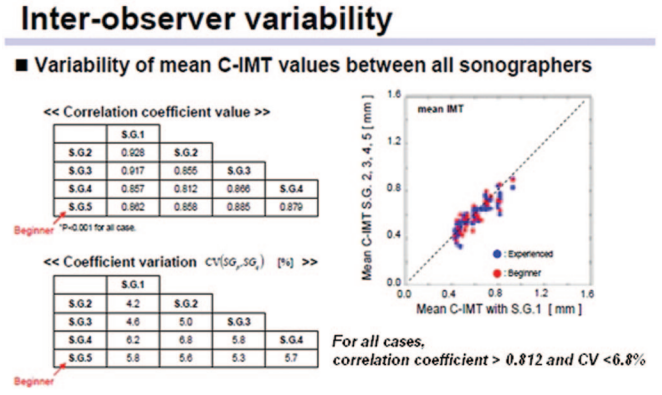
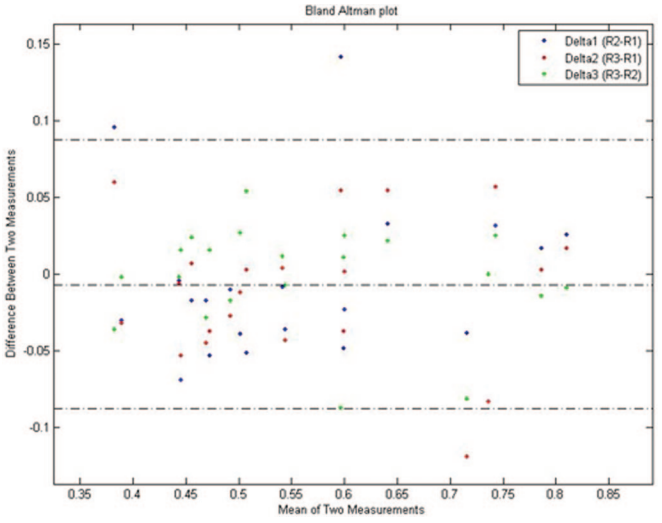
Most current methods for measuring carotid intima-media thickness (CIMT) require the user to manually identify a region of interest (ROI) and obtain the CIMT measurement offline from an ECG R-wave triggered image frame. We developed a new ultrasound instrument dedicated to carotid screening which combines real-time, automated R-wave triggered border detection and an auto-freeze function to capture the CIMT measurement, obviating the need for external ECG and offline reading.



We tested the inter-observer variability of our automated border detection program in a study in which 5 sonographers (4 experienced and 1 "beginner" with <2 months experience; S.G.1-5) each obtained a mean-CIMT measurement (single angle, far wall, distal common carotid artery-CCA) from 30 healthy individuals . Maximum difference from manual reading of ECG R-wave triggered images obtained with commercially available ultrasound systems was < 0.02mm. Intra-observer variability was very good (all coefficients of variation, or CV, were <6.8%, even for the "beginner").



To test the intra-observer variability of this device, we conducted a separate study in which a non-sonographer (<1 month training) obtained mean-CIMT (single angle, far wall, distal CCA) measurements in triplicate from 21 healthy individuals. Intra-operator variability was excellent (mean CV <5.0%). Coefficient of repeatability was 0.088mm. Of note, average time to obtain each auto-freeze measurement was 33 sec.



In summary, acquisition of CIMT measurements using our new ultrasound instrument with automated border detection, automated R-wave trigger, and auto-freeze features demonstrated very good reproducibility and excellent repeatability, even when used by a novice operator. Moreover, the capability to quickly obtain CIMT measurements in real-time and without a need to perform manual, offline measurement may be a desirable feature in the clinical setting.

Author Disclosures: T. Fukumoto: Employment; Significant; Panasonic Healthcare Co., Ltd. S. Lynum: Employment; Significant; Panasonic Healthcare Co., Ltd. M. Urabe: Employment; Significant; Panasonic Healthcare Co., Ltd. A. Kawabata: Employment; Significant; Panasonic Healthcare Co., Ltd. Y. Nishimura: Employment; Significant; Panasonic Healthcare Co., Ltd. T. Suzuki: Employment; Significant; Panasonic Healthcare Co., Ltd. M. Kato: Employment; Significant; Panasonic Healthcare Co., Ltd. I. Okabayashi: Employment; Significant; Panasonic Healthcare Co., Ltd. R. Bedi: Consultant/Advisory Board; Modest; Panasonic Healthcare Co., Ltd.. K. Ishikawa: None. A. Yen: Consultant/Advisory Board; Modest; CardioNexus Corporation. H. Hassan: Consultant/Advisory Board; Modest; CardioNexus Corporation. D. Panthagani: Consultant/Advisory Board; Modest; CardioNexus Corporation. A. Bandekar: Consultant/Advisory Board; Modest; CardioNexus Corporation. C. Hartley: Consultant/Advisory Board; Modest; CardioNexus Corporation.

W P142

Angiographic Staging Of 215 Moyamoya Patients: Defining A New Modified Staging And Correlating Results To Patient Demographics And Clinical Findings

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Background: Moyamoya (MM) disease is a progressive angiopathy involving the entire circle of Willis. Suzuki and Takaku in 1969 and then later Mugikura et al in 2002 presented a staging system emphasizing progression of disease in the anterior and posterior circulation. We present a modified staging system paying special attention to changes in the anterior, middle and posterior cerebral arteries. Additionally changes in occurrence of MM collaterals and in the cervical ICA defined as the "bottleneck sign" were reviewed and correlated to patient demographics and clinical findings. **Patient Selection:** Preoperative cerebral angiographies of 215 moyamoya patients undergoing surgical revascularization at our institute were reviewed and a new staging method applied. Mean age of was 32.5 years (1 to 69 years). This included 22% children, 78% adults, 75% females, 25% males, 31% Asians, 58% Caucasians. Unilateral to bilateral disease ratio was 1:1.8. **Results:** The distribution of the modified staging system was as follows: *Stage 1a:* intracranial ICA stenosis/occlusion = 12%, *Stage 2a*: segmental ICA involvement and ACA/MCA stenosis/occlusion = 35%, *Stage 3a*: A1 and M1 occlusion = 33% *Stage 4a*: supraclinoidal ICA occlusion with continued filling to the level of ophthalmic artery = 11%. *Stage 1p*: focal involvement of PCA = 5%, *Stage 2p*: segmental involvement of PCA = 10%, *Stage 3p*: disappearance of PCA = 2%, *Stage 4p*: proximal involvement of SCA or basilar artery = 3%. In 15% of the patients extracranial ICA stenosis in the form of a "bottle neck" was present at the level of its origin from the common carotid artery. This was always associated with *Stage 4a* of the disease. Typical MM collaterals were observed with *Stage 1a to Stage 2a*, disappearing with disease progression to *Stage 4a*. *Stage 4a* was more frequently seen in Caucasians. *Stage 2a and 3a* were the most common presentations in both children and adults. Females presented more often with bilateral disease and posterior circulation disease. Children presented more often with *Stage 3a* and posterior circulation disease. *Stage 2a* most commonly correlated to side of presenting TIA and Stroke. **Conclusion:** Using this modified staging system progression of disease was evaluated in both the anterior and posterior circulations. Appearance/disappearance of collaterals could be quantified. Late changes in the cervical ICA were documented and specific demographic and clinical correlations were made.

Author Disclosures: N. khan: None. M.P. Marks: None. J. Petralia: None. E. Tunovic: None. G.K. Steinberg: None.

W P143

Primary Central Nervous System Vasculitis: Circulating Endothelial Cells as Potential Diagnostic Biomarkers

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Background: Histological evidence of vasculitis is the only proof of primary central nervous system vasculitis (PCNSV) at present. But, a biopsy is often omitted due to the invasive character and possible complications of the procedure. The number of circulating endothelial cells (CEC) has been shown to be elevated in patients with ANCA-associated vasculitis. We hypothesize that the CEC value is also elevated in patients with PCNSV and may contribute to the diagnosis of PCNSV. **Methods:** CEC were assessed in 19 patients in the age of 30-84 years (13 male) with clinical and additional examination findings suspicious of PCNSV. In 11 of them a brain biopsy was performed. Three patients were under immunosuppressive treatment. The patients' data were compared to those of 16 healthy controls (age range: 42-58 years, 8 male), 74 controls with cerebrovascular risk factors (age range: 54-60 years, 41 male) and 49 patients with ischemic stroke (age range: 61-79 years, 24 males) as disease controls. CEC's were measured by immunomagnetic isolation from peripheral blood. Patients with infectious diseases, malignoma and systemic vasculitis etc. were excluded. **Results:** Three brain biopsies showed a vasculitis. Interestingly, in these patients CEC values outranged 400 cells/ml. In the

patients under successful immunosuppressive treatment the CEC value was significantly lower (range 0-52 cells/ml; $p < 0.05$). The CEC values in the control groups were also significant lower (healthy controls: range 0-16 cells/ml, $P<0.01$; patients with cerebrovascular risk factors: 0-20 cells/ml, $P<0.01$; patients with stroke: 8-144 cells/ml, $P<0.01$). In the remaining 13 patients with clinical and additional findings highly suspicious for PCNSV the median CEC value was 220 cells/ml, and thus significantly higher than in the immunosuppressive treated patients ($p<0.01$) and the healthy and disease control groups ($p<0,001$ for each group). **Discussion:** However, our data are not sufficient to finally describe the sensitivity or specificity of CEC for the diagnosis of PCNSV. But, for the first time we could show that CEC are significantly elevated in patients with active biopsy proven PCNSV. Thus, CEC may well be a potential biomarker for PCNSV, expecially in not performed or biopsy negative settings. Continuous analysis of CEC in patients who undergo brain biopsy for the diagnosis of PCNSV and the monitoring of CEC numbers in patients treated for PCNSV shall provide data for a final judgement about the diagnostic use of CEC in this pathology.

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W P144

Validation Of New Ultrasound Parameters For Assessment Of The Collateral Pathway Through The Ophthalmic Artery In Internal Carotid Artery Occlusion

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Background and Purpose: The external carotid artery (ECA) may function as a collateral pathway through the ophthalmic artery in internal carotid artery (ICA) occlusion. The conversion to low resistance doppler sonography waveform in the ECA has been termed 'internalization' because the abnormal tracings in the ECA mimic the ICA, however, the criterial indicator of the internalization has not been reported. We determined the criterion for judgment of internalization by neck ultrasonography (US). **Methods:** We retrospectively analyzed the patients with unilateral ICA occlusion that were able to undergo digital subtraction angiography (DSA) and neck US. The clinical features, each parameter of the neck US, the DSA data and ^{15}O-labeled positron emission tomography (PET) data were evaluated. Furthermore, the degree of collateral flow via the ophthalmic artery observed in DSA was graded into three groups (grade 0: no filling of ophthalmic artery; grade 1: retrograde flow in the ophthalmic artery with filling of the carotid siphon; grade2: to MCA and/or ACA). We used ANOVA to analyze the relationships of the ECA collateral flow Grade and the parameters of the neck US. **Results:** 45 patients who underwent both DSA and US (43 men; mean age 68.1 ± 7.9 years; 23 patients occluded on the right side) were analyzed. PET data were obtained for 32 patients (71.1%). Retrograde flow via the ophthalmic artery was detected in 27 cases (60.0%). The patients were divided into two groups those with (grade 1 or 2) and those without (garade 0) retrograde flow via the ophthalmic artery. Patient characteristics were no statistically different in age, sex, obstruction side and risk factors between the two groups. History of cerebral infarction and elevated oxygen extraction fraction (OEF) measured with PET were significantly higher in the patients with retrograde flow ($p<0.05$). Compared to each parameter of the neck US the optimal cut-off value of the ratio of the pulsatility transmission index (PTI: the ratio of pulsatility index (PI) of the occluded side ECA to PI of the ipsilateral common carotid artery) for detecting internalization was 0.94 with a sensitivity of 92.6%, and a specificity of 94.5%, respectively. The relationship between the ECA collateral flow grade and the PTI was statistically significant ($P<0.01$; one way ANOVA). **Conclusion:** PTI is the optimal parameter to determine the internalization of ECA as a collateral pathway through the ophthalmic artery as well as providing a platform for the easy detection of elevated OEF indicating misery perfusion in ICA occlusion.

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W P145

Patent Foramen Ovale Characteristics and Infarct Size in Cryptogenic Stroke with PFO

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Introduction and Hypothesis: Causal relationship between patent foramen ovale (PFO) and stroke is still controversial. We hypothesized that PFO characteristics (i.e., size or shunt amount) and ischemic lesion burden (i.e., infarct volume or number) might be correlated, if PFO plays a role as embolic source. **Methods:** Of ischemic stroke patients admitted to Asan Medical Center between January 2000 and April 2007, we identified patients who had (1) acute ischemic lesion on diffusion-weighted imaging (DWI) within 5 days of symptom onset, (2) undetermined cause of stroke according to TOAST classification and (3) only PFO detected by extensive cardiac work-up including transthoracic, transesophageal echocardiography and Holter monitoring. Volume, pattern and number of acute ischemic lesions on baseline DWI were obtained. Arterial occlusion relevant to index stroke was evaluated with MR angiography. Lesion patterns were classified as large territorial, perforator artery (large $>$ or $=$2cm, small $<$2cm), pial artery, or border zone infarcts. PFO characteristics on echocardiographic studies included size, shunt degree (minimal versus moderate versus severe, according to number of bubbles), shunt pattern (left-to-right versus right-to-left versus bi-directional) and presence of atrial septal aneurysm (ASA). The PFO size was measured as the maximum separation of the septum primum from the septum secundum in digitally, stored transesophageal echocardiographic images. Initial stroke severity was examined according to National Institutes of Health Stroke Scale (NIHSS) Scores. **Results:** 75 patients (male 56% and mean age 45.3 ± 13.9) were included for this study. 10 patients (13.3%) had ASA. Median DWI lesion volume was 7.0 cm^3 (range; 0.1-196.6 cm^3). In univariate analysis, PFO size was positively correlated with log-transformed infarct volume (LIV) (regression coefficient$=$0.469, $p=0.009$). After adjusting hypertension, previous stroke history and migraine (all $P<0.2$ by univariate analysis), PFO size remained independently associated with LIV (regression coefficient$=$0.481, $p=0.007$). Larger PFO size was associated with large territorial infarct (odds ratio [OR]$=$2.077, 95% confidence interval [CI] 1.119-3.858, $p=0.021$) and occlusion of relevant artery (OR$=$1.467, 95% CI 0.969-2.222, $p=0.07$). The initial NIHSS scores tended to be positively correlated with PFO size (Spearman's coefficient rho$=$0.223, $p=0.054$). Lesion number was negatively correlated with PFO size (Spearman's coefficient rho$=$-0.251, $p=0.03$). **Conclusions:** PFO size and ischemic lesion burden was positively correlated in cryptogenic stroke with PFO. These results support the idea that PFO may be an embolic source of stroke in patients with cryptogenic stroke.

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W P146

Impaired Cerebrovascular Reactivity Assessed By Transcranial Doppler In Hepatic Cirrhosis

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Background: In patients with hepatic cirrhosis systemic vasodilatation secondary to portal hypertension induces a continuous activation of two vascular regulatory systems, the renin-angiotensin-aldosterone and the sympathetic nervous, which stimulate a dysfunctional circulatory vasoconstriction involving kidneys, muscles, skin, and brain. This provides a substrate for damage to cerebral microvessels and probably, it may constitute a physiopathologic pathway of development and progression of hepatic encephalopathy (HE). The primary aim of this study was to evaluate the cerebrovascular reactivity (CVR) assessed by transcranial Doppler in patients with hepatic cirrhosis with and without HE. Material and Patients: Sixty cirrhotic patients were studied and severity was classified according with Child score. Also, HE was determined by *West Haven* evaluation. The proximal segments of the middle cerebral artery were examined on each side and the following parameters were evaluated: peak systolic blood flow velocity, end-diastolic blood flow velocity, mean flow velocity, and pulsatility index (PI). CVR was examined using the breath-holding index (BHI). The BHI values included in the analysis were the means of the 2 tests and of right and left values. CVR reflects the compensatory dilatory ability to maintain constant cerebral blood flow. **Results:** There were 62% women; mean age was 49 years. According with Child score 33 patients (55%) had severe hepatic damage (Child score $\geq$8) and 45% mild to moderate disease (Childe $<$8). Fifty percent (30 patients) had HE. Classification of HE correlated with anemia ($p<0.000$), hyponatremia ($p<0.008$), and severity of disease (Child $>$7, $P=0.049$). Patients with severe hepatic damage (Child $\geq$8) showed lower CVR with BHI (0.83; 95%CI 0.45-1.12) as compared with patients with mild to moderate hepatic damage (1.25; 95%CI 0.86-1.53; $P=0.006$) and higher PI (1.07, 95%CI 0.95-1.21 versus 0.87, 95%CI 0.83-1.05; $P=0.002$). Similar results were obtained when PI and CVR were compared between patients with and without HE. **Conclusions:** This study provides evidence of significant vasoreactivity reduction and increased PI in patients with severe hepatic damage and HE, as indicators of impairment of cerebral microvasculature circulation. This suggests that overactivation of systemic vascular mechanisms have an effect on cerebrovascular regulation, first, with functional damage, and, with progression of the disease, structural damage.

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W P147

Predictive Factors For A Neurological Deterioration In The Acute Phase Of Ischemic Stroke - Fukuoka Stroke Registry

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Background & Purpose: A neurological deterioration in the acute phase can be associated with a bad outcome in stroke patients. We investigated the predictors for a neurological deterioration in the acute phase of ischemic stroke. **Subjects & Methods:** Consecutive 1732 ischemic stroke patients who were admitted to the 7 stroke centers in Fukuoka, Japan within 24 hours after the onset were included in the present study. Stroke subtypes were classified according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification: Large-artery atherosclerosis, Cardioembolism, Small-vessel occlusion, and Others. We observed a neurological deterioration (a NIHSS score worsening of $\geq$1-point), stroke recurrence, or any death in the acute phase (the first 21 days) and also evaluated the outcome 3 months after admission. Modified Rankin Scale of 0 or 1 was defined as a good outcome. **Results:** A neurological deterioration was observed in 233 (13.5%) patients. A stroke recurrence or any death was observed in 76 (4.4%) patients. A neurological deterioration was significantly associated with a good outcome (OR; 0.17; 95%CI, 0.06$\sim$0.50). With regard to the TOAST classification, a neurological deterioration was most frequent in Large-artery atherosclerosis (21.1%) and was less frequent in Small-vessel occlusion (7.1%). The site of ischemic lesions on the magnetic resonance imaging (MRI) or computed tomography on admission was significantly associated with a neurological deterioration ($p<0.0001$): both cortex or cerebellar

lesions and brain stem or subcortex lesions (18.0%), only brain stem or subcortex lesions (15.1%), only cortex or cerebellar lesions (9.6%), and no ischemic lesions on MRI (7.3%). A stenosis of ≥50% or a total occlusion of the major brain artery, diabetes mellitus, a motor hemiparesis, NIH stroke scale score, systolic blood pressure (SBP), white blood cell, low density lipoprotein cholesterol, blood sugar, and HbA1c values on admission showed an association with a neurological deterioration on univariate analysis. On multivariate analysis, a major brain artery stenotic lesion (OR, 1.99; 95%CI 1.44～2.75), ischemic lesions including both cortex and subcortex (OR, 1.99; 95%CI, 1.26～3.16), motor hemiparesis (OR, 2.62; 95%CI, 1.69～4.05), and SBP ≥162mmHg (OR, 1.79; 95%CI, 1.32～2.42) were significantly associated with a neurological deterioration in the acute phase. In comparison with patients without any those 4 independent predictive factors, patients with 1, 2, 3, and all 4 factors have 5.1, 12.3, 18.4, and 22.4-fold risk for a neurological deterioration. **Conclusions:** A major brain artery stenotic lesion, the site of ischemic lesions, a motor hemiparesis, and SBP value on admission were significant predictors for a neurological deterioration in the acute phase of ischemic stroke.

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W P148

Significance of VEGF in Ischemic Stroke - Research for Biomarkers in Ischemic Stroke (REBIOS)

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Background and Purposes: Blood biomarkers for stroke diagnosis would be helpful, especially under the situations without imaging modalities. However, there is no biomarker clinically available for diagnosis of ischemic stroke so far. Heterogeneous mechanisms of ischemic stroke hampers the identification of biomarkers associated with ischemic stroke. In the present study, we aimed to discover blood biomarkers for diagnosis of ischemic stroke and to evaluate its predictive capability for prognosis. **Methods:** We designed Research for Biomarkers in Ischemic Stroke (REBIOS) study, and 132 patients with brain infarction (atherothrombotic (AT) 27, cardioembolic (CE) 39, lacunar (Lac) 39, and unclassified 27 cases) were recruited from the Fukuoka Stroke Registry, a prospective multi-centered study for acute stroke in Japan. Blood samples as well as clinical information were obtained from the patients at 5 points after the stroke onset, day 0 (within 24 hours after the onset), 3, 7, 14, and 90. Ninety molecules were measured by HumanMAP® v 1.6 (Rules-Based Medicine, Inc.). Age and sex -matched healthy subjects from the Hisayama study in Japan were enrolled as the control group (n=110). **Results:** Among the molecules we tested, we identified vascular endothelial growth factor (VEGF) as one of the biomarkers that increased significantly and immediately after the stroke onset in all subtypes (AT 581 <27< 154, CE 563 ± 204, Lac 595 ± 243 pg/ml at day 0), compared with controls (435 ± 130 pg/ml, P<0.0001). A receiver operating characteristic analysis demonstrated that ischemic stroke was differentiated from the healthy subjects with sensitivity 62% and specificity 82% (cut-off value: 480 pg/ml). VEGF values at day 90 remained significantly high in all stroke subtypes (AT 612 ± 176, CE 599 ± 204, Lac 651 ± 268 pg/ml), and were correlated strongly with those at day 0 (p<0.0001, r=0.79). In CE, VEGF values at day 0 were significantly higher in the group with poor prognosis (modified Rankin Scale 3 to 6) at day 90 than in the group with good one (640 ± 200 pg/ml vs 488 ± 154 pg/ml, P<0.05). Conversely, VEGF values at day 0 tended to be higher in the group with good prognosis in AT. **Conclusion:** Plasma VEGF levels could be a biomarker useful for diagnosis of ischemic stroke regardless of its subtype. The significance of VEGF in ischemic stroke may be different among its subtype, especially in terms of prediction of prognosis.

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W P149

Visinin-like Protein-1 (VILIP-1): A Novel Plasma Biomarker For The Detection Of Acute Cortical Ischemic Stroke

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Background: The diagnosis of acute ischemic stroke is largely based on clinical evaluation and the absence of hemorrhage on head CT. It has been estimated that up to 7-15% of acute strokes are clinically misdiagnosed. Therefore, biomarkers that can reliably detect acute neuronal injury may have great utility in improving diagnostic accuracy and clinical decision-making. Visinin-like protein-1 (VILIP-1), a calcium sensor protein expressed exclusively in neurons, has demonstrated utility as a neuronal injury marker in Alzheimer disease patients. Here, we examined the utility of plasma VILIP-1 in the detection of acute ischemic stroke. **Methods:** Suspected acute ischemic stroke patients were enrolled within 12 hrs of symptom onset after obtaining informed consent. NIHSS and plasma samples were obtained on presentation (<12), 24, and 72 hrs after symptom onset. Ischemic stroke patients were classified into cortical and subcortical localization based on clinical signs and symptoms as well as magnetic resonance imaging (MRI) when available (n=39). Plasma was assayed for VILIP-1 using a commercial chemiluminescence assay (Singulex, USA). In the subset of patients with cortical ischemic stroke who had MRI (n= 22), DWI (diffusion-weighted imaging) lesions were manually delineated by a board-certified neuroradiologist (RP) who was blinded to all clinical and VILIP-1 results. Infarct volumes were measured using Image-J v.1.43. Unpaired t-tests and Spearman correlations evaluated group comparisons and relationships between VILIP-1 levels and NIHSS or infarct volumes. **Results:** Seventy patients with discharge diagnosis of brain ischemia were enrolled, including 48 cortical strokes, 15 subcortical strokes, and 7 TIAs. Eleven patients were diagnosed as stroke mimics, including stroke recrudescence (5), post-ictal paralysis (4), diabetic cranial nerve palsy (1), and conversion disorder (1). In addition, 36 healthy age-matched controls were enrolled. Plasma VILIP-1 levels were higher in ischemic stroke compared to controls at 12 hrs (83.6 and 58.2 pg/ml, respectively, p=0.003), 24 hrs (94.3 pg/ml, p=0.048), and 72 hrs (118.8 pg/ml, P<0.0001). Moreover, plasma VILIP-1 levels were higher in cortical strokes compared to stroke mimics at 12 hrs (90.8 and 36.3 pg/ml, respectively, p=0.03). While cortical strokes had higher VILIP-1 levels compared to subcortical strokes (90.8 and 61.1 pg/ml, respectively, p=0.034), subcortical strokes were not different from controls (p=0.64) within 12 hrs of onset. Peak VILIP-1 levels values were at 72 hrs, at which time-point VILIP-1 correlated with both NIHSS (r=0.65, p=0.0008) and DWI-defined infarct volume on MRI (r=0.73, p=0.024). **Conclusion:** Our results suggest that plasma VILIP-1 levels correlate with NIHSS and infarct volume on MRI, and may have diagnostic utility for the acute diagnosis of cortical ischemic strokes.

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W P150

A Screening Approach for Endo- and Myocarditis in Ischemic Stroke Patients at Hospital Admission - a Preliminary Report

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Background and Purpose: Cardiac sources can be identified as etiology for ischemic stroke in up to one third of the cases. Thereby, early detection of potentially life-threatening courses due to severe cardiac insufficiency, arrhythmia and thrombus formation - as frequently found in endocarditis (EC) or myocarditis (MC) - is of great importance for planning diagnostic and therapeutic procedures. The present study aims to identify screening parameters that may help to detect stroke patients suffering from MC and EC at hospital admission. **Methods:** A hospital-based database with 950 cases of ischemic stroke was retrospectively screened for the occurrence of MC and EC, detected by echocardiography. Patients with EC (n=12) or MC (n=3) were compared to those devoid of EC/MC concerning age, clinical parameters (Glasgow Coma Scale [GCS], National Institute of Health Stroke Scale [NIHSS]), inflammatory (C-reactive protein [CRP], leukocyte count) and cardiac (troponin T, myoglobin, creatine kinase [CK], creatine kinase isoenzyme [CK-MB]) serum markers. Furthermore, MRI/CT-based differences in type of infarction (lacunar, territorial, border zone stroke) and lesion pattern (single territory vs. multiple territories) were analyzed. **Results:** Patients with EC/MC were significantly younger than non-affected patients (means, 61.1 years vs. 68.7 years; P<0.05). NIHSS and GCS did not differ significantly between the groups. Leukocyte count and CRP were significantly increased in patients with EC/MC (means, 11.4 exp9/l vs. 9.0 exp9/l; 74.0 mg/l vs. 15.3 mg/l; P<0.05 for each). Identifying patients with EC/MC, a receiver operating characteristics (ROC) analysis revealed superiority for CRP (area under curve [AUC], 0.832; P<0.001). Troponin T, myoglobin, CK and CK-MB tended to increased values in patients with EC/MC, which failed statistical significance. Surprisingly, percentage rates for type of infarction and lesion pattern did not differ significantly between patients with EC/MC and non-affected patients. **Conclusions:** CRP and leukocyte count were identified as helpful parameters for the detection of EC and MC in ischemic stroke patients at hospital admission. Significantly increased values should accelerate further diagnostic procedures - especially echocardiography - with the objective of EC/MC exclusion.

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W P151

Elevated Plasma Levels of Soluble Form of RAGE and High Mobility Group Box 1 in Patients with Acute Stroke

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Background and purposes: The receptor for advanced glycation end products (RAGE) and high mobility group box 1 (HMGB1) have been shown to mediate ischemic brain damage in experimental stroke model, but little is known about its clinical implication. Here we reported the plasma levels of HMGB1 and soluble form of RAGE (sRAGE) in patients with acute stroke. **Methods**: We prospectively recruited patients with acute ischemic and hemorrhagic stroke and age-and sex-matched healthy controls. Plasmas were collected from patients at 3 time points after stroke: within 48 hours, 3 days and 7 days. The plasma levels of HMGB1 and sRAGE were determined by the ELISA. **Results:** There were 118 patients (male, 62.7%; mean age, 64.8±15.5 years; ischemic stroke, 65.3%) with acute stroke and 110 controls. The NIH stroke scale (NIHSS) score at admission was 11.6±7.4. After acute stroke, **plasma** HMGB1 levels were significantly elevated in all 3 time points and kept increasing with time course (controls 6.4±2.9 ng/mL, vs. stroke, 15.8±31.1, 19.4±37.1, and 20.7±44.0 ng/mL, respectively; all *P*<0.001). By contrast, sRAGE levels were significantly elevated in samples collected within 48 hours but decreased gradually with time course (control 751.2±322.4 ng/mL, vs. stroke, 996.1±1073.4, 834.3±790.9, and 721.9±823.0 ng/ml, respectively, *P*=0.019, 0.152, and

0.853, respectively). There was no significant difference of the **plasma** levels of HMGB1 between ischemic and hemorrhagic stroke patients. However, level of sRAGE was significantly higher in ischemic than hemorrhagic stroke patients. The initial NIHSS score was correlated with the sRAGE levels, but not with the HMGB1 levels. **Conclusion:** This study suggested that the HMGB1 and its receptor RAGE were activated in acute stroke patients.

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W P152

The Validation Of The Use Of Cardiac Monitor In Ischemic Stroke Patients Post-thrombolytic Therapy

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Background & Objective: No clinical trials have tested the utility of cardiac monitoring in regards to blood pressure, ECG change, and cardiac events post stroke. The objective of the study is to validate the use of cardiac monitor in acute ischemic stroke patients post tissue plasminogen activator (tPA) administration. **Methods:** A retrospective chart review was undertaken for patients who received iv tPA. All patients had 24 hour cardiac monitor. The detection of new myocardial infarction (MI) and arrhythmias, management and short term outcomes were analyzed. **Results:** A total of 97 charts were analyzed. The mean age was 67.4±3.01 (average ± 95%CI), with 55.2% being male gender. Forty three percent had past history of stroke or TIA, 90.6% had history of hypertension (60.10% were treated), 37.90% had diabetes, 86.7 % patients had dyslipidemia (49.30% on treatment); 45.7% had prior ischemic heat disease, and 28.4% had cardiac arrhythmia [94.7% had atrial fibrillation (AF)/ flutter] by history, prior documentation or admission ECG. NIHSS at admission was 12.8±7.36. Positive Troponin, elevated Troponin and CK, and ST-T change on ECG were found in 5%, 2.6% and 16.9% of the patients, respectively. Systolic BP exceeding 180 mmHg and 210 mmHg were recorded in 40.10% and 8.4% of patients; among whom 19.3% received IV Labetalol and/or hydralazine. Cardiac tachyarrhythmia was recorded in 27% of patients; with majority were AF/flutter (88.89%), and new diagnosis of one case of SVT, one case ventricular arrhythmia, and one case of pulseless electric activity (PEA). New diagnosis of AF was in 3 patients (3.09%). Treatment was initiated for 10.2% of the patients with beta-blockers (8.2%), Digoxin (1%), and amiodarone (1%), respectively. The patient with PEA died after resuscitation. No treatment was warranted for the SVT and brief ventricular arrhythmia. Acute MI was diagnosed in 5.2% patients. None required invasive measures and all survived. **Conclusion:** This pilot study has demonstrated that 24 hour cardiac monitoring has a role in diagnosing new cardiac arrhythmia and hypertensive urgency in acute stroke patients post tPA. However, 24 hour monitoring does not seem to impact on MI diagnosis or treatment in this setting. Future analysis comparing non-monitored group for arrhythmia diagnosis and outcome measure are required for more complete validation of 24 hour cardiac monitoring.

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W P153

Differences In The Identification Of Cerebrovascular Profiles Between Two Etiological Stroke Classifications: Toast And Asco

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Introduction And Objectives: The current classifications of stroke are based on identifying their most likely cause. A new classification capable to describe a complete "stroke phenotyping" has been recently proposed, the ASCO scale: A, atherosclerosis; S, small vessel disease; C, cardiac source; O, other cause. Each of the 4 phenotypes is graded 1, 2, or 3. One for 'definitely a potential cause of the index stroke', 2 for 'causality uncertain', 3 for 'unlikely a direct cause of the index stroke (but disease is present)'. When the disease is absent, the grade is 0; when grading is not possible due to insufficient workup, the grade is 9. The main objective is to analyze the presence of "mixed" cerebrovascular disease in the stroke etiological classification, using the TOAST and ASCO classifications. **Materials And Methods:** Observational study of the first 30 ischemic stroke patients admitted to our Stroke Unit in 2010. The clinical records were given to two stroke expert neurologists, two general neurologists and two resident neurologists, who were blinded to the final etiological stroke classification. The physicians classified each stroke patient twice, according to TOAST and ASCO classifications. **Results:** ASCO scale showed more than one possible stroke profiles in 66-83% (minimum and maximum percentage between the six observers) of strokes. There was not a strong concordance between the TOAST and ASCO scales in the atherothrombotic and small vessel disease group. ASCO scale revealed atherothrombotic disease in 40%-65% of stroke not so classified by TOAST, and small vessel disease in 42% to 57% of the strokes that had not been diagnosed as lacunar strokes by TOAST. However, a cardiac source by ASCO was identified in all patients with cardioembolic stroke by TOAST. Up to 94% of patients with cardiac source as definitively cause of stroke (C1) by ASCO presented scores of 1-3 in the other items (A, S, O). This kind of "mixed" vascular disease is observed in 63%-80% of strokes caused by cardioembolism according to TOAST ($p<0{,}001$). ASCO revealed evidence for other stroke etiologies in most of strokes of undetermined origin by TOAST (50%-80%, 40%-75%, and 40%-99%, for atherosclerosis, cardioembolism and small vessel disease, respectively). **Conclusion:** The ASCO scale shows more than one stroke profile in most of patients. The concordance between ASCO and TOAST is strong in cardioembolism but poor in large and small vessel disease. ASCO shows other stroke profiles in most of strokes of undetermined origin by TOAST.

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W P154

Pelvic Magnetic Resonance Venography For Detection Of Deep Vein Thrombosis In Young Patients With Cryptogenic Ischemic Stroke And Patent Foramen Ovale

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Background: Despite comprehensive evaluation the cause of stroke remains unidentified in as many as 64% of young adults (<55 years old). Patent foramen ovale (PFO) has been related to ischemic stroke, particularly in patients with cryptogenic stroke. Paradoxical embolism has been suggested as one of the mechanisms for stroke in these patients, leading to the search for deep vein thrombosis (DVT). Prior studies demonstrated presence of pelvic DVT on pelvic Magnetic Resonance Venography (MRV) in 20% of young adults with cryptogenic stroke and known PFO. However, the sensitivity of pelvic MRV remains low and its utility in routine evaluation of patients with cryptogenic stroke and PFO is still unclear. **Methods:** Medical records of patients 15-49 years old admitted to Boston Medical Center between January, 2005 and February, 2010 with diagnosis of ischemic stroke were retrospectively reviewed. Patients diagnosed with PFO on Transthoracic (TTE) or Transesophageal echocardiogram (TEE) were selected and their lower extremities Duplex scan (LE Duplex) and pelvic MRV were reviewed. Both venous studies were performed following standard procedures, and MRV was obtained within 3±2 days of admission. Descriptive statistics are presented. **Results:** A total of 114 patients with ischemic stroke (62.3% men) were identified (mean age: 41; range: 19-49 years), representing 11.4% of all patients admitted with a diagnosis of ischemic stroke during the same period. TTE or TEE was done in 111 (97.4%) patients, including TTE in 110 (96.5%) and TEE in 58 (50.9%) patients. PFO was detected in 20 (17.5%) patients. Pelvic MRV and LE Duplex were available in 12 (60%) and 18 (90%) of these patients, respectively. One patient with PFO was found to have LE thrombosis confirmed by LE Duplex, but none of the pelvic MRV detected a DVT. **Conclusion:** While prior studies revealed high prevalence of pelvic DVT among young patients with cryptogenic stroke and PFO using pelvic MRV, we were unable to corroborate this observation in our sample. Our study is limited by its sample size and design. Given that pelvic MRV is a costly test, further studies are required to assess its role in the routine evaluation of patients with cryptogenic stroke and PFO.

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W P155

A New Contrast Agent Of A Drop Of Diazepam Added To Saline To Detect PFO With Transesophageal Echocardiography

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Background and Purpose: Patent foramen ovale (PFO) has been known as one of potential embolic sources for ischemic stroke, especially in cryptogenic stroke. Contrast transesophageal echocardiography (c-TEE) has been a sensitive technique to diagnose PFO. Usually, agitated saline (air bubble) is used as contrast agents, but air bubble is easy to be broken and it is frequently difficult to diagnose PFO. Therefore, stable contrast agent is expected. Diazepam is a benzodiazepine with water solubility non-water-soluble powders. Therefore, Diazepam seems to be better as contrast agents than saline. The aim of this study was to investigate whether use of a drop of Diazepam added to saline can improve the detection rate of PFO with c-TEE. **Methods:** We prospectively studied consecutive ischemic stroke patients admitted to our hospital. To detect PFO, c-TEE was performed 2 times using 2 kind of contrast agents as follow; saline only, and saline with a drop of Diazepam. We compared the detection rate of PFO between the 2 conditions. Next, we divided patients into 4 grade on the basis of the number of micro-bubble in left atrium within 3 cardiac cycles after opacification of the right atrium; non-PFO, small PFO; <10 micro-bubbles, moderate PFO; 10 to 50 micro-bubbles; large PFO; >50 micro-bubbles. We investigate the change of detection rate for PFO and PFO grade using a drop of Diazepam. **Results:** 559 patients (male 400, age 69.6±11.7 years) were enrolled in the present study. Detection rate of PFO was higher in cooled saline with a drop of Diazepam than saline only (36.9% vs. 20.4%, $P<0.0001$, Figure 1). For PFO grade for saline only and saline with a drop of Diazepam, non-PFO was 77.6% and 56.2%, small PFO was 14.2% and 26.0%, moderate PFO was 6.0% and 9.8%, and large PFO was 2.2% and 8.0%, respectively ($p<0.0001$, Figure 2). Therefore, using saline with a drop of Diazepam, the amount of stable micro-bubble increased and detection rate of PFO improved, in particular small and moderate PFO. **Conclusion:** Using of one drop of Diazepam can improve the detection rate of PFO with c-TEE, especially in small and moderate PFO.

Figure 1

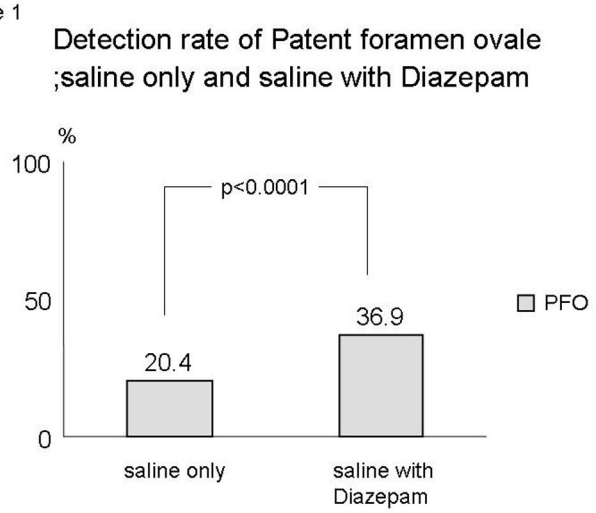
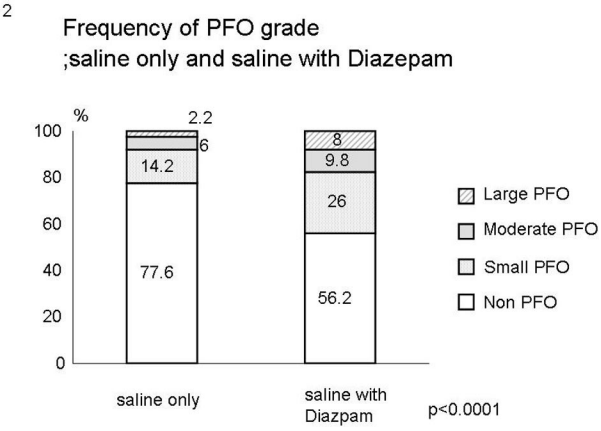


Figure 2



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W P156

The Cardio-Ankle Vascular Index As A Predictor Of Cerebral Microbleeds In Acute Ischemic Stroke Patients

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Background: Cerebral microbleeds (CMBs) are recognized association with hypertension, white matter hyperintensity (WMH), kidney dysfunction, and intracerebral hemorrhage. However, relationship between CMBs and arterial stiffness is still unclear. The cardio-ankle vascular index (CAVI) has been recently reported as a new index of arterial stiffness, which is less influenced by blood pressure than pulse wave velocity (PWV). We investigated the correlation between the presence of CMBs and CAVI in patients with acute ischemic stroke. **Methods:** We prospectively studied with acute cerebral infarction or transient ischemic attack (TIA) patients who underwent T2*-weighted gradient echo and fluid attenuated inversion-recovery (FLAIR) images on MRI. All patients had a detailed clinical assessments that included neurological investigations, blood tests, echocardiography, and CAVI examination. CAVI was automatically calculated from the pulse volume record, both systolic and diastolic blood pressure, and the vascular length from the heart to ankle. We divided all patients into CMBs group and no CMBs group. We compared clinical characteristics between two groups. **Results:** This study consisted of 88 patients (59 males, 67.0±13.7 years old), who were classified according to stroke subtypes into cardioembolic stroke (23 patients), large artery disease (16 patients), small-vessel disease (17 patients), other or undetermined cause of stroke (24 patients), and TIA (8 patients). T2*-weighted gradient echo MRI revealed CMBs in 42 patients (47.7%) and no CMBs in 46 patients (52.3%). CAVI value was significantly higher in CMBs group (10.5 vs 8.9, P<0.001). The optimal cut-off CAVI value to distinguish CMBs group from no CMBs group using a receiver operating characteristics (ROC) curve was 9.0, with a sensitivity of 81.0% and a specificity of 63.0%, respectively. All patients were categorized into three subgroups according to CAVI value tertile. The frequency of CMBs patients gradually increased in accordance with increasing CAVI value (tertile 1:19.4%; tertile 2:57.1%; tertile 3: 69.0%;ptivariate logistic regression analysis using male, hypertension, advanced WMH, and CAVI value >9.0 as variables with a P<0.1 on univariate analysis, CAVI value >9.0 was the only independent factor associated with CMBs (odds ratio 6.61; 95% confidence interval, 2.50 to 17.47, P<0.001). **Conclusion:** CAVI may be as a strong predictor of CMBs in acute ischemic stroke patients. These findings suggest that arterial stiffness may be pahophysiologically associated with CMBs.

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W P157

A Risk Score To Predict Paroxysmal Atrial Fibrillation In Acute Ischemic Stroke

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Background and Purpose: Atrial fibrillation (AF) is a major risk factor for ischemic stroke. However, paroxysmal AF (PAF) is often failed to detect during hospitalization in acute ischemic stroke patients. Our aim of this study was to investigate the factors associated with PAF and to develop a risk score to predict the presence of PAF. **Methods:** Consecutive ischemic stroke patients were retrospectively enrolled. The patients with chronic AF were excluded. The patients without AF underwent continuous ECG monitoring and/or 24 hours Holter ECG to detect AF. The patients were divided into two groups according to the presence of PAF (newly and a past history of PAF): the PAF group or the non-PAF group. The factors associated with PAF were investigated by multivariate regression analysis. Furthermore, we devised a new risk score to predict the presence of PAF. **Results:** 215 patients (male 138 (64%), mean age 70.2 years) were enrolled in the present study. The PAF group had 32 (14.9%) patients. Age, NIHSS score on admission, left atrial size, mitral valvular disease, D-dimer, the frequency of absence of lacunar imaging on CT or MRI and plasma BNP level were significantly higher in the PAF group than in the non-PAF group. Multivariate logistic regression analysis demonstrated that NIHSS score ≥8 (OR, 4.22; 95% CI, 1.38-12.88, P = 0.011), left atrial size ≥3.8cm (OR, 4.8; 95% CI, 1.65-13.66, P = 0.004), mitral valvular disease (OR, 7.5; 95% CI, 2.17-25.90, P = 0.002), and plasma BNP level ≥144 pg/ml (OR, 12.8; 95% CI, 4.12-40.00, P = 0.0213) were independent factors associated with PAF. We developed a risk score from these variables (total score 0 to 5): NIHSS score ≥8 (1 point); left atrial size ≥3.8cm (1 point); mitral valvular disease (1 point); plasma BNP level ≥144 pg/ml (2 points). The frequency of PAF was 0% (0/51) in score 0, 4% (3/75) in score 1, 14% (4/33) in score 2, 26% (8/32) in score 3, 50% (7/14) in score 4 and 100% (10/10) in score 5, respectively. **Conclusions:** Our risk score can predict the presence of PAF during hospitalization in acute ischemic stroke.

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W P158

Secular Trends in Ischemic Stroke Intravenous Thombolysis: 2000-2007

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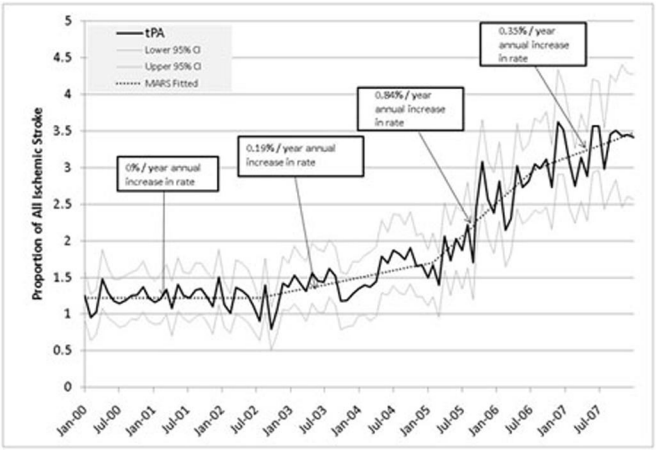
Introduction: Intravenous thrombolysis is used infrequently for stroke. Estimation of nation-wide changes in utilization over time can help inform the design and interpretation of interventions to improve tPA use. Our primary objective was to estimate the change in tPA use over time using a nationally representative sample. We also estimated the proportion of stroke patients who presented to hospitals that used tPA for stroke. **Methods:** The Nationwide Inpatient Sample is the largest all-payer database of U.S. acute care hospitalizations; it is designed to capture 20% of all inpatient stays. Ischemic stroke cases were identified using ICD-9 codes from the principal diagnosis. Use of tPA was identified using procedure code 99.10. The analysis was limited to cases admitted from the ED and to hospitals which any reported procedure codes (>90%). While accounting for the complex survey design, we estimated the national proportion of ischemic stroke patients receiving tPA for each month from 2000 to 2007. A model was constructed to fit the rates using multivariate adaptive regression splines (MARS) to evaluate for non-linear trends. Finally, hospitals were categorized as either treating any stroke patients with tPA for a year versus not. We used logistic regression to compare the odds of a stroke case being admitted to a non-treating hospital over the years queried. **Results:** The NIS contained 470842 stroke cases from 2000-2007 meeting the inclusion criteria corresponding to a population estimate of 2.3 million stroke hospitalizations. The monthly rate of tPA treatment ranged from 0.8% to 4.3%. The monthly rates along with 95% CI are presented in the figure. The best fitting MARS model provided slope transition points of Aug-02, Feb-05, and Aug-06 (R squared using cross validation 0.93). The annualized rates of increase for each period are depicted in the figure. The total proportion of stroke cases presenting to hospitals using stroke tPA was 59.7% in 2000 versus 75.4% 2007 (OR: 2.1 [95% CI 1.6-2.7]). **Conclusions:** The use of tPA has increased substantially from 2000 to 2007 in U.S. hospitals. The rate of increase in tPA use has not been stable over time, with several apparent transitions within the upward trend. While some of this increase may be attributable to improved coding, the inclusion of a broad cross section of hospitals strongly suggests nationwide improvement in use.



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W P159

Post-Graduate Academic Neurovascular Fellowship for Advanced Practice Nurses and Physician Assistants Significantly Increases tPA Treatment Rates: Results from the First Graduating Class of the NET SMART Program

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Background: Standard academic training for acute care advanced practice nurses (APNs) and physician assistants (PAs) has evolved into a "generalist-hospitalist" model that includes less than 30 minutes didactic content on stroke, while APNs credentialed in primary care receive no content on stroke diagnosis and treatment. **Methods:** We developed and implemented a first-of-its-kind, post-graduate, federally-funded neurovascular fellowship program for APNs and PAs that utilizes a hybrid internet-based didactic/clinical training approach in partnership with vascular neurologists across the U.S. All program content is evidence-based, updated regularly, and externally vetted by expert vascular neurologists to ensure accuracy and relevancy; learning materials are accessible via the internet 24/7/365. Fellows must pass written exams, and vascular neurologist overseen clinical skills testing to complete each section of the program, as well as a final on-site clinical validation session to ensure mastery of program content and skills prior to graduation. The primary aim of the NET SMART program is to increase the early identification and treatment of acute stroke patients, with outcomes measured during and after program completion. **Results:** The first graduating class consisted of 18 (17 APNs; 1 PA) fellows, representing 12 US states. Employing practice sites were 28% university-affiliated comprehensive stroke centers (CSC); 5% university-affiliated primary stroke centers (PSC), 39% community hospital CSC, and 28% community hospital PSC; 94% of graduates worked at a certified or state-designated stroke center with 17% of these programs receiving their designation while the graduate was enrolled. Baseline tPA treatment rates on entry into the fellowship averaged 3.3%, and increased over a period of 1.4 years on average to 11.6% at the time of program completion (paired $t=9.34$; mean difference=8.3, 95%CI=6.4-10.2; $P<.001$) without a significant increase in acute stroke patient admissions and an average sICH rate of 4.4% (range 2%-6.25%). 100% of sponsoring vascular neurologists rated themselves as confident in their graduates' ability to appropriately select candidates for reperfusion therapy. **Conclusions:** APN/PA completion of the NET SMART fellowship is associated with a safe and significant increase in tPA treatment across a variety of stroke center settings. Use of this peer-reviewed educational model builds confidence in the use of mid-level providers to deliver safe reperfusion therapy, while providing standardized, accessible evidence-based education that retains APN/PA resources within their original practice settings.

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W P160

Engaging Clinicians, Patients and Family Members in the Development of Decision Support for Hyperacute Stroke

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Background: Decision support tools (DSTs) are warranted to expedite assessment of eligibility for thrombolysis and (where appropriate) communication of risks/benefits to patients/families. Based on findings of an interview study, relevant research literature, an international survey of available examples and a locally designed decision analytic model we designed draft paper-based DSTs that expressed short-term outcomes (symptomatic intracerebral haemorrhage, death, independence/dependence at 6-months) and long-term outcomes (QALYs; life expectancy - overall and expected time in an independent and dependent state; and 5-year survival), with and without thrombolysis, as a function of patient characteristics (age, stroke severity, onset to treatment time, systolic BP). Objectives: To obtain feedback from (i) clinicians on DSTs to expedite eligibility decision making for thrombolytic treatment (structured look-up tables and tables of decisions rules for different levels of benefit from thrombolysis), risk presentation (bar graphs, pictograms and flowchart diagrams), and communication of risks/benefits to patients/families; and (ii) patients/families on risk communication tools (bar graphs, pictograms and flowchart diagrams). **Methods:** DSTs were presented to 12 stroke clinicians (7 stroke physicians, 5 stroke nurses) and 15 patients/families (8 patients, 7 family members) within interactive group workshops. We elicited their views and preferences on the form and content of draft DSTs, including their perceived value during the hyperacute stroke phase. **Results:** Clinicians were generally supportive of presenting short-term outcomes to patients/families, although views on the most effective format to achieve this did not reach consensus. Mixed views were reported on the utility of long-term outcomes for supporting eligibility decisions. The volume of material prompted clinicians to suggest the development of a computerised version of the DSTs. The challenge of integrating the DSTs within existing care pathways was also highlighted by clinicians. Patients/families expressed negative reactions to the presentation of information on average life expectancy, and preferred the balanced presentation of 'short-term' risks and benefits using pictograms or clustered bar graphs (used within verbal presentation by trusted clinicians). **Conclusions:** Computerised DSTs are likely to be the most efficacious format for supporting clinical decision-making within the hyperacute period of stroke. Short-term outcomes using pictograms or clustered bar graphs (showing natural frequencies) are feasible options for the balanced presentation of risks/benefits of thrombolytic treatment to patients and families.

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W P161

Introduction of Enhanced Prehospital Stroke Tool Improves Delivery of Acute Stroke Care

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Introduction: Participation by emergency medical services (EMS) plays a crucial role in achieving excellent acute stroke care. In order to raise the level of acute stroke recognition, we have moved from the concept of a simple scale to something more complex, incorporating education and participation in our hospital's stroke program. **Methods:** For this study we have worked with a single EMS group over a 12 month period, providing them with a stroke assessment tool containing an abbreviated National Institute of Health Stroke Scale (NIHSS), time of onset and assessment, glucose, Coumadin use, epilepsy and surgical and trauma history. EMS obtained NIHSS certification, attended scheduled educational programs, stroke committee and Joint Commission meetings, community presentations, and helped develop the hospital's stroke DVD. The Emergency Trauma Center (ETC) was included in this program and asked to respond positively to calls from EMS reporting their assessment tool results. We tracked: 1. Percentage of patients with acute stroke who received intravenous (IV) or intrarterial (IA) recombinant tissue plasminogen activator (rt-PA) 2. Symptom to drug time 3. Door to CT time 4. Door to drug time. NIHSS results presented by EMS were compared to results obtained by the neurologist seeing the patient acutely. **Results:** 101 patients reported to the ETC with possible acute stroke. 50% of these patients were determined to be mimics, a higher figure than usually reported, suggesting that EMS "erred" on the side of inclusion. 1. 20% of eligible patients were treated with IV or IA rt-PA, nearly double the year before and among the highest figure in the country. 2. Symptom to drug time was 150 minutes. 3. Door to CT time averaged 15.5 minutes 4. Door to drug time was 67.6 minutes. The abbreviated NIHSS was very close to the full NIHSS obtained by the neurologist, though some patients improved or worsened once they arrived in the ETC. **Conclusion:** We have demonstrated that alliance with EMS, through the use of a stroke assessment tool, recognized by the ETC, educational programs explaining the tool and stroke care standards and participation by EMS in all aspects of our Stroke Center programs can increase rt-PA administration and improve time to evaluation and treatment. Other benefits such as improved communication and respect between EMS and ETC cannot be easily measured, but certainly occurred to the delight of all who participated.

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W P162

Hospital Pre-notification of Stroke Patients by Emergency Medical Services Improves Stroke Time Targets

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Introduction: Pre-arrival notification to hospitals by emergency medical services of patients with suspected stroke is recommended to reduce delays in time-dependent therapies. We

hypothesized that hospital pre-notification would reduce stroke time targets recommended by the National Institute of Neurological Disorders and Stroke (NINDS). **Methods:** We used the Robert Wood Johnson University Hospital (RWJUH) Brain Attack Database, which includes demographic and clinical data on all emergency department (ED) patients alerted to the stroke team as a Brain Attack between January 1, 2009 and June 30, 2010. Outcome variables included the time from door to stroke team arrival, CT completion, CT interpretation, EKG, laboratory results, treatment decision, and intravenous (IV) rt-PA administration. The primary independent variable was Brain Attack activation before ED arrival (pre-hospital) versus on or after ED arrival (no pre-hospital). Analysis of covariance was used with patient predictors (age, sex, initial NIHSS) as covariates in addition to the one of interest (pre-notification vs. no pre-notification). Statistical significance was defined as a p-value ≤ 0.05. **Results:** There were 231 patients (116 pre-notification, 115 no pre-notification) alerted as a Brain Attack from the RWJUH ED within the study period. Patients with pre-hospital notification were older, had more severe strokes, and were treated with IV rt-PA twice as often (Table 1). Pre-notification of a Brain Attack resulted in a significant reduction in all studied stroke time targets, except the door to treatment decision time and rt-PA administration (Table 2). **Conclusions:** Pre-hospital notification of suspected stroke patients reduces time to stroke team arrival, CT scan completion, and CT scan interpretation. IV thrombolysis occurred twice as often in the pre-notification group, however, there was no difference in door to rt-PA administration time.

Table 1. Patient Characteristics

	Pre-notification N=116	No pre-notification N=115	p-value
Age (mean±SD)	69.5±11.1	61.5±17.1	0.0002
Female	61 (53%)	55 (47%)	0.469
Arrival			
EMS	115 (62%)	71 (38%)	<0.0001
Walk-In	1 (2%)	44 (98%)	
NIHSS (mean±SD)	11.1±7.6	6.1±6.9	<0.0001
IV rt-PA	32 (28%)	17 (15%)	0.024

Table 2. Outcome variables

Variable	Time (minutes) Mean±SD			p-value
	Pre-notification N=116	No pre-notification N=115	Absolute Difference (95% CI)	
Door to Stroke Team Arrival	-2.5±7.6	16.1±15.2	18.6 (15.5-21.8)	<0.0001
Door to ECG	5.8±5.2	14.3±23.3	8.5 (4.1-13.0)	0.0002
Door to CT completion	25.5±11.4	38.4±17.8	12.9 (9.0-16.8)	<0.0001
Door to CT interpretation	38.2±17.3	50.4±20.2	12.2 (7.3-17.1)	<0.0001
Door to Lab Results	45.2±16.4	54.1±16.7	8.9 (4.5-13.2)	<0.0001
Door to Decision	52.6±31.4	47.2±15.4	-5.4 (-21.7-10.9)	0.422
Door to rt-PA administration	65.8±26.9	62.0±17.6	-3.8 (-18.4-10.8)	0.554

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W P163

Paramedics and Prehospital Stroke Research Trials: Effective Education Strategies

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Background: In clinical trials, initiation of experimental therapies for time urgent neuro-emergency conditions like stroke is increasingly occuring in the prehospital EMS system, allowing delivery within the first minutes after onset. However, paramedic exposure to conducting research has been limited. In the Field Administration of Sroke Therapy - Magnesium (FAST-MAG) study, the first phase 3 clinical trial of prehospital neuroprotective therapy for stroke, strategies have been devised to address paramedic perceptions of barriers. **Methods:** A survey was performed of 61 paramedics in Los Angeles County by nurse coordinators and research assistants from the FAST-MAG study, complemented by direct observations and interactions with medics by 12 FAST-MAG nurse-coordinators responsible for 228 fire stations. **Results:** Leading paramedic concerns include 1) avoiding delay in transport times, 2) cell phone connection difficulties, 3) calls to enrolling lines that do not result in patient enrollments (screen failures), and 4) need for explicit informed research consent, rather than implied consent. To minimize potential delays, FAST-MAG procedures were designed to occur simultaneously with routine care, such that the paramedics call an enrolling line and an on-call physician elicits the consent. By tracking the times from paramedic arrival on scene to ED arrival, study staff demonstrated that study procedures are not increasing time spent in the field over historical norms or national averages. Establishing a proper phone connection can be hampered by variable cell phone reception and unanswered calls. We have iteratively improved our response system, including implementing a simultaneous ring, voice over internet phone system. In addition, improved cell tower coverage has reduced dropped calls. Paramedic expectations are now framed by educating that 50-60% of patients meeting paramedic screening criteria will not meet the complete study entry criteria. Additionally, several exclusion criteria have been migrated to the paramedic stage from the MD stage, reducing screen failures and increasing paramedic autonomy. Federal regulations require explicit informed consent and determination of the competency of the patient to provide consent, or if appropriate, the availability of a proper legally authorized representative. Repeated education has highlighted these concepts but paramedics continue to have questions regarding the consent process. Solutions: Paramedics are knowledgeable professionals who can perform prehospital research procedures reliably and efficiently. Knowledge of paramedic concerns permits refinements in study design and training. The addition of research principles in paramedic education curricula would provide basic knowledge about research, promote paramedic enthusiasm to conduct research and encourage initiation of their own research.

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W P164

The Impact of Ambulance "Ramp Time" Delays on Acute Stroke Pathways

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Background: Over recent years rapid care pathways implemented in the pre-hospital and Emergency Department (ED) settings have been successful in reducing times to evaluation and treatment for acute stroke patients. However, over a similar period of time hospitals in Australia have experienced increased ED overcrowding and increased patient presentations by ambulance. This has resulted in delays transferring the patient after triage from an ambulance stretcher to an ED cubicle ("Ramp Time"). Patients remaining on ambulance stretchers in the ED (including stroke patients) cannot be appropriately assessed or investigated. Little is known about the impact of "Ramp Time" delays on rapid care pathways for stroke patients. We hypothesised that among stroke patients presenting by ambulance: ● Stroke patients experiencing "Ramp Time" delays could be identified, ● Demographic and clinical factors associated with prolonged "Ramp Times" (triage to ED cubicle time >15 minutes) could be identified. Methods From January to June in 2010, all ambulance-transported patients presenting to one of three hospital emergency departments with a final ED diagnosis of stroke or TIA were assessed. Hospital medical records were retrospectively analysed. Results 527 patients were included in the study. (351 Stroke and 176 TIA). Around half of patients (46%, n=243) experienced some "Ramp Time" delays with the majority of delayed cases (n=172) remaining on the ambulance stretcher. Median Ramp Time delay was: 17 minutes (IQ range 6 - 46); maximum delay was 241 minutes. An unexpected finding was that a number of ambulance transported stroke patients (n= 76) were off-loaded after triage into a waiting room normally occupied by walk in patients. These patients experienced longer median delay times of 37 minutes (IQ range 13-102). No demographic or clinical variables were associated with prolonged "Ramp Time" delays. Patients with a triage assessed urgent priority code (1 or 2) were associated with shorter delay times (p=<0.001). **Conclusions:** "Ramp Time" delays were experienced by half of stroke patients including those who presented rapidly following symptom onset and those recognized as stroke at triage. No clinical variables other than an urgent triage code reduced the likelihood of prolonged delays. Other factors like ED overcrowding may contribute to delays. Ambulance "Ramp Time" delays in the ED may restrict the timely application of rapid care pathways for many stroke patients and requires further investigation.

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W P165

The Analysis Of The Influence Of Demographic And Logistic Factors On Effectiveness And Safety Of Treatment With Rt-pa The Patients With Acute Ischemic Stroke In Agricultural Region In South-east Poland.

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Material and Methods: Between September 2006 and December 2009 in the stroke center in Sandomierz 1034 patients with acute ischemic stroke (ais) was treated, including 143 patients (14,31% of all patients with ais) treated i.v. rt-PA and 5 patients treated with combined therapy i.v. and i.a. (aged 42-88, mean 69,14±9,73 ; 83 men (56,08%) , 65 women (43,92%); time window 0-6 hours for the i.v. and combined therapy). We analysed status of the patients in the moment of admission, after 1 and 3 months after symptoms onset according to National Institutes of Health Stroke Scale (NIHSS) and modified Rankin Score (mRS). We analysed also the influence of demographic and logistic factors on effectiveness and safety of treatment. **Results:** The average time from the onset of the disease to the beginning of the treatment was 150,13±46,06 (42,5-interquartile range) minutes. In the moment of admission the average NIHSS was 12,20±4,86 (8,0) and average mRS was - 4,15±0,81 (2,0). After 1 month mean NIHSS and mRS were respectively: 4,40±5,12 (5,0); and 2,46±1,98 (3,00); and after 3 months: 4,00±9,46 (5,00); 2,25±2,11 (3,5). No correlation between onset- to - needle time, and patients' status at 30th and 90th day was found. We stated statistically significant correlation between distance from place of onset to our center and patients status at 30th day (p<0,017). Also there were statistically significant difference between clinical status of patients

(using mRS) from urban and country populations (p<0,013). **Conclusions:** Place of living(town and country) and distance from place of symptoms onset to hospital determines effectiveness of treatment, evaluated after 30 days using mRS. There is still requirement for improving organisation of prehospital procedures in agricultural regions.

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W P166

Extension Of The IV tPA Window Does Not Impact Performance Of A Resident-Based Acute Stroke Protocol

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Background: Extending the IV tPA window to 4.5 hours might lead to a lack of urgency in the treatment of patients with acute ischemic stroke, particularly using a resident-based acute stroke protocol. In November 2008, we instituted an extended 3-4.5 hour IV tPA stroke protocol. We hypothesized that door-to-needle (DTN) times might be longer: (1) in the 0-3 hr window and (2) within the extended window owing to newer exclusion criteria and the reduction of time pressure after the change in our protocol. **Methods:** Since 2004, we have utilized a resident-based stroke protocol placing neurology residents in decision-making roles for tPA administration. Patient demographics, NIHSS, and quality control metrics including DTN times, symptomatic intracerebral hemorrhage (sICH) rate, and discharge locations were prospectively collected. In November 2008, we adopted the ECASS III trial-based IV tPA extended treatment protocol. To test how the extended window may affect safety and efficiency, we assessed DTN times, sICH, and discharge outcomes in two comparisons: (1) 0-3 hr metrics pre-extended window (2004-2007) vs. 0-3 hr metrics post-extended window (2008-2010) ; and (2) 0-3 hr metrics vs. 3-4.5 hr metrics since initiation of extended tPA window. T- or Wilcoxon Rank Sum Tests were used for parametric and non-parametric continuous data, respectively. Chi-squared or Fisher's Exact Tests were used for parametric and non-parametric binary data, respectively. **Results:** From 2004-2007, 113 patients were treated with IV tPA. Since initiation of the extended tPA window (11/08 to 7/10), 94 patients were treated with IV tPA: 78 patients < 3 hours, 16 patients between 3-4.5 hours. Comparing the pre-extended window metrics (2004-2007) to post-extended window metrics (2008-2010), there was no significant difference between mean DTN times (60 vs. 61 minutes, p=0.78) or rate of sICH (3.5% vs. 2.6%, p=0.70). "Favorable" discharge location (home or inpatient rehabilitation) was 76% pre-extended window vs. 77% post-extended window, p=0.90; "unfavorable" discharge (nursing home or death prior to discharge) and 24% pre vs. 23% post, p=0.90. Since initiation of the extended window in 2008, there was no difference in median DTN times between the 0-3 and 3-4.5 hr windows (60 vs. 66 minutes, p=0.15), nor did rates of sICH differ (2.6% vs. 0%, p=1.0). Furthermore, discharge outcomes were similar: 77% for 0-3 hrs vs. 69% for 3-4.5 hours (p=0.53) for favorable discharge location and 23% vs. 31% (p=0.53) for unfavorable discharge location. **Conclusions:** Our resident-based stroke protocol provided efficient and safe delivery of IV tPA to acute stroke patients up to 4.5 hours. The protocol did not demonstrate "relaxed" DTN times due to a longer window in either the 0-3 or the 3-4.5 hour cohorts.

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W P167

CT Angiography Based Protocol Does Not Delay Thrombolysis In Acute Ischemic Stroke

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Introduction: Despite information provided by CT Angiography regarding site of occlusion, extent of at risk tissue, thrombus burden and collateral status, its use is not uniformly accepted. Lack of additional utility over NCCT in decision making and delay in door to needle time are arguments used against the use of a CTA based protocol in acute ischemic stroke management. We compare interval times during a CTA based acute ischemic stroke protocol with an earlier non-CTA based protocol at our center. **Methods:** We reviewed our experience with stroke thrombolysis in a university hospital in Calgary, Canada from April 1996 to December 2009. 850 patients treated with thrombolytic therapy (IV and IV/ IA TPA) during this period with complete data were included in the analysis. Time to treatment was divided into the following interval times: onset to door, door to needle and onset to needle.Patients were categorised into three groups: Group 1(April 1996 - Dec 2002) (Noncontrast CT Scan based thrombolysis) n=297, Group 2 (Jan 2004- Dec 2009) (CT Angiography based thrombolysis).The period from Jan to Dec 2003 (n=49) was considered a washout period and not included in the analysis as we gradually integrated the CTA protocol into standard care that year.Interval times were compared between the 2 groups using non-parametric test of medians and by multiple linear regression. **Results:** 801 patients were included in the final analyses. Median onset to door times in group 1 and Group 2 were 55 minutes (IQR 48),and 61 minutes (IQR 57) respectively, (p=0.019). Median door to needle times in group 1 [67 minutes(IQR 43)], and group 2 [62.5 minutes (IQR 52)] respectively (p=0.519), Median Onset to needle times in Group 1 (139 minutes (IQR 73)] and Group 2 (141.5 min(IQR109.5) (p=0.468). In multivariable analysis, age and baseline INR influenced onset to needle times and door to needle times in both the groups Older age resulted in marginally shorter times and elevated INR resulted in longer onset to needle times, presumedly due to the wait for confirmed laboratory measured INR. **Conclusions:** CTA based thrombolytic approach for acute ischemic stroke does not prolong door to needle time in routine clinical practice.

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W P168

A Four-Year Retrospective Evaluation of Blood Pressure Management Before IV Thrombolysis

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Delays in intravenous (IV) t-PA administration can prolong ischemia and worsen outcomes during stroke. Severe uncontrolled hypertension is a contraindication to tPA and adequate blood pressure (BP) reduction is necessary. Stroke guidelines offer limited therapeutic strategies. Hypothesis: During the acute treatment of ischemic stroke: 1) severe hypertension can significantly contribute to delays in the initiation of IV t-PA administration, and 2) the repetitive and/or aggressive administration of IV antihypertensive agents can cause potentially significant hypotensive excursions during or immediately after the IV t-PA infusion. **Methods:** Electronic medical records from the Medical University of South Carolina were retrospectively examined to identify ischemic stroke patients presenting from May 2006 to May 2010. The records of patients with a diagnosis of ischemic stroke were used to determine the incidence of severe hypertension requiring acute BP reduction before IV t-PA administration. BP reduction practices were described and evaluated in terms of therapy used, efficacy (time to achieve targeted BP) and safety (hypotensive excursions). **Results:** During the evaluation period, 93 patients received IV t-PA and 17 (18%) of them required acute BP reduction. Of these patients, 11 (65%) received IV bolus labetalol first line. Eight patients (47%) required the continuous infusion of nicardipine. Patients required a median number of either 3 separate doses or titration adjustments [range: 1-9] of any IV antihypertensive agents to achieve and/or maintain the targeted BP. Seven (47%) patients required more than one antihypertensive agent. Following the initial CT scan, the average time delay between the first IV antihypertensive agent given and the administration of IV t-PA after achieving the targeted BP was 27 minutes [range: 5-55]. Although no patient experienced clinically significant hypotension requiring treatment, potentially significant hypotensive excursions (i.e. systolic BP < 130 mm Hg) were identified in 3 (18%) patients during the first 3 hours following the initial IV tPA bolus. Patients who received the continuous administration of nicardipine often required a dose reduction during the acute management. **Conclusions:** The incidence of acute BP reduction prior to IV t-PA administration is relatively low. However, severe hypertension often requires polypharmacy and can significantly contribute to delays in the initiation of IV t-PA administration. We propose that specific antihypertensive regimens should be studied in the setting of acute ischemic stroke to optimize rapid BP reduction prior to IV t-PA administration while preventing potentially significant hypotensive excursions.

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W P169

Female Sex Is Associated With Unfavorable Outcomes Following Low-dose Intravenous Rt-pa Therapy: The Samurai Rt-pa Registry

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Background: Sex differences in the effect of intravenous (IV) rt-PA therapy for ischemic stroke are controversial. The aim of this study was to elucidate the sex differences in the stroke outcome after low-dose IV rt-PA (0.6mg/kg alteplase) therapy. **Methods:** A retrospective, multicenter, observational study was conducted to clarify the practical conditions of low-dose IV rt-PA therapy in 10 stroke centers in Japan (SAMURAI rt-PA Registry: Stroke 2009;40:3591-3595). Studied were consecutive patients with a premorbid modified Rankin Scale (mRS) ≤ 2 who were treated with IV rt-PA from October 2005 through July 2008. We assessed baseline data, including sex, age, comorbidities (hypertension, diabetes, hyperlipidemia, and atrial fibrillation), time from onset to treatment, NIH stroke scale (NIHSS) score, Alberta Stroke Programme Early CT score (ASPECTS), and presence of internal carotid artery (ICA) occlusion identified on MR angiography or carotid ultrasound. Outcomes were a favorable outcome defined as an mRS score 0-2 and death at 3 months, as well as symptomatic intracerebral hemorrhage (sICH) within 36 hours: i.e. a parenchymal ICH associated with neurological deterioration corresponding to an increase of ≥4 point from the baseline NIHSS score. **Results:** Of 554 patients (358 men, 71±11 years) who were studied, 282 (50.9%) had a favorable outcome and 35 (6.3%) died at 3 months. Symptomatic ICH was identified in 16 patients (2.9%). Women were older (mean age 75±11 vs. 69±12 years, P<0.001), more frequently had atrial fibrillation (50.8 vs. 37.5%, p=0.004), and had higher median initial NIH Stroke Scale score (13 vs. 12, p=0.009) than men. There were no significant sex differences in hypertension, diabetes, hyperlipidemia, time from onset to treatment, ASPECTS, and ICA occlusion. Women had less favorable outcome (41.3% vs. 56.2%, p=0.001) than men. There

were no significant sex differences in mortality (8.7% vs. 5.0%, p=0.102) and sICH (3.1% vs. 2.8%, p=0.999). After multivariate analysis using the stepwise backward selection procedure with age and other baseline data, women were inversely related to favorable functional outcome at 3 months (odds ratio 0.63, 95%CI 0.40-0.99, p=0.044). **Conclusion:** Initial stroke symptoms were severer in female patients who were scheduled to receive intravenous rt-PA therapy than in male ones. After adjustment for the initial severity and other baseline features, women were independently related to unfavorable stroke outcome 3 months after rt-PA.

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W P170

Low-dose Intravenous rt-PA Therapy for Acute Stroke Patients without intracranial artery occlusion

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Background and Purpose: Information about cerebral artery occlusive lesions is not taken into account for the CT-based patient selection of intravenous rt-PA therapy. The safety and efficacy of intravenous rt-PA for patients without cerebral artery occlusion (CAO) have not been elucidated. This study was aimed to clarify characteristics and outcomes in stroke patients without CAO who were treated with 0.6 mg/kg alteplase from the SAMURAI rt-PA registry, a retrospective, multicenter, observational study. **Methods:** Studied were 416 patients with premorbid modified Rankin Scale (mRS) of 0-1 who underwent MRA to identify CAO before rt-PA therapy. Endpoint events were intracranial hemorrhage (ICH) within the initial 36 hours, and favorable (modified Rankin Scale [mRS] 0-1) and unfavorable (mRS 4-6) outcomes, and mortality at 3 months. **Results:** CAO was documented in 327 patients (78.6%, 211 men, 71.9±11.3 years old), but not in 89 patients (21.4%, 65 men, 67.0±11.5 years old). As compared to patients with CAO, those without CAO were younger (p<0.001) and more frequently diabetic (27.0% vs. 16.8%, p=0.031), and had less commonly atrial fibrillation (13.5% vs. 48.3%, P<0.001), higher initial systolic (154.2±15.4 mmHg vs. 149.4±19.4 mmHg, p=0.030) and diastolic blood pressure values (85.7±13.4 mmHg vs. 81.0±14.7 mmHg, p=0.006), higher ASPECTS on DWI (median 9 vs. 8, P<0.001), lower initial NIHSS score (median 7 vs. 14, P<0.001), more commonly lacunar infarction (19.1% vs. 1.5%, P<0.001) but less frequently cardioembolic stroke (30.3% vs. 68.5%, p=0.007). With regards to endpoint events, patients without CAO had less frequently ICH within the initial 36 hours (11.2% vs. 22.9%, p=0.015), more frequently favorable outcome (56.2% vs. 33.6%, P<0.001), less commonly unfavorable outcome (16.9% vs. 43.3%, P<0.001), and no mortality at 3 months (vs. 7.7%, P<0.001) than those without CAO. After adjustment with various baseline features, absence of CAO was no longer associated with favorable outcome(OR 1.37, 95% CI 0.77-2.41), unfavorable outcome (0.58, 0.28-1.12), and ICH within the initial 36 hours (0.67, 0.30-1.37). Among patients without CAO, higher initial NIHSS score (OR 1.08, 95% CI 1.00-1.17 per 1-score increase, p=0.048) were associated with 3-month unfavorable outcome after multivariate adjustment with underlying features. **Conclusions:** Although 3-month outcomes of stroke patients without CAO after rt-PA were better than those of patients with, these associations became insignificant after adjustment with baseline features. The initial neurological severity was associated with 3-months outcome in patients without CAO.

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W P171

Re-exacerbation Within 24 Hours After T-pa Infusion Was Associated With Small-vessel Disease

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Background and Purpose: We sometimes experience re-exacerbation within 24 hours after IV t-PA. The purpose of this study was to examine the characteristics of re-exacerbation patients within 24 hours after t-PA infusion. **Methods:** Consecutive stroke patients with t-PA within 3 hours of onset between October 2005 and March 2010 were studied. After t-PA infusion, we evaluated NIHSS in every 15 minutes for first one hour, every 30 minutes until six hours, and every one hour until 24 hours. We divided the patients into four groups, Improvement(Im) group; improved in NIHSS≥4 points, Unchanged(Un) group; exacerbated or improved in NIHSS<4 points, Exacerbation(Ex) group; exacerbated in NIHSS≥4 points, and, Re-exacerbation(Re-Ex) group; after t-PA infusion improvement of NIHSS≥4 points, however, the neurological symptom was re-exacerbated in NIHSS≥4 points. We compared age, sex, stroke subtype, risk factors, right to left shunt (RLS), use of antiplatelet and anticoagulant medication, BMI, initial NIHSS, time from onset to t-PA infusion, laboratory data on admission, and hemorrhagic infarction on MRI T2* amng four groups. **Results:** 222 patients (male 135 patients, median 76 years old) were enrolled into the present study. Re-Ex group had 16(7%) patients, Ex group had 23(10%) patients, Im group had 99(45%) patients, and Un group had 84(38%) patients. There was no difference in age, male, risk factor, RLS, initial NIHSS, antiplatelet and anticoagulant drug use, BMI, initial NIHSS, and time to t-PA, and laboratory data on admission among four groups. However, Re-Ex group most frequently had small-vessel disease and hemorrhagic cerebral infarction among 4 groups (44% and 25% for Re-Ex group, 9% and 22% for Ex group, 5% and 6% for Im group, and 17% and 14% for Un group, P<0.001 and P=0.041). Multivariate logistic regression analysis identified small-vessel disease was an only independent factor associated with re-exacerbation within 24 hours after t-PA infusion (OR 12.5, 95% CI 2.57-61.14, P=0.018). **Conclusion:** Re-exacerbation within 24 hours after t-PA infusion was associated with small-vessel disease.

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W P172

Safety of a 'Drip and Ship' Intravenous Thrombolysis Protocol for Patients with Acute Ischemic Stroke

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Introduction: The 'drip and ship' approach for intravenous thrombolysis (IVT) is becoming the standard of care for patients with acute ischemic stroke (AIS) in communities without direct access to a stroke specialist. We aimed to demonstrate the safety of our "drip and ship' IVT protocol in terms of symptomatic intracerebral hemorrhage (sICH). **Methods:** Retrospective study of consecutive patients with AIS treated with IVT from January 2003 to June 2010. Information on patients' demographics, clinical characteristics, neuroimaging, sICH, and outcome was obtained from our stroke registry. A group of patients were treated with IVT by an emergency physician in phone consultation with a board-certified vascular neurologist (BCVN) at one of our three stroke network affiliated hospitals (SNAH). These patients were subsequently transferred to our JCAHO-certified primary stroke center (CPSC) after completion of IVT ('drip and ship' protocol). The other patients were treated directly by a BCVN at CPSC. The study received IRB approval. **Results:** We studied 147 patients treated with IVT. Of them, 21 patients received IVT at SNAH and 126 patients were treated at CPSC. There were no significant differences between the two groups in mean age (57 versus 60 years) and mean stroke symptom onset-to-needle time (159 versus 144 minutes). The patients who received IVT at SNAH had a lower median NIHSS score on admission compared to the patients treated at CPSC (4.5 versus 11, p < 0.001). Among patients treated at SNAH, two patients had sICH. This number was not significantly higher among patients treated at CPSC (6 out of 126). **Conclusions:** This study suggests that our 'drip and ship' protocol for IVT is safe. The patients treated with the 'drip and ship' approach had lower NIHSS scores on admission as compared to the patients treated at CPSC. Further research is warranted.

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W P173

IV rt-PA Administration in the Expanded Time Window (3-4.5 hours) in Practice: Utilization and Outcomes

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Introduction: A randomized double-blind trial (ECASS III) demonstrated that intravenous recombinant tissue plasminogen activator (rt-PA) administered between 3 and 4.5 hours after the onset of symptoms significantly improved clinical outcomes in patients with acute ischemic stroke. In May 2009, the American Stroke Association guidelines recommended the use of IV rt-PA for patients presenting within 3 and 4.5 hours after symptom onset. **Objective:** To determine the rate of patients treated with IV rt-PA within the 3 and 4.5 hour time window and associated outcomes in general practice. **Methods:** We retrospectively reviewed all patients who were treated with IV rt-PA at two comprehensive stroke centers from September 2008 to July 2010 and identified a total of 98 patients. In addition, we identified patients who arrived to the ED of those centers within 2.5 to 4 hrs of symptom onset between January 2007 and June 2010 and received only endovascular treatment. We compared the rates of favorable outcome (determined by using modified Rankin scale 0-2 at discharge and 3-month follow up), and NIHSS score improvement by ≥ 4 points or 0 at discharge among patients treated with IV rt-PA within 3-4.5 hrs with those who received IV rt-PA within 0-3 hrs, and subsequently with patients presenting at similar time window treated only with endovascular treatment. **Result:** The 98 IV rt-PA treated patients had mean admission NIHSS score +SD: 11.4±6.6, mean age+SD: 66±17 and 47 (48%) were women. 14% of patients received IV rt-PA within 3-4.5 hours. Baseline characteristics were not different between both comparison groups. Favorable clinical outcome at discharge (50% vs. 56%, p=0.77), 3 months (64% vs. 64%, p=1.0), and NIHSS score improvement (43% vs. 58%, p=0.38) were not different between those treated within 3-4.5 and 0-3 hrs time windows. There appeared to be a non-significantly higher rate of favorable outcomes at discharge (25% vs. 50%, p=0.24), and at 3 months (42% vs. 64%, p=0.43) among patients treated with IV rt-PA within 3-4.5 hrs compared with those treated with primary endovascular treatment. **Conclusion:** An additional 14% of patients received IV rt-PA because of treatment window expansion from 3 to 4.5 hours with comparable outcomes to those treated within 3 hours after symptom onset. The shift of those patients from primary endovascular treatment does not appear to adversely affect patient outcome.

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W P174

Frequency of Complete Resolution of Motor Symptoms among Stroke Patients Evaluated within 2 Hours of Symptom Onset

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Background: Many patients found to have stroke signs during paramedic evaluation in the field will have complete and rapid resolution of those signs. There may be clinical factors which identify whether a patient is more likely to have clinical resolution (CR) on subsequent examination. Previous studies have evaluated the proportion of patients with cerebral ischemia and hemorrhage with complete resolution of signs but have not focused on patients evaluated in the field in the first hours after symptom onset. **Objective:** To determine the frequency and predictors of rapid CR of motor signs of unilateral weakness among stroke patients evaluated in the field using the Los Angeles Prehospital Stroke Screen (LAPSS) which incorporates the Los Angeles Motor Score (LAMS), a 0-5 scale quantifying unilateral weakness of the face, arm, and hand. **Methods:** The study population is comprised of consecutive subjects enrolled in the Field Administration of Stroke Therapy-Magnesium (FAST-MAG) clinical trial were evaluated in the field using the LAPSS within 2 hours of their last-known-well-time (LKWT) and randomized to receive intravenous Magnesium Sulfate or placebo. A second evaluation was performed by the FAST-MAG study nurse coordinator in the emergency department (ED). CR was defined using the definition of a follow-up ED evaluation LAMS score of 0 indicating no weakness. Clinical, demographic, and enrollment-related factors were compared in those with CR and those without. **Results:** A total of 1029 subjects were evaluated in the field using the LAMS an average of 45 minutes after LKWT. Median (range) of field LAMS 4 (1-5), and 131 (13%) experienced CR of motor weakness (LAMS=0) on the follow-up evaluation performed a median of 108 minutes following the field LAMS. A host of clinical factors were evaluated for an association with CR including age, gender, ethnicity, time to evaluation, blood pressure, medical history (hypertension, diabetes, dyslipidemia, atrial fibrillation, coronary artery disease, valvular heart disease) and results of initial imaging. The only variable which significantly predicted complete clinical resolution was absence of intracerebral hemorrhage on initial imaging. There were 240 cases (23%) with ICH on initial ED imaging of which only 2 (<1%) experienced CR, compared to 15% of the 789 with no evidence of ICH on initial imaging. **Conclusions:** Among patients with motor stroke signs <2 hours in duration from symptom onset evaluated in the field, approximately 13% will have complete resolution of motor weakness on subsequent evaluation in the ED. We were not able to find any predictors of CR which would be beneficial in the field. Those patients with resolution of motor symptoms in the first few hours are highly unlikely to have intracerebral hemorrhage. The FAST-MAG study will be able to evaluate whether treatment with Magnesium Sulfate affected rates of CR.

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W P175

Mri Based Tia Triage Study

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Rapid Diagnostic Evaluation of TIA Using a Clinical Decision Area Triage Approach Background The AHA scientific statement on the evaluation of TIA recommends an urgent evaluation including a brain MRI and neck vessel imaging within 24 hours after symptom onset. The purpose of this ongoing prospective study is to determine whether an ER-based triage system that performs acute evaluation, including brain MRI and neck vessel imaging within less than 24 hours, is feasible and associated with a low rate of early stroke. Methods In January 2010 we initiated a new triage protocol for suspected TIA patients at the Stanford Emergency Department (ED). Patients considered likely to have suffered a TIA are transferred to the Clinical Decision Area (CDA) which is a short term (<24 hours) observation unit where patients undergo brain MRI and neck vessel imaging, close cardiac and neurological monitoring and a consult from a stroke neurologist. If the CDA evaluation reveals an acute ischemic lesion on DWI, a symptomatic intracranial or extracranial stenosis or other unstable condition, the patient is admitted to the Stanford Stroke Service. Patients with a negative evaluation in the CDA are discharged and followed up in the outpatient TIA clinic. Patients are assessed for outcome events at 7, 30 and 90 days. Results Sixty seven suspected TIA patients were enrolled over 6 months. Sixty four (96%) arrived at the ED within 24 hrs of symptom onset. Sixty-two underwent DWI and 65 had neck vessel imaging. MRI was performed within 24 hrs of symptom onset in 48 patients (77%), and within 24 hrs of ED arrival in 55 patients (89%). Thirty seven patients had a final diagnosis of stroke (n=11) or TIA (n=26). In addition, 11 patients had a diagnosis of a possible TIA. Median ABCD2 score was 4 (IQR=3-4). An acute ischemic lesion on DWI was detected in 16 patients (24%) and a symptomatic vessel stenosis was present in 6%. Forty-six patients were transferred from the ER to the CDA. Nineteen patients (28%) were admitted to the Stroke Service (8 directly from the ED and 11 from the CDA). Forty eight patients were discharged home (35 from the CDA and 13 from the ED). Only one patient suffered a subsequent stroke; 30 day stroke rate was 0.014 (95% CI: 0.002-0.08). The patient with a subsequent stroke was discharged from CDA after normal initial evaluation [MRI, MRA, EKG] then experienced a minor stroke, NIHSS=1, seven days after discharge. **Conclusion:** Urgent TIA evaluation, including obtaining an MRI and vessel imaging within 24 hours, is feasible using an ED-based clinical observation unit. Preliminary data suggest this approach is associated with low stroke rates.

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W P176

TIA Patients' Arrival Time To The Emergency Department Within A Population: No Association With Symptom Severity, Duration, Or ABCDD Score

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Background: Ongoing trials are investigating the efficacy of early intervention after TIA in preventing subsequent ischemic events. Arrival patterns among TIA patients are of interest from both a public health and clinical trial perspective. Previously we reported that over time TIA patients within our population are arriving more quickly for emergency care. We sought to describe specific factors that impact emergency department (ED) arrival times in TIA. We hypothesized that greater symptom severity, longer symptom duration, and higher ABCDD score (a score used to predict risk of future stroke in TIA) would shorten arrival times in TIA patients within our large biracial population. **Methods:** Using ICD-9 codes 430-436, we ascertained and physician-verified all TIA events (symptom duration <24 hours) presenting to a local ED within our population of 1.3 million in 2005. Time of symptom onset and ED presentation, symptom duration, initial retrospective NIHSS score, description of clinical deficits, patient demographics, and medical history were recorded as documented in the medical record. The relationships between ED arrival time and symptom severity, symptom duration, and ABCDD score were analyzed with generalized estimating equations. **Results:** The total number of TIA events presenting to an ED in 2005 was 834. The mean age was 69, 42% were male, and 12% were black. Overall, 56% resolved prior to arrival. The percent with exact/estimated/unknown onset and arrival times was 57%, 32%, and 11%, respectively. Symptom duration was known or estimated in 829 events; duration was <10 minutes in 10%, 10-59 minutes in 30%, and at least 60 minutes in 61%. Initial NIHSS score was available for 704 events, with a median score of 1 (interquartile range: 0, 2). ABCDD score was known for 818 events; 22% had a score of 0-3, 50% had a score of 4-5, and 29% had a score of 6-7. There was no association between symptom severity, symptom duration, or ABCDD score and time to ED arrival. **Conclusion:** Contrary to our hypothesis, we found that within our population the time from symptom onset to ED arrival for TIA patients was not associated with duration or severity of symptoms, or with ABCDD score. As with ischemic stroke patients, documentation of symptom onset times remains problematic, with only half of the TIA events having exact times documented. Patients at highest risk for subsequent ischemic stroke do not appear to seek emergency care more quickly than patients at lower risk. Continued public health campaigns are needed to emphasize stroke risk factors and encourage quick action even if symptoms resolve.

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W P177

Abnormalities on CT Angiogram in patients presenting to the Emergency Department with Transient Ischemic Attack

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Introduction: Clinical scores to predict the stroke risk in patients with TIA do not incorporate imaging data, which could improve the prognostic accuracy. Evidence for the incidence of intracranial CT angiography (CTA) abnormalities and their prognostic significance in patients presenting with TIA are scant. **Methods:** We retrospectively indentified all patients with an emergency department (ED) discharge diagnosis of TIA by ICD-9 code (435) between 1/2009 - 3/3010, and who underwent CT angiography at time of evaluation. ED diagnosis of TIA was validated, and clinical and demographic data were abstracted from electronic medical records by a neurologist blinded to radiographic findings. Follow-up was evaluated up to 1 year after index event. Two neurointerventionalists, blinded to clinical data, reviewed and scored each CTA independently. Each reader located and viewed 10 pre-specified extracranial and 13 intracranial arterial segments per study. Degree of stenosis was categorized into none, mild (1-49%), severe (50-99%), or occluded. A third neuroradiologist adjudicated any differences. Dichotomous variables were compared using Chi squared test or Fisher's exact if appropriate. Multivariate logistic regression was used to identify predictors of CTA abnormalities, and to evaluate the association of CTA abnormalities with stroke outcome. **Results:** Of 99 patients with an ED discharge of TIA, 57 had undergone CTA and had validated TIAs. The mean age was 72 ±12 years, and 54% were women. Mean ABCD2 score was 4.5 ±1.6, with 60% having an ABCD2≥4. Seven patients (12%) had at least one intracranial vessel segment with severe stenosis, and 2 (4%) patients had intracranial occlusions. Seven patients (12%) had at least one extracranial vessel segment with severe stenosis. No extracranial occlusion was seen in this cohort. In 9 patients (16%), their severe stenoses or occlusions could account for their presenting symptoms. Three subjects (8%) had strokes within 1 year of the index TIA, and 6 (16%) had recurrent TIA. There were no significant differences in follow-up stroke (7% vs. 11%, p=0.7), TIA (11% vs. 33%, p=0.11), or combined vascular event (4% vs. 11%, p=0.38) between subjects with no severe stenoses, and those with at least one severe intra or extracranial stenosis or occlusion. Among the 3 patients with stroke during the follow-up period, one had severe stenoses in both the anterior and posterior intracranial circulations, and 2 had no severe stenosis. **Conclusions:** Severe intra- or extracranial vascular stenoses or occlusions are relatively common among patients presenting to the ED with TIA. The

relationship between these abnormalities and clinical outcomes should be studied with larger sample sizes to evaluate their prognostic value.

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W P178

Management of Patients with Suspected Transient Ischemic Attack is Safe in an Outpatient Clinic Based on Rapid Diagnosis and Risk Stratification

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Introduction: Patients with transient ischemic attack (TIA) are at high risk of short-term stroke, myocardial infarction and vascular death. Stroke risk is reduced substantially by rapid treatment initialization. Stroke Unit treatment is recommended for all TIA patients. We addressed the question whether outpatient evaluation of patients with suspected TIA is a safe approach. **Objective:** To establish an outpatient TIA clinic on weekdays at a German city hospital, to provide stroke work-up within one day, and to prospectively determine the short-term stroke and vascular risk during 3 months follow up. **Methods:** Stroke work-up included cerebral imaging, duplexsonography, transcranial Doppler screening for patent foramen ovale, ECG, blood tests, $ABCD_2$ score and ancle-brachial-index within 1 day. All TIA patients received secondary prophylaxis immediately. TIA patients fulfilling predefined criteria for high stroke risk in the next days ($ABCD_2$ Score$\geq$ 4 points and TIA within 72 hours, symptomatic extra- or intracranial stenosis, newly detected atrial fibrillation, recurrent TIA) were referred to the Stroke Unit. The remaining patients were sent home the same day. 90 days telephone follow-up was obtained. Freedom from stroke was estimated by the Caplan Meier method. **Results:** From February to December 2009, 135 consecutive patients with suspected TIA (57 male, mean age 59 years $\pm$17,1) were seen. Diagnostic work-up revealed TIA or minor stroke in 76 (56%), migraine with aura in 18 (13%), vertigo of non-vascular origin in 10 (7%), transient global amnesia in 4 (3%), focal seizures in 4 (3%), and other diagnoses in 23 patients (17%). Median time from symptom onset to presentation at the TIA clinic was 48h (range 1h to 3 months). Patients with TIA/minor stroke presented significantly more frequently with high $ABCD_2$ Score ($p = 0.03$). 15 patients (11%) were admitted to the Stroke Unit. 90 days stroke rate was 1.5% ($n = 2$) , compared to 5.9% predicted by the $ABCD_2$ Score. Stroke etiology was patent foramen ovale in one patient and embolic with unknown cause in the other patient. Freedom from stroke after 3 months was 98.5 $\pm$1.1 %. No patient reported cardiac or peripheral arterial ischemic events within 3 months. **Conclusion:** Based on rapid risk stratification, diagnostic evaluation of suspected TIA can be performed safely in an outpatient setting at a German city hospital. TIA mimicks are frequent. Vascular events within 3 months follow up are rare. The fact that cardiac causes of embolism were found or suspected in the two patients with stroke during follow-up may indicate that cardioembolic risk assessment needs to be improved in this setting.

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W P179

Subtypes and Hospital Length of Stay in Patients with a Missed Diagnosis of Ischemic Stroke in the Emergency Department

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Introduction: We have previously shown within a population that 18% of acute ischemic stroke (AIS) events were not given a diagnosis consistent with stroke in the Emergency Department (ED). These missed diagnoses were more likely in patients who presented with altered mental status or nonfocal weakness. Here, we further characterize the subtypes of AIS that were missed in the ED, and we evaluate the impact of a missed diagnosis on hospital length of stay (LOS). We hypothesized that patients with large vessel disease or embolic stroke would be less likely to be missed and patients with a missed diagnosis would have an increased LOS. **Methods:** ICD-9 codes 430-436 were screened to identify all stroke cases that presented to EDs of all 16 adult hospitals in the Greater Cincinnati/Northern Kentucky region in 2005. Cases were abstracted by research nurses and confirmed by study physicians. For this analysis, transient ischemic attacks, hemorrhagic strokes, and in-hospital strokes were excluded. An ED diagnosis of AIS was defined as a neurologic diagnosis indicative of stroke, including "rule-out stroke" and/or focal neurologic deficit description (ie. "left sided weakness" or "aphasia"). AIS subtypes were categorized by study physicians into large vessel, small vessel, cardioembolic, other identified cause, or an undetermined etiology. "Other" causes of stroke included cocaine use, dissection, surgery (peri- or immediate post-op), angio/cath/PTCA, cancer, hypercoagulable states, or venous thrombosis. Stroke subtypes and LOS were compared between patients with and without an ED diagnosis of AIS using Pearson's chi-squared test or the Mann-Whitney U-test, as appropriate. **Results:** Of 1498 confirmed AIS cases presenting to an ED, 275 (18.4%) had an ED diagnosis that was inconsistent with AIS. Sex, age, race, and medical history were similar between those with and without a missed diagnosis. Missed diagnosis of AIS was associated with stroke subtype ($p=0.039$); large vessel, 14.7% (35/238) missed, small vessel 17.0% (53/312), cardioembolic 17.8% (58/326), other causes 33.3% (15/45), and undetermined 19.8% (114/577). Patients with a missed diagnosis of stroke were more likely to have an increased LOS (5 days vs. 4 days, $P<0.001$). **Conclusion:** In our region, nearly 1 out of 5 cases of AIS were not given an ED diagnosis of AIS. The probability of a missed ED diagnosis was higher among cases with an "other" subtypes of stroke, and patients with a missed diagnosis also had a longer hospital LOS. A missed diagnosis could lead to missed opportunities for early treatment, therefore, a heightened awareness of atypical causes of ischemic stroke is necessary in patients presenting to the ED with atypical symptoms.

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W P180

tPA Contributes To Impairment of ATP and Ca Sensitive K Channel Mediated Cerebrovasodilation After Piglet Photothrombosis Through Upregulation of JNK MAPK

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Introduction: The sole FDA approved treatment for acute stroke is tissue type plasminogen activator (tPA). However, tPA potentiates impairment of pial artery dilation (PAD) in response to hypotension after photothrombosis in pigs. ATP and Ca sensitive K channels (Katp and Kca) are important regulators of cerebrovascular tone and mediate PAD in response to hypotension. Mitogen activated protein kinase (MAPK), a family of at least 3 kinases, ERK, p38 and JNK, is upregulated after photothrombosis, with JNK contributing to vasodilator impairment. This study examined the effect of photothrombosis on Katp and Kca-mediated cerebrovasodilation and the roles of tPA and MAPK in this effect. **Methods:** Photothrombotic injury (PTI) was produced by directing a laser (532 nm) onto piglet pial arteries after injection of erythrosine B. Drugs were given 30 min before or 2h after PTI. Phosphorylated and total ERK, p38, and JNK MAPK were measured by ELISA in the CSF of piglets equipped with a closed cranial window. Data ($n=5$) were analyzed by ANOVA, with significance at p less than 0.05. **Results:** PTI blunted PAD induced by the Katp agonists cromakalim, calcitonin gene related peptide (CGRP) and the Kca agonist NS 1619, which was exacerbated by tPA given before or after injury. JNK and p38 were upregulated after PTI, which was potentiated by tPA while ERK was unchanged. The JNK antagonist SP600125, given before or after PTI, prevented impairment of PAD in response to cromakalim and CGRP, but did not effect the response to NS 1619. The p38 antagonist SB203580 potentiated impairment of PAD by cromakalim, CGRP, and NS 1619 after injury, while the ERK antagonist U 0126 had no effect. **Discussion:** These data indicate that photothrombosis impairs K channel mediated cerebrovasodilation. tPA augments loss of K channel function after injury by upregulating JNK, while p38 may serve in a protective role. These data suggest that photothrombosis produces cerebrohemodynamic dysregulation during hypotension by impairing Katp and Kca mediated cerebrovasodilation via upregulation of JNK. These data suggest that thrombolytic therapy for treatment of CNS ischemic disorders can produce cerebrohemodynamic dysregulation through impairment of ionic controls of cerebrovascular tone.

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W P181

MicroRNA 17-92 Cluster Mediates Erythropoietin-induced Cerebral Angiogenesis

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Introduction: MicroRNAs, a class of non-coding small RNAs, regulate angiogenesis. Erythropoietin (EPO) enhances angiogenesis in the ischemic brain. However, the role of microRNAs in EPO induced angiogenesis has not been elucidated. In the present study, we tested the hypothesis that miR17-92 cluster mediates EPO-induced angiogenesis. **Methods and Results:** Cerebral endothelial cells (CECs) were isolated from microvessels of adult non-ischemic rats ($n=10$) or rats subjected to 7 days of the right middle cerebral artery occlusion (MCAo, $n=6$). MicroRNA microarray analysis of CECs revealed that ischemia downregulated and upregulated many miRNAs including miR-19a, a member of miR17-92 cluster. Real-time RT-PCR shows an increase in miR-19a in ischemic CECs (1.6 ± 0.1 vs 1.1 ± 0.04 in non-ischemia, $n=3$, $P<0.05$), which confirms microarray finding. Incubation of CECs with EPO (10 U/ml) significantly ($p<0.05$) upregulated miR-19a (7.2 ± 0.6 vs 1.0 ± 0.03, $n=3$), which was associated with substantial increases in capillary tube formation (3.5 ± 0.9 vs 2.1 ± 0.5 mm/mm^2), an in vitro angiogenesis assay. Western blots show that EPO significantly reduced thrombospondin 1 (TSP1, 0.7 ± 0.2 vs 1.0 ± 0.003, $n=3$) and connective tissue growth factor (CTGF) by 25% compared with the control. Transfection of CECs with miR17-92 cluster decreased TSP1 and CTGF protein levels to 79% and 72% of scrambled control, respectively, leading to significantly increased tube formation (8.2 ± 0.5 vs 4.9 ± 1.4 mm/mm^2, $n=5$) compared with levels in CECs transfected with scramble, which is consistent with fact that the miR17-92 cluster targets the TSP1 and CTGF in endothelial cells and downregulation of TSP1 promotes angiogenesis. In addition, EPO increased c-Myc protein levels in CECs (2.1 ± 0.1 vs 1.0 ± 0.001, $n=3$, $P<0.05$). **Conclusions:** The c-Myc has been shown to upregulate expression of the miR17-92 cluster. Thus, the present study indicates that EPO triggers c-Myc which upregulates miR17-92 cluster, leading to enhancement of angiogenesis by targeting anti-angiogenic genes TSP1 and CTGF.

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W P182

Infarct Size Prediction Using A Combined Technique Of Laser Doppler Flowmetry And Near-infrared Fluorescent Thrombi Imaging In A Mouse Model Of Embolic Stroke

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Background: There is a notion that failure of bench-to-clinic translation is partly due to the fact that experimental studies vary considerably in quality and reliability. Embolic stroke models have been great assets to stroke researchers, however they provide less control over the location and extent of the thrombi. **Objectives:** 1) To describe a near-infrared fluorescent (NIRF) imaging technique to measure the distribution and extent of the cerebral thrombi on ex vivo mouse brain and 2) to show how the technique, in combination with laser Doppler flowmetry (LDF) monitoring in vivo, could be helpful in predicting infarct size variability. ●**Methods:** Autologous blood clots were labeled with a Cy5.5 NIRF imaging agent that can detect activity of the factor XIII coagulation enzyme. In 10-week-old mice (n=45), the NIRF labeled clot emboli (3.70mm^3) were injected into the proximal portion of the left middle cerebral artery (MCA), while monitoring the cerebral blood flow (CBF) for 30 minutes using a LDF machine. Twenty-four hours later, the animals were euthanized, and the brains were removed and imaged ex vivo using a NIRF imaging machine. The brains were then used for immediate TTC staining to delineate the infarct area. After normalization, pixel counts of Cy5.5 NIRF signal in the left MCA and adjacent arteries, which represent thrombi extent, were calculated. The left hemisphere infarct volumes were measured and expressed as a percentage of the intact right hemisphere volume. **Results:** We confirmed that molecular optical labeling of thrombi and NIRF imaging allowed clear visualization of cerebral thrombi ex vivo. Representative brain sections showed corresponding thrombus filling the vessels. Next we observed that the decrease of CBF on LDF following placement of thrombi was rather variable (44.9±16.1% of the baseline, range 17~78%). Moreover, we could demonstrate that substantial heterogeneity existed in the distribution and extent (150.6±121.4 pixels, range 0~557) of remaining thrombi at 24h. Accordingly, infarct size was quite variable (30.6±10.1%, range 9.9~52.8%). The CBF decrease was positively correlated with the infarct size ($r=0.41$, $P<0.05$). The thrombi extent was also positively correlated with the infarct size ($r=0.40$, $P<0.05$). A multiple regression analysis revealed that both CBF decrease and thrombi extent could independently (and when combined, better) predict the infarct size ($r=0.53$, $P<0.05$). It was estimated that as initial CBF decreases 20% or final thrombi extent increases 150 pixels, infarct size increases by approximately 4%. **Conclusion:** The combined technique of LDF monitoring and thrombi imaging will serve as a useful tool in animal stroke research by directly (exclusion of modeling-failure cases) or indirectly (post-hoc statistical adjustment of infarct size) reducing data variability, consequently increasing statistical power of a study.

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W P183

Neuroprotective Effect of TAK-937, a Novel Cannabinoid Receptor Agonist, in Rat Permanent and Thrombotic Middle Cerebral Artery Occlusion Models

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Introduction: TAK-937 is a novel, highly potent and selective cannabinoid (CB1/CB2) receptor agonist. We examined the effect of TAK-937 in a permanent middle cerebral artery occlusion (MCAO) model in rats. In addition, the effect of TAK-937 in combination with tissue-type plasmsminogen activator (t-PA) was examined in a rat thrombotic MCAO model. **Methods:** Thrombotic MCAO was induced by photo-irradiation of MCA with rose bengal administration. Permanent MCAO was induced by coagulation of MCA electrically in male young-adult and aged rats. TAK-937 across a dose range between 10 to 100 ig/kg/hr or vehicle was intravenously infused starting 1, 3, 5 or 8 hr to 24 hr after MCAO (n=7~18 for each group). t-PA at 3 mg/kg was intravenously administered as a bolus injection in 20% of total volume, followed by an infusion of the remainder over a period of 30 min 1, 1.5 or 2 hr after MCAO (n=5~7 for each group). Infarct volume was determined by 2, 3, 5-triphenyltetrazolium chloride staining method 24 or 48 hr after MCAO. In combination studies, t-PA was administered at 3 mg/kg together with TAK-937 at either 30 or 100 μg/kg/hr. These were compared with the results of single administration of t-PA at 3 mg/kg, and TAK-937 at 10 and 30 μg/kg/hr (n=5~8 for each group) and their infarct volume was determined 24 hr after MCAO. **Results:** TAK-937 significantly reduced infarct volume in a dose dependent manner when administered up to 5 hr after in young-adult rats with permanent MCAO ($p<0.025$). No such effect was observed when TAK-937 was administered 8 hr after MCAO. Moreover, TAK-937 at 100 μg/kg/hr showed significant reduction of infarct volume in aged rats with permanent MCAO ($p<0.05$). t-PA administered 1 hr after MCAO significantly reduced the infarct volume in rats with a thrombotic MCAO ($p<0.05$) but such effect was not observed when t-PA was administered later than 1 hr. Combined treatment of t-PA with 30 or 100 μg/kg/hr of TAK-937 1 hr after MCAO showed further reduction in infarct volume compared to t-PA alone ($p<0.025$). **Conclusion:** TAK-937 exerted neuroprotective effects in both young adult and aged rats with a wide therapeutic time window in a rat permanent MCAO model. Furthermore, TAK-937 produced an enhanced therapeutic effect when given in combination with t-PA in a rat thrombotic MCAO model.

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W P184

Visualization of Clot Lysis in a Rat Embolic Stroke Model

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Objectives: The purpose of this study was to develop a novel MRI method for imaging clot lysis in a rat embolic stroke model, and to compare tissue plasminogen activator (tPA) based clot lysis with and without recombinant Annexin-2 (rA2). **Methods:** Experiment 1: In vitro optimization of clot visualization using multiple MRI contrast agents in concentrations ranging from 5 to 50μL in 250μL blood. Experiment 2: In vivo characterization of the time course of clot lysis using the clot developed in the previous experiment. Diffusion, perfusion, angiography, and T1-weighted MRI for clot imaging were conducted prior to and during treatment with vehicle (n = 6), tPA (n = 8) or rA2+tPA (n = 8) at multiple time-points. Brains were removed for ex vivo clot localization facilitated by Evans Blue (EB) staining of the clot developed in experiment 1. The T1 and EB clot visualization is displayed in Figure 1.

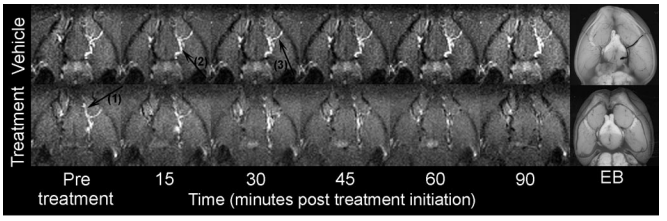

Figure 1: In vivo Maximum Intensity Projection of the clot utilizing T1-weighted imaging in a representative vehicle (top) and tPA (bottom) treated animal, respectively. Note the progressive clot lysis in the tPA-treated but not the vehicle animal. T1-weighted imaging results match well with Evans Blue (EB) stained clot found on histology 3.5 hours post embolization. Arrow 1, 2 and 3 points to clot visible in anterior cerebral artery, internal carotid artery, and middle cerebral artery respectively.

Results: Clots created with 25μL Magnevist© were the most stable and provided the highest contrast-to-noise ratio. In the vehicle group, clot length as assessed by T1-weighted imaging correlated with histology ($r = 0.93$). Clot length and CBF-derived ischemic lesion volume were significantly smaller than vehicle at 15 minutes post-treatment initiation in the rA2+tPA group, while in the tPA group no significant reduction from vehicle was observed until 30 minutes post-treatment initiation. The rA2+tPA group had a significantly shorter clot length than the tPA group at 60 and 90 minutes post-treatment initiation, and significantly smaller CBF deficit than the tPA group at 90 minutes post-treatment initiation (see Figure 2).

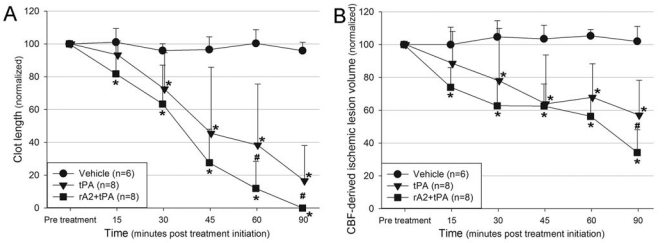

Figure 2: Temporal evolution of A) T1-weighted imaging derived clot length and B) perfusion lesion volume in the experimental groups. *Significant difference between treatment group and control. #Significant difference between treatment groups. $p < 0.05$. Note, n = 5 for the last imaging time-point in figure B for the rA2+tPA group.

Conclusion: We introduce a novel MRI based clot imaging method for in vivo monitoring of clot lysis. Lytic efficacy of tPA was enhanced by rA2.

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W P185

Inhibition of Calcium/Calmodulin Dependent Protein Kinase IV is Detrimental in Experimental Stroke

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Background: Calcium/Calmodulin Dependent Protein Kinase Kinase (CaMKK) is a kinase well known for its role in calcium signaling, which is critical in stroke pathology. We have previously

demonstrated that inhibition of CaMKK is detrimental in stroke. CaMKK directly activates CaMK IV (Calcium/Calmodulin Dependent Protein Kinase IV). Although CaMK IV is a known cellular survival factor, its role in stroke remained unknown. In this study, we assessed the hypothesis that inhibiting CaMK IV is detrimental in experimental stroke. **Methods:** Stroke was induced by reversible middle cerebral artery occlusion (MCAO-90 minutes) in male CaMKK IV knockout (KO) mice and littermate (WT) mice. The matrix metalloproteinases (MMP) inhibitor SB-3CT or vehicle was injected at the onset of stroke to CAMK IV KO mice. Stroke outcome was determined with TTC-staining at 24 hrs. Neurological scoring was done prior to sacrifice. Immunohistochemistry was used to assess blood brain barrier protein collagen IV loss. Gel zymography was used to measure the activity of MMP 9. Data are presented as mean±sem. **Results:** CaMK IV KO mice had significantly increased cortical (KO 64.9 ± 4.9% vs. WT 48.9±4.1%, P<0.05), striatal (KO 77.8±5.8% vs. WT 62.2±2.5%, P<0.05) and total (KO 61.0±5.1% vs. WT 43.4±3.7%, P<0.05) (n=7/pg) infarct volumes compared to WT littermates. This was reflected in exacerbated neurological deficits (KO 3.1±0.3 vs. WT 2.3±0.2, P<0.05) in KO mice. Stroke-induced mortality was seen in 6 out of 13 in CaMK IV KO mice with increased intracerebral hemorrhagic transformation rate whereas no WT control mice died. A dramatic loss of collagen IV (55%) was seen in CaMK IV KO mice 4 hours after stroke, an effect not seen in WT controls. The exacerbated blood brain barrier disruption in KO was associated with enhanced MMP 9 activity after stroke. Treatment of MMP 9 inhibitor SB-3CT reversed the detrimental phenotype of CaMK IV KO mice and reduced mortality rate and decreased infarct size. There were no differences in physiological parameters between CaMK IV KO and WT groups. In addition, local cerebral blood flow measured by Laser Doppler Flow was equivalently reduced during ischemia (KO 11.2±1.1% versus WT 12.3±1.1%, n=4/pg) and was restored equally in early reperfusion. **Conclusion:** Our data demonstrated that genetic deletion of CaMK IV is detrimental after experimental stroke and this effect was secondary to BBB disruption and activation of MMP9 activation. This suggests that CaMK IV may represent a novel therapeutic target for stroke treatment and to restore BBB dysfunction.

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W P186

Anesthesia Confounds in Experimental Stroke and Preconditioning

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Prolonged anesthesia is often required in the application of imaging and recording modalities to experimental stroke, but its potential impact on the parameters under study is not always considered. A specific confound was identified in the course of monitoring CBF transients as an index of peri-infarct depolarizations (PIDs) using speckle contrast perfusion imaging, in a model of lesion-induced preconditioning in Spontaneously Hypertensive Rats. Animals (5-12 per group) experienced initial surgery under brief isoflurane anesthesia to produce small cortical freeze lesions (cold lesions, CL), or a sham procedure. The following day rats were subjected to permanent tandem MCA/CCA occlusion, again under isoflurane anesthesia. CL rats allowed to recover from anesthesia exhibited significantly smaller 24 h edema-corrected infarct volumes than a Naïve group, with no effect of the Sham procedure, demonstrating a robust preconditioning phenomenon (Naïve 116 ± 14, Sham 113 ± 11, CL 85 ± 14 cubic mm; P < 0.05 CL vs. Naive). However, animals maintained under isoflurane anesthesia for perfusion imaging exhibited comparably reduced PID incidence in Sham and CL groups (both 3 ± 1 vs. 7 ± 2 in Naïve), and no differences in infarct volume after the acute 4 h monitoring interval (Naïve 99 ± 20, Sham 85 ± 11, CL 94 ± 9 cubic mm). In contrast, transition to á-chloralose immediately after occlusion increased overall PID incidence and eliminated the Sham effect, but maintained reduced PID number in the CL group (Naive 17 ± 5, Sham 15 ± 6, CL 6 ± 2; P < 0.05 CL vs. Naive). Furthermore, 4 h infarct volumes in these groups faithfully replicated the initial preconditioning study (Naive 112 ± 13, Sham 111 ± 16, CL 90 ± 18 cubic mm; P < 0.05 CL vs. Naive). These results identify a subtle influence of prior isoflurane exposure on acute stroke pathophysiology when under anesthesia with the same agent. Replacement of isoflurane with á-chloralose accelerates infarct progression, acutely replicates subsequent histopathological outcome in the model under study, and reveals a specific impact of cold lesion preconditioning on the incidence of PIDs, considered to be of direct mechanistic relevance to infarct evolution. Although á-chloralose itself markedly attenuates absolute brain blood flow and metabolism it has been widely used in studies of neurovascular coupling. It now appears to be of specific utility in avoiding confounding effects of repeated isoflurane anesthesia in experimental stroke.

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W P187

Neuroprotective Effect of TAK-937, a Novel Cannabinoid Receptor Agonist, in a Rat Transient Middle Cerebral Artery Occlusion Model

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Introduction: TAK-937 is a novel, highly potent and selective cannabinoid (CB_1/CB_2) receptor agonist. This study examined the effects and explored the mechanism of actions of TAK-937 in a rat transient middle cerebral artery occlusion (MCAO) model. **Methods:** Male Sprague-Dawley (SD) rats were subjected to 2 hr transient MCAO by inserting an intraluminal suture. TAK-937 at 3, 10, 30 and 100 μg/kg/hr or vehicle was intravenously administered for 22 hr from 2hr after MCAO and their infarct volume was determined in a dose-response study (n=16~20 for each group). Functional outcomes (neurological symptom and foot-fault test) and brain atrophy were also evaluated 4 weeks after 2 hr transient MCAO and TAK-937 at 30 and 100 μg/kg/hr or vehicle treatment (infusion for 22 hr) (n=23~27 for each group). Effects of TAK-937 at 30 μg/kg/hr (infusion for 22 hr) on infarct volume were also examined in 2 hr transient MCAO in female and ovariectomized (OVX) SD rats (n=10~15 for each group). In a study to assess contribution of hypothermia to the neuroprotective effects of TAK-937, brain temperature of freely moving male SD rats was telemetrically monitored and maintained between 37 and 38 °C during intravenous infusion of TAK-937 at 100 μg/kg/hr for 24 hr after MCAO using a multi-channel brain temperature controlling system (n=10~11 for each group). Subsequently, infarct volume was determined. **Results:** In the dose response study, infarct volumes at 3, 10, 30 and 100 μg/kg/hr of TAK-937 were reduced in a dose-dependent manner compared with infarct volume in the vehicle treated animals by 3.5 (p>0.025), 23.5 (p<0.025), 48.9 (p<0.025) and 66.3% (p<0.025), respectively. TAK-937 at 30 and 100 μg/kg/hr significantly ameliorated neurological symptom, motor impairment and brain atrophy until 4 weeks after MCAO (p<0.025). TAK-937 at 30 μg/kg/hr also reduced infarct volume in female and OVX rats (p<0.05). When the hypothermic effect of TAK-937 at 100 μg/kg/hr (about 4 degree Celsius) was completely reversed to the same level of brain temperature in the vehicle group by warming, the neuroprotective effect of TAK-937 was partially attenuated (p<0.01) although significant reduction in cerebral infarct volume was still observed (p<0.05). **Conclusion:** TAK-937 exerts neuroprotective effects in a transient MCAO model in male, female and OVX rats. This neuroprotective effect may be mediated in part by the induction of hypothermia. TAK-937 also brings long-term improvement in functional outcomes and brain atrophy at 4 weeks.

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W P188

Very Brief Focal Cerebral Ischemia Induces A Delayed Immune Response In Peripheral Blood Of Rats

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Background: Inflammation is a common event observed in both acute and chronic neurological conditions including stroke, Alzheimer's disease, and multiple sclerosis. Currently, inflammation is considered a critical determinant outcome following acute brain injury. A prominent inflammatory response occurs following both ischemic stroke and hemorrhagic stroke. Although one third of patients with transient ischemic attack (TIA) go on to have ischemic strokes, the link between TIA and subsequent ischemic stroke has not been identified. Related to this issue, we have shown that inflammatory response occurs in the brain[1] and the peripheral blood[2] in rats at 24h postischemia in both animal models of TIA and stroke. However, the delayed inflammatory response has not been identified in TIA patients or animal models. In the current study we investigate whether brief focal ischemia in rats, simulating TIA in humans, produces delayed inflammatory response in peripheral blood. **Method:** Adult rats (n=3 in each group) were subjected to 10 minutes of middle cerebral artery occlusion followed by 48h or 72h of reperfusion and compared to 24h of reperfusion. Whole blood was obtained and RNA expression assessed on whole genome Affymetrix microarrays. **Results:** Compared to 24h, 48h and 72h reperfusion resulted in significantly altered expression of 90 and 428 genes, respectively (absolute fold change ≥ 1.5 and false discovery rate ≤ 0.05). Among these genes, 3 and 25 genes were involved in inflammatory response at 48h and 72h postischemia, respectively. Most of these inflammatory related genes (24 out of 25) were not regulated at 24h postischemia compared to naïve controls as we previously demonstrated[2], which suggested a delayed inflammatory response. The inflammatory related genes were mainly involved in the pathways of 'T cell receptor signaling', 'CTLA4 signaling in cytotoxic T lymphocytes', 'calcium-induced T lymphocyte apoptosis', and 'cytotoxic T lymphocyte-mediated apoptosis of target cells'. These results provide evidence that delayed adaptive immune responses occur at 72h postischemia in the peripheral blood of rats. We postulate that this will also occur in humans. **Conclusion:** Very brief focal ischemia induces a delayed immune response in peripheral blood of rats. The data supports the possibility that human patients with TIAs may have similar changes in blood gene expression, and that some of these changes may depend on the duration of post cerebral ischemia. **Keywords:** transient ischemic attack, inflammation, microarray, gene expression, blood, rat **Reference:** 1. Brain Res. 2008; 1234:183-97. 2. JCBFM. 2010; 30(1):110-8.

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W P189

TLR3 Ligand Attenuates Cerebral Ischemia/Reperfusion Injury

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Introduction: Innate immune and inflammatory responses have been implicated in cerebral ischemia/reperfusion (I/R) injury. Toll-like receptors (TLR) play a critical role in the induction innate immunity and inflammatory response. However, it is unclear whether modulation of TLR will induce protection against cerebral I/R injury. The TLR3 mediated signaling pathway directly stimulates production of interferon-â and local injection of interferon-â has been shown to decrease cerebral I/R injury. We hypothesized that modulation of TLR3, with Poly I:C ligand, will induce protection against cerebral I/R injury. **Methods:** To evaluate our hypothesis, we treated male C57BL/6 mice with the TLR3 ligand, Poly I:C (n=8, 75 μg/25 g body weight) or placebo (n=8) by i.p injection one hr before the brains were subjected to cerebral ischemia (60 min) followed by reperfusion (24 hrs). Untreated mice (n=8) were subjected to cerebral I/R. We also

treated TLR3 knockout mice with Poly I:C one hr prior to cerebral I/R. Infarct size was examined by TTC staining. Morphology of neurons in brain sections was examined by Nissl staining. Cellular proteins were isolated for Western blot analysis. **Results:** Poly I:C treatment significantly decreased infarct size by 55.9% compared with untreated I/R mice (10.0±1.72 vs. 22.7±2.73). Morphologic examination showed that there was less neuronal damage in the hippocampus of Poly I:C treated mice compared with untreated I/R mice. Poly I:C induced protection was abolished in TLR3 knockout mice. Western blot analysis showed that cerebral I/R increased the levels of Fas by 28.2%, FasL by 54.1%, phospho-ASK-1 by 52.0%, phospho-JNK by 64.3%, and NF-êB binding activity by 32.1%, respectively, in untreated mice compared with sham control (n=5/group). In contrast, Poly I:C administration significantly attenuated I/R-increased the levels of FasL, Fas and phospho-ASK1, phospho-JNK, and NF-êB binding activity. **Conclusion:** Poly I:C treatment induces protection against cerebral I/R injury through a TLR3 dependent mechanism. TLR3 ligand-induced protection involves a decrease in the I/R-activated Fas-mediated apoptotic signaling pathway. Modulation of TLR3 could be a potential approach for protection against stroke.

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W P190

Activation of AMP-activated Protein Kinase Differs in Young and Aging Mice after Stroke

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Introduction: Adenosine monophosphate-activated protein kinase (AMPK) is an evolutionary conserved energy sensor that regulates cellular metabolism and is activated via phosphorylation (pAMPK). Numerous stimuli can increase the activation of AMPK, including increasing AMP/ATP ratio. Acute activation of AMPK is detrimental in models of focal stroke as both pharmacological inhibitors and genetic deletion of the catalytic isoform of AMPK are neuroprotective. The AMP/ATP ratio increases with age and chronic exposure to metabolic stress may accelerate the aging process. However, AMPK activity decreases in peripheral tissues with age. Whether this also occurs in the aging brain, and how this contributes to the ability of the aging brain to cope with an acute stressor such as stroke is not known. This study investigated the activation of AMPK and the response to AMPK inhibition after induced stroke in both young and aging mice. Hypothesis: Stroke induced pAMPK expression will be higher in young than in aging mice. The AMPK inhibitor, Compound C administration will protect young, but not aging, mice from stroke. **Methods:** Focal stroke was induced by middle cerebral artery occlusion (MCAO) in young (8-10 weeks old) and aging (16-18 months old) C57BL6 male mice. Compound C was intraperitoneally administered at the onset of MCAO. Behavioral deficits and infarct volumes were assessed 4 or 24 hours after MCAO. Separate cohorts were utilized for Western blotting for pAMPK. **Results:** Levels of pAMPK were higher in aging brain compared to young mice at baseline. Stroke induced robust activation of AMPK as measured by phosphorylation in young mice, yet this response was muted in the aging brain. Male mice had a reduction in infarct volume with age, with smaller infarcts in aging animals but more severe behavioral deficits. Inhibition of pAMPK reduced infarct volumes in young animals (Total infarct, vehicle vs. drug: 55.9±2.4 vs. 32.8±4.0 %, n=6 animals/gp, $P<0.05$), but had no effect in aging mice. Compound C administration led to significant hypothermia in both age groups, which contributed to an additive neuroprotective action in young mice, but not in aging. **Conclusions:** Aging increases baseline pAMPK levels, but aging mice have an ameliorated stroke-induced pAMPK response. Neuroprotective agents that are efficacious in young animals may be ineffective in aging.

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W P191

Angiogenic Factor Expression And Vascular Damage After Stroke In Type 2 Diabetic Mice

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Diabetes mellitus is a major health problem associated with both microvascular and macrovascular disease. Disequilibrium of angiogenesis promoters and inhibitors in Diabetes may lead to exuberant but dysfunctional neovascularization. In this study, we investigated the changes and the molecular mechanisms of cerebral vascular damage after ischemic stroke in type-2 diabetic (T2DM) mice. Adult male db/db T2DM and non-diabetic wild-type (WT) mice were subjected to sham and transient middle cerebral artery occlusion (MCAo) and sacrificed 24 h after surgery. The angiogenic factors were measured by angiogenic protein array. In the blood serum, Endothelial Growth Factor (EGF), platelet-derived growth factor (PGDF)-AA and angiopoietin-1(Ang1) level were decreased, while Plasminogen Activator Inhibitor-1(PAI-1), Monocyte Chemotactic Protein-1 (MCP-1), Macrophage Inflammatory Protein-1 (MIP-1), Matrix Metalloproteinase-8 (MMP8) and Matrix Metalloproteinase-9 (MMP9) were increased in sham T2DM-mice compared to WT-mice. We compared the difference of angiogenic factors between WT-MCAo and DM-MCAo mice in the ischemic brain. Angiogenin, PAI-1, MCP-1, MMP9 and endothelin-1 were increased, while TIMP-4 and Ang1 were decreased in the ipsilateral hemisphere of T2DM-MCAo mice. Using immunostaining, T2DM significantly increased brain hemorrhage and vascular density, but decreased vascular perimeter and arterial diameter in the ischemic border compared to WT-MCAo mice ($p<0.05$). T2DM also exhibited decreased BBB function as measured by tight junction protein (occludin) and a-SMA expression in the ischemic brain compared to WT-mice ($p<0.05$). T2DM had significantly decreased Ang1, Tie2 and PDGF expression and increased MMP9 and Ang2 expression in the ischemic brain compared to WT-mice. To investigate the mechanism underlying T2DM induced vascular damage, mouse brain endothelial cell (MBEC) primary culture, MBEC capillary tube formation and arterial explant cell migration assays were employed. MBEC capillary tube formation was significantly increased, but arterial cell migration significantly decreased in artery extracted from T2DM-mice compared to WT-mice. Ang1, Tie2 and PDGF gene expression significantly decreased, while Ang2 and MMP9 gene expression was significantly increased in culture with MBECs derived from T2DM mice compared to MBECs from WT mice ($p<0.05$). High glucose also significantly decreased vascular stabilization using an in vitro co-culture MBEC and smooth muscle cell (SMC) model compared to normal glucose control. Ang1 treatment attenuated the decreased arterial cell migration and increased capillary tube formation stabilization in T2DM-MBECs ($p<0.05$). Our data indicate that, T2DM disequilibrium regulates angiogenic promoters and inhibitors and plays an important role in T2DM-induced vascular damage after stroke.

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W P192

The RXR Agonist, Bexarotene Reduces Infarction Volume in Transient Cerebral Ischemia

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Activation of several nuclear transcription factors, including peroxisome proliferator-activated receptor α and γ, and liver X receptors (LXR) is neuroprotective in animal models of ischemic stroke. These receptors form heterodimers with the nuclear receptor, retinoid X receptor (RXR). This complex can be activated by agonists to either receptor. Activation modulates gene transcription either by binding to target gene promoters or through transrepression of other transcription factors. Mechanisms of transrepression include competing for coactivators, direct binding to transcription factors, and inhibiting corepressor clearance. We hypothesize that RXR agonists, which activate heterodimers containing PPARα, PPARγ and LXR simultaneously may be a more potent neuroprotective stimulus than agonists for either factor alone. The RXR agonist, bexarotene, is FDA approved to treat cutaneous manifestations of T-cell lymphomas and acute myeloid leukemia. The primary toxicity with chronic treatment is hypertriglyciderimia and hypercholesterolemia. We tested the neuroprotective actions of bexarotene, an RXR agonist, in the suture model of transient focal ischemia. Male Wistar rats were treated with IV bexarotene dissolved in saline or saline at the time of two hour middle cerebral artery occlusion (MCAO). All animals underwent physiologic monitoring including cerebral blood flow (CBF), arterial blood pressure and arterial blood gases. There was no difference in the physiologic parameters of any group of animals. Reperfusion was confirmed by CBF at the time of suture removal. Rats were euthanized 24 hours later and infarct volume calculated. Treatment with either 5 or 10 mg/kg bexarotene resulted in reduced infarction volumes relative to that in saline treated rats (p0.5) in both experiments. Activation of PPARs and LXR are anti-inflammatory and this is felt to contribute to their neuroprotection. We find that the inflammatory infiltrate in brains from bexarotene treated animals is significantly reduced following MCAO ($p<0.001$; Mann Whitney U test. Saline treated: n= 318 hpf/4 rats; Bexarotene 5mg/kg: n=530 hpf/6 rats; Bexarotene 10mg/kg: 448 hpf/5 rats. These data demonstrate that bexarotene is neuroprotective in an animal model of cerebral ischemia even when administered 3 hours after ischemic onset. Administration of bexarotene is associated with a reduced inflammatory infiltrate and this may be the mechanism of neuroprotection.

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W P194

Hypoxia Inducible Factor-1α Contributes To Brain Edema After Stroke By Regulating Aquaporins And Glycerol Distribution In Brain

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Introduction: The purpose of this study was to determine, in a rodent model of cerebral ischemia, whether a molecular cascade involving HIF-1α, AQP-4 and AQP-9 is causally related to the regulation of glycerol in brain tissues and the formation of brain edema. **Methods:** Middle cerebral artery occlusion (MCAO) followed by 2 hour reperfusion were performed in male Sprague-Dawley rats (250-280g). The anti-AQP-4, anti-AQP-9 antibody, or 2-Methoxyestradiol (2ME2, an inhibitor of HIF-1α) were given at the time of MCAO. The rats were sacrificed at 1 and 24 hours after reperfusion and their brains were examined for protein expression, glycerol concentration and brain edema. Extracellular and intracellular glycerol concentration of brain tissue was calculated with enzymatic glycerol assay. The protein expressions of HIF-1α, AQP-4 and AQP-9 were determined by Western blotting. Brain edema was measured by brain water content. **Results:** Compared to control, significant edema ($p < 0.01$) and significantly increased glycerol ($p < 0.05$) was observed after stroke. Stroke also significantly ($p < 0.05$) enhanced expression of HIF-1α, AQP-4, and AQP-9. Edema was significantly ($p < 0.01$) decreased after inhibition of AQP-4, AQP-9 or HIF-1α, respectively. Extracellular glycerol was also significantly ($p < 0.01$) decreased after inhibition of AQP-4, AQP-9 or HIF-1α while intracellular glycerol was not, even increased ($p < 0.01$) 1 hour after stroke. Inhibition of HIF-1α significantly ($p < 0.01$) suppressed the expression of AQP-4 and AQP-9. **Conclusion:** HIF-1α plays a role in regulating cerebral glycerol and brain edema formation via a molecular pathway involving AQP-4 and AQP-9. Pharmacological blockade of this pathway in stroke patients may provide novel therapeutic strategy.

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W P195

Hypothermia Identifies Extracellular Calcium-sensing Receptor (CaSR) As A Potential Therapeutic Target

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Background: Hypothermia has been shown to be effective in improving neurological outcome from cardiac arrest. The mechanisms of protection are multifold, but may be useful in identifying appropriate therapeutic targets. The extracellular calcium-sensing receptor (CaSR), originally found in parathyroid cells, senses minute changes in extracellular [Ca^{2+}] and promotes intracellular Ca^{2+} release. It is also expressed in the brain where calcium overload worsens ischemic brain injury, but the role of CaSR in brain ischemia is completely unknown. **Methods:** To study the role of CaSR in brain ischemia, we subjected male mice (C57/BL6) to global cerebral ischemia (a model that results in brain injury much like that seen following cardiac arrest) by subjecting them to 10 min bilateral carotid artery occlusion followed by reperfusion for 3d. We then assayed CaSR expression in mice exposed to therapeutic hypothermia (33C for 3h starting at the onset of reperfusion) and in mice with selective hippocampal CaSR deficiency by immunohistochemistry and immunoblots. **Results:** Forebrain ischemia led to increased expression of CaSR, especially within neurons of the susceptible hippocampus but not in astrocytes. Mild hypothermia protected CA1 neurons from ischemic damage and inhibited CaSR induction. Mice deficient in hippocampal CaSR were protected compared to wildtype (n=7/group, $P<0.05$). Since GABA-B receptor-1s (GABA-B-R1) can heterodimerize with CaSR and suppress its expression, and GABA-B-R1 is involved in inhibitory neurotransmission, we studied GABA-B-R1 deficient cultured hippocampal neurons. CaSR was increased in neurons lacking GABA-B-R1, suggesting a new role of CaSR in potentiating ischemic neuronal death, and may be inversely linked to GABA-B-R1. **Conclusion:** CaSR may be a new therapeutic target for treatment of ischemic brain injury.

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W P196

Three Variations of an Angiographic Rabbit Model of Acute Embolic Stroke

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Background: Models of stroke in rabbits have successfully mimicked stroke volumes, hemorrhage, and recanalization rates. Techniques developed in rabbits have successfully transitioned into human therapies. Smaller models are more popular but often fail in translation to humans. To refine the rabbit model, three modified angiographic techniques were used to mimic different types of clinically relevant embolic stroke. **Hypothesis:** Delicate angiographic techniques can produce different types of infarct depending on embolic agent. **Methods:** We report control rabbits with embolization but no therapy, N=76, from a total of 640 test animals. New Zealand White rabbits (5.2 $\pm$ 0.07 kg) received subselective internal carotid angiography from a femoral artery approach using a 3 F catheter and magnification angiography techniques. Internal carotid artery (ICA) injection of emboli occluded the branches. Fresh clot was prepared by clotting fresh rabbit blood in 1.0 mm diameter plastic tubes for 3 to 6 hours at 37°C and cutting to 1 mm length. Aged clot used 1.5 mm plain glass tubes with clotting for 6 hours at 37°C, then cooling to 4°C for 72 hours and cutting to 4 mm length. Groups included 1) fresh clot (N=50), 2) aged clot (N=13), and 3) insoluble embolic spheres 700-900 microns in diameter for modeling atheroma (N=13). Follow up angiograms identified occluded vessels. Vital stains on 4 mm sections were used to measure infarcts and histology measured hemorrhage. **Results:** Fresh clot animals resulted in very small infarcts averaging 0.45% of total brain volume. These were sometimes difficult to see on angiography and a high proportion, 60%, cleared completely with autolysis and recanalization within 24 hours. These small strokes often resembled transient ischemic attacks but were too mild to compare stroke therapies. Aged clot animals produced moderate anterior infarcts averaging 4.5%, a volume with clinical relevance. These were well tolerated in all but one with stray clot to the brain stem. Autolysis cleared 23%. Sphere animals produced similar moderate anterior infarcts averaging 4.3% in size that were well tolerated. The aged clot and spheres were well seen on angiograms, usually involving the middle cerebral artery or a combination of the middle and anterior cerebral arteries. There was no autolysis with spheres. Rabbits survived long term, up to 90 days, unless emboli reached the posterior cerebral artery or superior cerebellar artery. This occurred in about 4% of all cases and most of these required early euthanasia due to the severity of the stroke. Stroke volumes achieved using aged clot and spheres were useful in separating results of therapies. **Conclusion:** Angiographic models using small fresh clots, larger aged clots, and insoluble spheres are reliable and useful models of transient ischemic attack, strokes from large embolic thrombus, and strokes from insoluble atheroma, respectively.

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W P197

Perfusion-diffusion Mri Of Non-human Primate Stroke

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Background: Numerous interventions have been developed and shown effective in rodent models; however, none of these has been proven effective in human besides rtPA. The rodent stroke model simply does not adequately reflect the complexity and dynamics of human stroke. It is the Stroke Therapy Academic Industry Roundtable (STAIR) recommendation that NHP stroke models need to be established for assessing novel interventions before clinical trials. Non-human primate (NHP) stroke model and non-invasive imaging technologies, such as MRI, are of significant importance albeit challenging. This study described the development of a baboon stroke model and the spatiotemporal evolution of the ischemic lesion by perfusion and diffusion MRI on a clinical scanner. **Methods:** Three normal female baboons (15-20kg) were subjected to permanent (n=1) or 90-min (n=2) MCAO using an endovascular approach (balloon occlusion at M1). Animals were anesthetized with ~2% isoflurane during stroke surgery and 0.8~1.0% isoflurane with vecuronium (0.1mg/kg) during MRI. Multimodal MRI including anatomical, perfusion (arterial spin labeling), diffusion, and MRA were performed on a clinical Siemens 3T scanner. Images were acquired every 30 min from 1 hour post-reperfusion up to 6 hours (permanent) or 4 hours (transient). Data were processed using custom-codes written in Matlab. Quantitative cerebral blood flow (mL/100g/min) and apparent diffusion coefficient (mm2/s) maps were calculated. Lesion volume was derived with thresholding (CBF>70mL/100g/min and ADC<0.53x10-3 mm2/s). Final infarct was determined with T2 images. **Results:** Perfusion-diffusion mismatch was robustly detected in the one animal underwent permanent stroke. In the transient ischemia group, hyperperfusion were detected repeatedly. The percent ipsi-lesional to contra-lesional CBF and ADC were ~149.6% and ~72.5% respectively at one-hour post-reperfusion. The percent ipsi- to contra-lesional ADC ratios degraded (~63.8%) overtime indicating the tissue progress to infarct. The percent ipsi- to contra-lesional CBF ratios remain relatively constant (~136.8%) up to four hours after reperfusion, and the defined lesion volume approximates the final infarct. **Conclusions:** This study described for the first time of monitoring both the spatial and temporal evolution of perfusion and diffusion characteristics on NHP stroke model using a clinical MRI scanner. Repeated perfusion measurements on large NHP were not feasible previously with DSC-MRI. The perfusion-diffusion mismatch approximates the penumbra was shown. An interesting hyperperfusion was observed within the diffusion lesion in transient stroke. Future studies will utilizes this multimodal MRI protocol to evaluate the spatiotemporal changes of baboon stroke, which provides a potential platform for developing novel interventions.

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W P198

Neuroprotective Effect Of A Brain-targeting Form Of Docosahexaenoic Acid After Stroke: An MRI-based Study

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Introduction and Purpose: Epidemiologic studies report cardio-vascular protection conferred by omega-3 fatty acids, in particular docosahexaenoic acid (DHA). Few experimental studies have addressed the neuroprotective potential of DHA in acute stroke treatment. DHA accumulation in brain has been evidenced through a specific uptake of DHA-containing lysophosphatidylcholine (lysoPC). Our aim was to use multimodal MRI to assess in vivo neuroprotection conferred by DHA and by a stabilized biomimetic form of LysoPC-DHA (AceDoPC) in an animal model of acute stroke. Methods Rats underwent a one-hour proximal MCA occlusion with the intraluminal thread model. Immediately following reperfusion, animals were randomly and blindly treated by i.v. injection of i) saline (n=8), or ii) plasma from donor rats (n=10), or iii) DHA (n=10) or iv) AceDoPC (n=10), both solubilised in plasma. Twenty-four hours after reperfusion, animals were submitted to behavioral tests and sacrificed. MRI was performed on a 7T Bruker magnet at H0 during occlusion and at H24 before sacrifice. The MR exam covered the entire MCA territory and included a 2D angiography, DWI, DSC-PWI, and T2w imaging. Initial and final lesions were defined respectively as hypointense signal on H0 apparent diffusion coefficient (ADC) maps and hyperintense signal on H24 T2w images (Fig. 1). After sacrifice, brain tissue was used to measure F2-isoprostane content. Results Median neuroscores exhibited a non significant trend to decrease in treatment groups (6.5, 6 and 4 in plasma, DHA and AceDoPC groups respectively) compared to the saline group (8), reflecting fewer deficits in treated animals. Mean initial lesion size was comparable in the four groups, as well as PWI/DWI mismatch. Between H0 and H24, lesion size increased in the saline group (mean±SD: +18%±20%), was stable in the plasma group (-3%±29%), decreased in the DHA group (-17%±15%, P<0.05), and further decreased in the AceDoPC group (-34%±27%, P<0.05). Lipid peroxidation was decreased in the AceDoPC group compared to the other groups. **Discussion and Conclusion:** The results provide an in vivo evidence of neuroprotection in acute stroke by a biomimetic stable form of LysoPC-DHA solubilised in plasma, AceDoPC. Enhanced brain accumulation is further suggested by decreased oxidative stress. MRI may play an important role for the controlled evaluation of new stroke treatments and thus help translate experimental findings into the clinic.

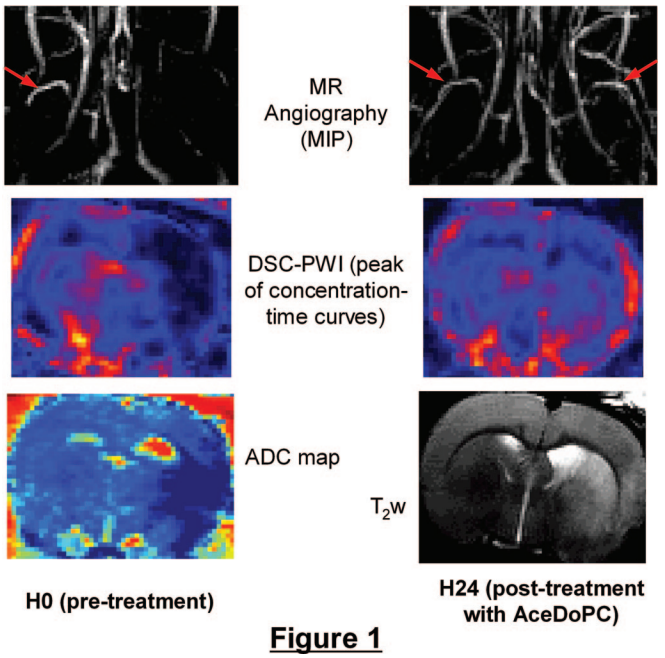

Figure 1

Author Disclosures: F. Chauveau: None. T. Cho: None. M. Perez: None. M. Guichardant: None. A. Riou: None. P. Aguettaz: None. M. Picq: None. M. Lagarde: None. Y. Berthezène: None. N. Nighoghossian: None. M. Wiart: None.

W P199

ADAMTS13 Is Neuroprotective Against Brain Ischemia-Reperfusion Injury By Improving Post-ischemic Microcirculation And Inflammation

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ADAMTS13 (A Disintegrin And Metalloproteinase with ThromboSpondin type-1 motifs 13) specifically cleaves the bond between tyrosine-1605 and methionine-1606 in the A2 domain of von Willebrand factor (VWF) multimer and thus reduces its prothrombotic and proinflammatory activities. VWF can activate platelets and leukocytes on the stimulated vascular endothelial cells. These activated platelets and leukocytes together contribute to both microcirculation impairment and inflammatory reactions after reperfusion in the ischemic brain. Therefore, ADAMTS13 may ameliorate the ischemia-reperfusion injury of the brain by cleaving the VWF. We investigated the role of ADAMTS13 in the ischemia-reperfusion pathology in the brain with using middle cerebral arterial occlusion (MCAO) model of ADAMTS13-gene-knockout mice. The ADAMTS13-deficient (ADAMTS13 KO) and wild-type (WT) mice were subjected to 30 minutes' MCAO followed by 23.5-hour reperfusion. The infarct volume was estimated on the brain tissue stained with TTC 23.5 hours after reperfusion. Plasma HMGB1 (high-mobility group box1) level was analyzed by Westernblot 24 hours after MCAO. The immunoreactivity of the ischemic brain tissue against HMGB1/NeuN or HMGB1/MPO (double immunofluorescent labeling) was also analyzed. The regional cerebral blood flow (rCBF) of the ischemic cortical tissue was measured by laser Doppler flowmetry during the period between 30 minutes before and 24 hours after MCAO. We also investigated if infarct volume after MCAO was reduced by intravenous infusion of ADAMTS13 protein in mice stroke model. ADAMTS13 KO mice had increased volume of brain infarction compared with WT. The plasma HMGB1 increased more in ADAMTS13 KO mice than in WT after MCAO. Ischemia induced more remarkable neuronal death and more inflammatory cells expressing HMGB1 in ADAMTS13 KO-mice cortical tissue compared to WT. The rCBF in ADAMTS13 KO mice progressively decreased more remarkably than that in WT during reperfusion phase after ischemia. In addition, extrinsic ADAMTS13 reduced infarct volume in mice after MCAO. ADAMTS13-gene-deletion aggravates brain damage, systemic and local inflammatory responses, and rCBF after ischemia-reperfusion. ADAMTS13 administration improves ischemic brain injury. This suggests that ADAMTS13 plays a possible neuroprotective role against brain ischemia by regulating the VWF-dependent thrombosis and inflammation in the reperfusion injury.

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W P200

Cytokine Expression in the Brains and Serum of MyD88-/- and TRIF mutant mice following permanent Middle Cerebral Artery Occlusion

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Background: Toll-like Receptor (TLR) signaling plays an important role in cerebral ischemia. To better understand the downstream TLR signaling events, we determined downstream effector cytokine/chemokine expression in mice with deletions or mutations of the two major adaptors of the TLR signaling pathway using a model of focal ischemia. **Methods:** We examined the cytokine expression profile in the brains and serum of MyD88 -/-, TRIF mutant and wild type (WT) mice at baseline, 3 and 24 h following permanent Middle Cerebral Artery Occlusion (pMCAO) using the 25-plex mouse cytokine/chemokine bead array. We also evaluated neutrophil infiltration in the brains of MyD88-/- and TRIF mutant mice and WT mice 24h after pMCAO. **Results:** The most striking differences were in serum IL-6 levels 3h after pMCAO; MyD88-/- , 14.7 ± 3.4 pg/ml, TRIF mutant; 88.3 ± 54.7 pg/ml and WT mice;172.6± 23.6 pg/ml; (p=0.027). Similar differences, with lower serum IL-6 levels, were detected 24h after pMCAO; MyD88-/-, ~ 2.5± 3.7 pg/ml, TRIF mutant; ~19.0± 16.2 pg/ml and WT mice; 44.7 ±12.6 pg/ml ;(p=0.05). In addition, brain and serum Interferon-inducible Protein 10 (IP-10) expression, which occurs primarily via the TRIF pathway, were significantly lower in TRIF mutant mice compared to MyD88-/- and WT mice. Brain IP-10 at 3h: TRIF mutant mice; 710.5 ± 223.0 pg/ml/g, MyD88-/- mice; 1087.5± 190.4 pg/ml/g and WT mice; 2077.2 ± 803.6 pg/ml/g; (p= 0.049). Serum IP-10 at 24h: TRIF mutant, 94.2 ± 19.9 pg/ml, MyD88-/- , 120.8 ± 26.6 pg/ml and WT, 156.1 ± 11.2 pg/ml; (p=0.049). Neutrophil chemoattractants, Keratinocyte Chemoatracttant (KC) and Granulocyte Colony Stimulating Factor (G-CSF) were also markedly lower in the serum and brains of MyD88-/- mice following pMCAO compared to WT and TRIF mutant mice and corresponded with a strong trend towards fewer neutrophils/field in the brains of MyD88-/- mice; 8.3±9.3 compared to WT, 17.3±8.0, and TRIF mutant, 35.2± 24.3 following pMCAO. **Conclusions:** The pattern of inflammatory chemokine/cytokine expression in MyD88-/- and TRIF mutant mice, following focal cerebral ischemia, is consistent with the phenotypes expected following disruption of either pathway. In addition, neutrophil chemoattractants, KC and G-CSF are produced in a MyD88-dependent manner and may direct neutrophil migration to the site of ischemia after pMCAO. Nevertheless, the less pronounced inflammatory environment in MyD88-/- mice does not confer protection in cerebral ischemia. Therefore these results suggest the possibility of another, yet-to-be determined, TLR signaling pathway involved in production of damaging mediators during cerebral ischemia.

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W P201

Rapamycin Enhances Autophagic Mediated Protection in a Permanent Middle Cerebral Artery Ligation Stroke Model

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Background: Under stress conditions, including nutrient depravation and ischemia, autophagy promotes cell survival by recycling proteins and organelles through lysosomes. Excessive autophagy, however, can lead to cell death, including apoptotic (PCD type I) and autophagic cell death (PCD Type II). During stroke, it is unclear whether autophagy promotes neurovascular unit cell survival or death. We hypothesized that increased autophagy after stroke is "protective" and that inducing autophagy by pharmacologic agents would reduce infarct size. **Methods:** We induced ischemia in C57BL/6J mice using a permanent MCA ligation model, with sacrifice 48 hours or 7 days after stroke. Mice were treated i.p. with chloroquine (30, 60, or 90 mg/K/d for 2 days), an autophagy inhibitor, rapamycin (1.25 or 2.5 mg/K/d for 2 days), an autophagy activator via inhibition of mTOR, or treated with vehicle (saline or 10% DMSO in 100 ul). The autophagy markers LC3 p62 and Beclin-1 were analyzed by Western blot and immunohistochemistry, additional Markers included Bcl2, and infarct size was measured by TTC staining. **Results:** Chloroquine at 30, 60 and 120 mg/kg reduces lesion size in a U shaped function between 28 & 34% ($p>0.01$). Rapamycin reduced lesion size 64.0% at 1.25 mg/kg and 62.5% at 2.5 mg/kg. The reduction in lesion size for chloroquine and the 10 mg/kg rapamycin was statistically significant (Kruskal-Wallis One Way ANOVA $p=0.016$). LC3 is decreased in the infarct side, suggesting turnover of LC3 by the fusion of autophagosomes and lysosomes. P62 increased, suggeating increased chaparone mediated clearance of damaged protein aggregates. Chloroquine increased LC3 by preventing its turnover and had no significant change on p62 levels. Rapamycin led to increased LC3 and p62, consistent with increased induction of autophagy. Summary: 1) Stroke increases autophagy and Bcl2 levels. 2) Since chloroquine and rapamycin both decreased lesion size, this suggests cross-talk between autophagy and other programmed cell death pathways and/or direct effects of the drugs on such pathways. 3) Modulation of autophagy may offer a new therapeutic avenue for stroke.

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W P202

Preconditioning Induces Sustained Neuroprotection by Inhibition of AMPK

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Background: Brief non-injurious cerebral ischemia (Ischemic preconditioning) induces neuroprotection and protects the brain from subsequent injury, a process also known as ischemic tolerance. We have previously shown that Adenosine monophosphate-activated protein kinase (AMPK), a key regulator of energy balance, is increased following stroke. This enhanced AMPK activity is detrimental in stroke as AMPK inhibition or genetic deletion of AMPK is neuroprotective. The objective of this study was to determine if ischemic preconditioning alters AMPK activity and thus induces sustained neuroprotection. **Methods:** Focal ischemia was induced by reversible middle cerebral artery occlusion (MCAO- non-injurious-3min (IPC); injurious-90 minute (referred as stroke hereafter)) in mice (male, 20 to 25 g; C57BL/6N, Charles River Laboratories). Stroke was performed 72 hours after IPC or sham surgery. Compound C (i.p 5mg/kg), an AMPK inhibitor (Calbiochem, San Diego, CA) was given at the onset of stroke. Different cohorts were used for infarct analysis ($n=8$/group) or molecular studies ($n=4$/group). Infarct volume was analyzed by TTC at 24hrs post-stroke. Protein levels were expressed as a ratio to a control actin band after densitometry analysis. **Results:** Three minutes of MCAO caused no visible injury; IPC 72 hrs before stroke induced significant neuroprotection (Total infarct: 33.1 ± 3.9; $n=7$) compared to stroke (Total Infarct: 45.01 ± 3.4; $n=8$) $P<0.05$. In addition, these improvements were correlated with changes in AMPK activity in WT mice. Preconditioning activated AMPK at 4 hrs (Sham-operated 4hrs 0.43 ± 0.22; IPC 4hrs 0.71 ± 0.13), but decreased AMPK activity at 72 hrs (Sham 72hrs 0.45 ± 0.18, IPC 72 hrs 0.32 ± 0.13; stroke 0.83 ± 0.11; IPC+ stroke 0.52 ± 0.16). Interestingly, Compound C treatment abolished the beneficial effects of IPC, Compound C (35.71 ± 4.11; $n=6$/gp) IPC+ compound C (33.28 ± 4.74; $n=6$/gp. $p>0.05$). **Conclusions:** Preconditioning is neuroprotective. IPC activated AMPK at early time points; however it reduced AMPK activation at 72 hours compared to sham IPC mice. Mice subjected to IPC had reduced AMPK activation after stroke. The effect of IPC is abolished in compound C treated mice. In conclusion, these studies suggest that AMPK plays an important role in mediating the beneficial effects of ischemic preconditioning. AMPK inhibition ameliorates ischemic tolerance.

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W P203

A Role For Spleen CCR2+ Monocytes In Stroke-Induced Injury In Hyperlipidemia

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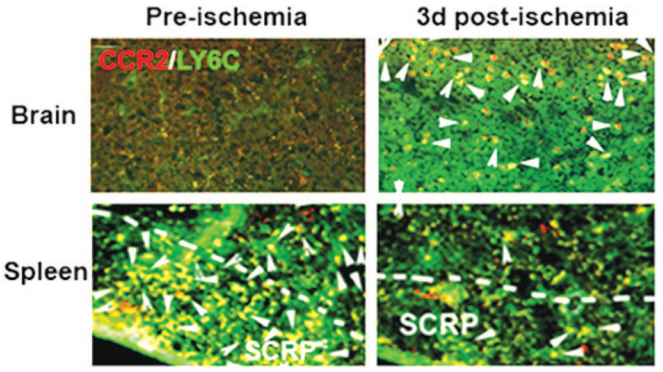
Infiltration of peripheral monocytes/macrophages is implicated in stroke pathology. However, *in vivo* evidence regarding monocyte deployment and mobilization to the infarct area is scarce. Recent studies indicate that hyperlipidemia, a prevalent co-morbid condition, increases the number of pro-inflammatory (CCR2+/LY6C^{hi}), but not anti-inflammatory (CCR2-/ LY6C^{low}) monocytes. In addition, we have previously reported that hyperlipidemia increases infarct size and pro-inflammatory inflammatory markers in the brain and peripheral macrophages. The present study investigates whether CCR2+/LY6C^{hi} monocytes in the spleen, an important reservoir for monocytes deployment upon injury, contribute to stroke pathology. Male wild type mice fed normal chow (WT) and ApoE KO mice fed a high fat diet (AKO) for 8 weeks were subjected to 30 min transient middle cerebral arterial (MCA) occlusion and subsequent infarct size and CCR2 expression in the brain and spleen were determined. FACS analysis prior to ischemia showed an increased number of CCR2+ monocytes in the spleen from AKO mice compared to WT (22.4 vs 11.9%). Three days after ischemia, both mice exhibited a significant reduction in spleen size ($p<0.001$) with a greater reduction in AKO mice relative to WT (30.7 vs.14.3%). Correlation among infarct volume, spleen weight, and brain CCR expression revealed that the larger the injury induced in AKO mice, the greater the reduction in spleen size ($p<0.001$ $n=9$), and the higher the expression of CCR2 in the post-ischemic brain ($p<0.001$, $n=13$). No such correlations were observed in WT mice. In AKO mice, stroke increased CCR+/LY6C+ monocytes (yellow indicated by arrowheads, upper right panel) in the infarct territory at 3 days whereas the number of cells were reduced in the subcapsular red pulp (SCRP) of spleen, a region where monocytes are clustered (lower panel). This study indicates that CCR2+ monocytes are deployed from the spleen following focal cerebral ischemia and contribute to stroke-induced inflammation and injury. The previously unrecognized role of spleen monocytes in cerebral ischemia suggests a novel strategy to limit ischemic brain injury by targeting CCR2 in peripheral monocytes.



Author Disclosures: E. Kim: None. Y. Bao: None. L. Qin: None. S. Cho: None.

W P204

MSCs Decrease TGF β1 Expression In Microglia Which Downregulate Astrocytic PAI-1 Expression After Stroke

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Introduction: Endogenous tissue plasminogen activator (tPA) activity promotes neurite remodeling after stroke. Astrocyte-derived plasminogen activator inhibitor-1 (PAI-1) modulates tPA activity in brain. We have previously shown MSCs decrease astrocytic transforming growth factor beta1 (TGF β1) expression which subsequently decreases the PAI-1 level in an autocrine manner in the ischemic brain; however, the role microglia as a source of TGF β1 and PAI-1 regulation has not been investigated. **Materials and Methods:** Adult C57BL/6 mice were subjected to permanent middle cerebral artery occlusion (MCAo) followed by injection of 1×10^6 MSCs ($n=6$) or phosphate-buffered saline ($n=6$) into the tail vein 24 hrs later. Animals were sacrificed at 14 days after stroke and paraffin slides were used for immunostaining. In vitro coculture systems with MSCs, astrocytes and microglia were also employed, and were subjected to oxygen and glucose deprivation (OGD) to mimic the ischemic condition. Western blot and RT-PCR were employed to detect the gene expression in protein and mRNA level. **Results:** At day 14 after stroke, activated microglia aggregated in the IBZ and highly expressed TGF β1, and MSC treatment significantly decreased TGF β1 expression in microglia ($32.0\pm4.3\%$, $P<0.05$). In vitro, RT-PCR results showed TGF β1 mRNA level in both astrocytes (C8-D1A, ATCC, CRL-2541) and microglia (EOC 20, ATCC, CRL-2469) were increased after OGD ($97.2\pm14.1\%$ and $162.3\pm24.5\%$, respectively, $P<0.01$) compared to normoxic conditions, and coculture of astrocytes and microglia significantly increased TGF β1 levels under normal ($27.2\pm11.2\%$ and $62.5\pm14.3\%$, in astrocytes and microglial cells, respectively, $P<0.05$) and OGD conditions ($87.1\pm24.3\%$ and $131.7\pm34.8\%$, in astrocytes and microglial cells respectively, $P<0.01$). Addition of MSCs into the astrocyte and microglial coculture system significantly decreased the TGF β1 mRNA level in normal ($47.3\pm17.2\%$ and $43.7\pm14.1\%$, in astrocytes and microglial cells, respectively, $P<0.01$) and OGD conditions ($73.7\pm24.8\%$ and

77.3±14.3%, in astrocytes and microglial cells, respectively, P<0.01). PAI-1 mRNA was below the threshold of detection in microglia. OGD or coculture of astrocytes with microglia increased the PAI-1 mRNA in astrocytes, and addition of MSC to the coculture significantly decreased PAI-1 level in microglia cocultured astrocytes under OGD conditions (52.5±13.3%, P<0.01). Western blot results also confirmed the similar protein level changes in astrocytes and microglia. **Conclusions:** MSCs decrease TGF â1 expression in IBZ microglia which contribute to the downregulation of PAI-1 level in astrocytes.

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W P206

Aggressive Blood Pressure Control with Clevidipine in Patients with Acute Intracerebral Hemorrhage is Rapid and Well Tolerated: The ACCELERATE Trial

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Introduction: Clevidipine, a rapidly-acting, vascular-selective, L-type dihydropyridine calcium channel blocker, lowers blood pressure (BP) by reducing systemic vascular resistance and has a pharmacokinetic half-life of approximately 1 minute. The ACCELERATE trial evaluated blood pressure (BP) reduction with IV clevidipine in patients with acute intracerebral hemorrhage (ICH). **Methods:** Patients presenting with symptoms of ICH within 12 hours and systolic BP (SBP) >160 mmHg were enrolled and treated with open-label IV clevidipine. Clevidipine was started at 2.0 mg/h and titrated every 90 seconds until SBP ≤160 mmHg was achieved, then titrated to keep SBP between 140 to 160 mmHg. Glasgow Coma Scale (GCS) score, NIH Stroke Scale (NIHSS) score, and hematoma volume were measured. **Results:** Thirty-five patients (27 men, mean age 64 years) were enrolled and received clevidipine. Prior to treatment, median GCS score = 14, median NIHSS score = 13, mean hematoma volume = 29 mL, mean SBP = 186 mmHg and mean diastolic BP = 85 mmHg. Mean time to infusion from symptom onset was 5.5 hours. Mean on-drug infusion duration from initiation to end of treatment was 28 hours. For patients who met study criteria (n=33), median time to achieving target SBP (<=160 mmHg to >=140 mmHg) was 5.5 min (95% CI 3,10). All patients achieved SBP ≤160 mmHg within 30 min, and 97% did so without additional or alternative antihypertensives. At 6 hours after termination of infusion, mean change in NIHSS score was 1.6 (mean baseline 13.7, post-baseline 15.3); and mean change in GCS score was -1.4 (mean baseline 12.9, post-baseline 11.5). Minimal intracerebral hematoma volume change was observed after SBP reduction with clevidipine. In patients requiring intracranial pressure (ICP) monitoring, cerebral perfusion pressure was maintained in an optimal range and no meaningful increases or other changes in ICP were observed. No patients had SBP <90 mmHg within 30 min after clevidipine initiation. Adverse events (AEs) were consistent with previous clinical experience; the most common was pyrexia (7 patients). Hypotension was reported as an AE for 3 patients; BP increased with resolution of AE after clevidipine dose was reduced or the infusion stopped. **Conclusions:** Clevidipine rapidly and effectively reduces BP in patients with acute ICH and was well tolerated in ACCELERATE patients (n=35), with evidence of a good safety profile consistent with previous experience in other clinical settings. Minimal changes were observed in GCS and NIHSS at 6 hours post-discontinuation and in hematoma volume on 24-hour CT scans.

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W P207

A Low Proportion of Patients with Intracerebral Hemorrhage Meet the Eligibility Criteria of the Surgical Trial in Intracerebral Hemorrhage II Study

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Background: Spontaneous supratentorial intracerebral hemorrhage (ICH) is a devastating condition with a high morbidity and mortality, and optimal management of the condition remains controversial. The Surgical Trial in IntraCerebral Hemorrhage II (STICH II) study was initiated to look at the role of early surgery versus conservative management for individuals with superficial lobar ICH, as the initial STICH trial showed the greatest benefit from early surgery in this subgroup. STICH II commenced in November 2006 with the aim of recruiting 600 patients, but as of June 2010 only 329 have been recruited worldwide. Even at the co-ordinating centre, Newcastle upon Tyne, where recruitment is highest, only 29 have been recruited. Despite our best efforts we have failed to recruit to STICH II. The aim of this study was to assess the reasons for poor recruitment overall and, in particular, at our centre. To do this, we estimated how many patients with ICH referred to the Greater Manchester Neurosciences Centre (GMNC) met the inclusion and exclusion criteria of the STICH II trial. **Methods:** The number of patients eligible for STICH II was determined from the GMNC neurosurgical referral database and from admissions to the local Stroke Unit over one year (January 1st to December 31st 2008). The referral database is a prospectively recorded database of all patients referred to the on-call neurosurgery service (catchment area 3.2 million). Eligibility was determined by the predefined STICH II inclusion and exclusion criteria, and equipoise was agreed by two neurosurgeons. **Results:** Of the 434 ICH referrals in 2008, 168 (38.7%) were lobar ICH; 53 (31.5% of lobar ICH) of these met the radiological and GCS criteria for STICH II, but only 16 (9.5% of lobar ICH; 3.7% of all ICH) had equipoise agreed on by two neurosurgeons. Thirty-five ICH patients were admitted to the Stroke Unit, and twelve (34.3%) of these had lobar ICH; none were eligible for STICH II when accounting for the radiological and GCS criteria. These figures suggest that only 360 of the almost 10,000 patients who suffer an ICH each year in the UK would be eligible for recruitment into STICH II. **Conclusions:** The number of patients meeting the eligibility criteria for recruitment into STICH II is small, in part because of the difficulty in establishing equipoise - a well-recognized problem in neurosurgical clinical trials. Time constraints in a busy neurosurgical emergency referral system undoubtedly exacerbate recruitment problems. Overall, this necessitates an aggressive recruitment approach for STICH II, focusing on neuroscience centers with neurosurgical units.

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W P208

Genome Wide Association Study of Intracerebral Hemorrhage

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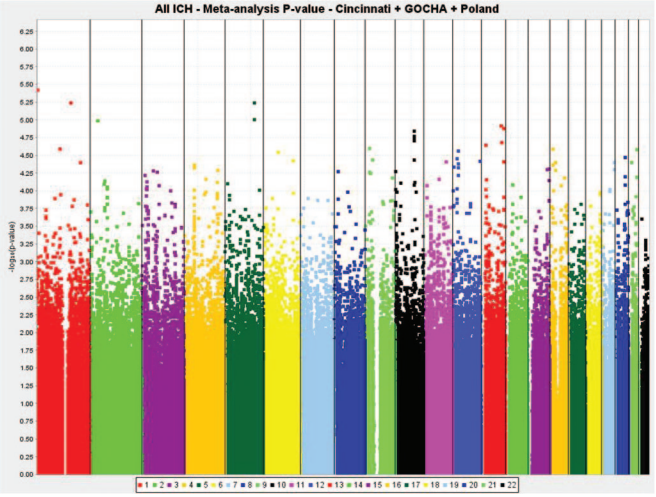
A genetic predisposition to spontaneous intracerebral hemorrhage (ICH) is well established. Genome-wide association studies (GWAS) are underway in Caucasian ICH cases from population and multi-center based studies. We report the results of a GWAS meta-analysis for all, lobar and deep ICH. **Methods:** The Genetic and Environmental Risk Factors for Hemorrhagic Stroke study prospectively recruits cases of ICH in the Greater Cincinnati/Northern Kentucky area and identifies controls through random digit dialing. Cases and controls were collected by buccal swab and were genotyped using the Affymetrix 6.0 platform. The Genetics of Cerebral Hemorrhage on Anticoagulation (GOCHA) Study is a multi-center US-based study recruiting ICH cases from hospital-based cohorts and controls from the same institutions. ICH cases and community-dwelling controls were contributed by the Jagiellonian University (Krakow, Poland) ICH Study. Controls for all 3 groups were matched by age (+/-5 yr), race and sex. The GOCHA and Jagiellonian cases and controls were genotyped using the Illumina 650 platform. Quality control analyses included batch effects, missing data, genetic outliners and HWE. Data were imputed using Impute 2.0 and HapMap 3 CEU data. The meta-analysis is based on an additive model using the inverse normal method weighted by respective sample size. All analyses were adjusted for admixture, age, sex, and high cholesterol. In addition, ICH was adjusted for hypertension (HTN), warfarin, and apolipoprotein E4 (APOE4); lobar was adjusted for APOE2 and APOE4; and deep was adjusted for HTN. **Results:** A total of 772 ICH cases and 872 controls including 326 lobar and 383 deep ICH cases were genotyped; 301/333 ICH cases/controls on Affymetrix 6.0 and 471/539 cases/controls on Illumina 1M. No regions reached genome-wide significance in meta-analysis or individual analyses. The Figure presents the $-\log_{10}$(p-value) for association with all ICH by genomic location. For a minor allele frequency of 0.2 and a type 1 error rate of 5x10E-7, our meta-analysis had 0.80 power to detect an OR=1.6 for ICH; OR=1.85 for lobar; and OR=1.80 for deep. Genomic control inflation factor was 1.01. **Conclusion:** In the largest GWAS of ICH reported to date, no association with a large effect size for ICH was identified after adjustment for multiple comparisons. This is consistent with ICH having a complex etiology with multiple smaller risk factors. The analysis demonstrates feasibility of collaboration between the study groups to enhance power to identify smaller effect sizes.



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W P209

Spatial Trajectory of Hematoma Enlargement Predicts Clinical Deterioration and Mortality in Patients with Acute Intracerebral Haemorrhage

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Background: Early hematoma growth (HG) has been shown to be an independent determinant of death and disability after intracerebral haemorrhage (ICH). Depending on ICH location, a predominant spatial growth direction may affect functionally critical and clinically eloquent structures leading to early clinical worsening. We aimed to investigate the spatial HG behaviour and the impact of the main HG trajectory on clinical course and outcome in patients with acute ICH. **Methods:** We prospectively studied patients with acute primary supratentorial ICH evaluated $<$ 6 hours of symptom onset. Patients underwent baseline ($<$6h) and 24h CT scans, and a CTA ($<$6h) for the blinded detection of spot sign (SS). ICH volumes were measured at baseline ($<$6h) and follow-up (24h) CT scans. ICHs were classified as lobar, basal ganglia, thalamic, or multiple locations. The main 3-dimention ICH diameters were calculated at baseline and follow-up CTs, the largest longitudinal (L) and transversal (T) diameters in the axial plane and the largest altitudinal (A) diameter in the coronal. HG trajectory (mm) was calculated from each 3-D ICH diameter. Early neurological deterioration (END) was defined as increase $\geq$4 points in the NIHSS score or death at 24 hours. 90-day mortality was recorded. **Results:** A total of 138 acute primary supratentorial ICH were included in this study. 31.4% of them were lobar, 38% were located in basal ganglia, 17.5% in the thalamus, and 13.1% in multiple locations. Mean baseline ICH volume was 28.8 $\pm$ 35.1 mL. HG occurred in 49 (35.3%) patients. The trajectory of HG was significantly larger in the L (2.89 $\pm$ 0.49 mm) compared to T (1.8$\pm$ 0.51 mm) and A (2.1$\pm$ 0.56 ml) hematoma diameters (p=0.004, Krusskal-Wallis test). L trajectory of HG was significantly correlated with a higher degree of clinical worsening in lobar (r=0.59; p=0.002) and basal ganglia (r=0.61; p=0.001) hematomas, while T trajectory was associated with clinical worsening in thalamic hematomas (r=0.67; p=0.017). Only L growth $>$2.7mm (sensitivity 69%, specificity 71%) was significantly (p$<$0.001) associated with 3-month mortality. CTA SS was seen on 26 (19%) patients. CTA SS was internally and externally located in 8 (30%) and 18 (70%) patients, respectively. Distribution of CTA SS strongly predicted the main trajectory of HG. In 91% of patients, growth trajectory followed the location of CTA SS. Among patients with lobar and basal ganglia hematomas, CTA SS located along the L diameter was significantly (p=0.034) associated with early clinical deterioration. **Conclusions:** In patients with acute ICH, the spatial behaviour of HG may predict early clinical course. L trajectory of HG predicts clinical deterioration and mortality in lobar and basal ganglia ICHs. The presence and distribution of CTA SS heralds the main direction of HG and its longitudinal distribution predicts clinical worsening.

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W P210

The Effect Of Leukoaraiosis Burden On Admission Hematoma Volume And Hematoma Growth In Patients With Spontaneous Intracerebral Hemorrhage

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Background: Hematoma expansion occurs in approximately one-third of patients presenting with intracerebral hemorrhage (ICH). The disruption of the neighboring secondary vessels around the primary vascular rupture site has been implicated as one of the contributing factors to hematoma expansion. Leukoaraiosis (LA), an established risk factor for ICH, is pathologically characterized by arteriosclerotic changes in cerebral vessels, enhanced capillary permeability and impaired blood brain barrier functions, all of which in theory might favor secondary vascular rupture and therefore increase the risk for hematoma expansion. On the other hand, the lower capillary density and increased gliosis observed in brains with LA might prevent this domino effect. In this study our aim was to assess the effect of LA burden on admission hematoma volume and hematoma expansion in patients with spontaneous ICH. **Methods:** A consecutive series of patients with a diagnosis of ICH and admission computed tomography (CT) imaging within 24 hours of symptom onset and a follow-up CT imaging within 72 hours symptom onset were included into the study. LA burden was determined by using the Fazekas scale on admission CT images. Hematoma volume was calculated by using the ABC/2 method. Significant hematoma growth was defined as an increase of $\geq$33% or 12.5 mL with respect to baseline volume. Spearman's correlation and chi-square tests were used to assess the bivariate relationships between LA burden and outcome variables (admission hematoma volume and hematoma expansion). Multivariable models were developed to analyze the independent effect of LA burden on outcome variables. **Results:** The study population comprised of 116 patients (70 male, 46 female). Neither the periventricular LA burden (p=0.50), nor the subcortical LA burden (p=0.66) showed any correlation with admission hematoma volume. A total of 26 patients (22%) had significant hematoma expansion on follow-up. Periventricular and subcortical LA burden was similar between patients with and without significant hematoma expansion (p=0.52 and p=0.87, respectively). A relationship between LA volume and admission hematoma volume or hematoma expansion was also not evident in multivariable models. **Conclusion:** We were unable to show any association between the amount of LA and hematoma volume or expansion. Further studies with larger number of patients and volumetric LA measurements are needed to totally negate the role of LA as a determinant of admission hematoma volume or hematoma expansion in the setting of ICH.

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W P211

Charlson Comorbidity Index Independently Predicts Long-term Functional Outcome in Patients after Intracerebral Hemorrhage

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Objective: Medical comorbidities are common in patients with intracerebral hemorrhage (ICH). While it seems reasonable that comorbid conditions influence recovery from ICH, studies of early mortality and long-term outcome have not systematically included adjustment for comorbid conditions. In fact, there is currently no standard method of assessing patient comorbidities for ICH studies. The Charlson Comorbidity Index (CCI) is a tool commonly used in outcome studies for other diseases and has been validated across many conditions, including ischemic stroke. The CCI is determined as the sum of point values ascribed for various patient comorbid conditions. The purpose of this current study was to assess whether the CCI could be determined in a cohort of ICH patients and whether it was associated with long-term outcome independent of other commonly assessed predictors. **Methods:** We performed a prospective observational cohort study of all patients with ICH admitted through the emergency departments at two UCSF hospitals from 6/1/2001-5/31/2004. Components of the ICH Score (admission Glasgow Coma Scale score, initial hematoma volume, presence of intraventricular hemorrhage, infratentorial ICH origin, and age) were recorded along with other clinical, neuroimaging, and in-patient care parameters. Outcome was assessed using the modified Rankin Scale (mRS) at multiple time points post-ICH out to 12 months. The CCI was derived by using information from hospital discharge ICD-9 CM codes as well as patient history obtained during the acute ICH hospital admission. CCI scores were categorized as 0, 1, 2, and 3 or greater. In order to assess whether the CCI was independently predictive of long-term outcome, multivariable ordinal logistic regression was performed adjusting for components of the ICH Score as well as the use of early DNR orders (within the first hospital day). **Results:** A total of 243 patients were included in the study with CCI scores of 0 (36.2%), 1 (25.5%), 2 (16.1%), and 3 or greater (22.2%). Only twenty eight percent of patients with high CCI scores ($\geq$3) achieved a 12-month mRS of 3 or better (disabled but ambulatory) compared with 49% of patients with CCI scores of 0 (p=0.011). High CCI ($\geq$3) was independently predictive of 30-day mortality (OR 8.8, p=0.026) even after adjustment for the above described predictors and withdrawal of medical support. CCI was also independently predictive of worsened 12-month functional outcome, with higher CCI having a greater impact (CCI=2, OR=2.3, p=0.062; CCI $\geq$3, OR=3.5, p=0.001). **Conclusion:** The Charlson Comorbidity Index can be determined in patients with ICH and is independently associated with early mortality and long-term functional outcome. This effect is independent of the use of early DNR orders or withdrawal of support and therefore is unlikely to be principally due to physician use of early care limitations.

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W P213

Prediction of 1 Year Functional Outcome in Patients With Intracerebral Hemorrhage: The "Functional ICH Score"

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Objectives: The ICH score was developed to predict 30-day mortality after intracerebral hemorrhage (ICH). We aimed to design a model to predict 1 year functional outcome after ICH and compare its performance with the ICH score (acknowledging that the latter was not designed for this purpose). We hypothesized that admission NIH Stroke Scale (NIHSS) is a more powerful outcome predictor than admission Glasgow Coma Scale (GCS). **Methods:** The DASH study is a prospective NIH funded study assessing the diagnostic utility of brain MRI in spontaneous ICH or intraventricular hemorrhage (IVH). We evaluated the association of baseline variables with 12-month poor outcome (i.e. modified Rankin scale (mRS) $\geq$4) and with mortality using logistic regression. Variables significant in the univariate analysis at $\alpha<0.2$ were entered in the multivariate analysis and kept in the model at $\alpha<0.01$. **Results:** Of 166 prospectively enrolled patients, 138 had a 1 year mRS score and were included in the analysis. Baseline characteristics were: age 63$\pm$17 years, 49% females, IVH in 44%, median (IQR) hematoma volume (HV) 15 (6-38) mL, admission GCS 14 (9-15), and admission NIHSS 8 (2-17). Overall mortality rate was 27%, and 46% of patients had a poor outcome at 1 year. In the univariate analysis, history of hypertension, age, HV, IVH, GCS, NIHSS and history of coagulopathy/thrombocytopenia predicted poor outcome and mortality, while hemorrhage location (deep versus other) and diabetes predicted only poor outcome. In the multivariate analysis, age and NIHSS were the strongest independent predictors of poor outcome and mortality: OR = 2.2 and 1.7 ($p<0.001$) with increase of NIHSS by 5 points; and OR=2.6 and 1.8 ($p<0.001$) for 10 years of age increase, respectively. In addition, IVH (OR=3.8, p=0.01), deep location (OR=9.5, $P<0.001$), and coagulopathy/thrombocytopenia (OR=2.8, p=0.089) independently predicted poor outcome. The sum-score points of a 6 point "functional ICH score" were: NIHSS (0-8=0, 9-19=1, $\geq$20=2), age (<70 = 0, $\geq$70 = 1), IVH (no=0, yes=1), hemorrhage location (deep=1, other=0) and coagulopathy/thrombocytopenia (no=0, yes=1). The "functional ICH score" predicted poor outcome at 1 year better than the ICH score: area under ROC curve 0.85 and 0.73, respectively (p=0.044). No patient with a "functional ICH score" =0 had poor outcome and no patient with a score of 4 or 5 had good outcome compared to 22% poor outcome in patients with an ICH score =0 and 25% good outcome with a score =4. Both scores performed similarly in predicting mortality. **Conclusions:** The "functional ICH score" may be a useful tool to help predict 1 year functional outcome after ICH. Age and admission NIHSS (rather than GCS) are strong predictors of outcome at this time point. Future studies are needed to validate these findings.

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W P214

Hematoma Expansion in Anticoagulant Associated Intracerebral hemorrhage Despite Prothrombin Complex Concentrate Treatment

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Background: Anticoagulant associated intracerebral hemorrhage (AAICH) has high mortality rate and poor neurological outcome. Rapid reversal of anticoagulation remains the cornerstone of medical therapy. Prothrombin complex concentrate has been shown to rapidly reverse coagulopathy. We aim to determine whether rapid INR reversal with PCC decreases the rate of hematoma growth in patients with AAICH. **Methods:** We conducted a prospective study in patients presenting with acute AAICH who received PCC. All patients had standardized CT assessment 24 hours after treatment. Hematoma volume was planimetrically measured on serial scans. Rates of hematoma expansion were compared to control patients with acute AAICH presenting in the two year period prior to approval of PCC for treatment of AAICH. Patients in the control group received fresh frozen plasma (FFP) and/or vitamin K and also underwent follow-up CT scan. The goal of therapy was an INR1/3 from baseline. **Results:** A total of 16 patients received PCC and 19 were treated with FFP/vitamin K. The median GCS in the PCC 15 (IQR= 2) and control 14 (IQR=4) groups was comparable (p=0.31). Baseline International Normalized Ratio (INR) was also similar in the PCC (3.7, IQR=2) and control groups (3, IQR=2, p-0.47). The PCC and control groups were balanced with respect to time from onset to baseline scan (236min, IQR= 355min vs 325 min, IQR=744 min, p=0.15) and baseline hematoma volume (median=21.2 ml, IQR= 43.6 vs median=25.9, IQR=74.2,p=0.64). Treatment with PCC resulted in a more rapid INR correction (128.5 min, IQR=617) than FFP/vitamin K (540min, IQR=730, p=0.005). Hematoma expansion rates were not different in PCC treated (4/16, 25%) and FFP/vitamin K treated patients (2/19, 10.5 %, $\lambda 2$ =0.46, p= 0.50). There was a trend towards higher absolute hematoma expansion volumes in PCC treated patients (mean= 8.3$\pm$13.0 ml) relative to the FFP/vitamin K group (-3.28 ml$\pm$13.9 ml, p=0.07). Multivariate regression analysis did not reveal a relationship between baseline INR (R= 0.4, p=0.43), GCS (R=0.1, p=0.65, systolic blood pressure (R= 0.2, p=0.29), age (R=0.07, p=0.27) or PCC treatment (R= -0. 5, p= 0.67) and significant hematoma expansion. **Conclusion:** Although PCC is associated with rapid reversal of INR, hematoma expansion remains frequent. Correction of the INR is necessary in AAICH treatment, but may not be sufficient to prevent expansion in all patients. A randomized controlled trial of PCC versus FFP/vitamin K in AAICH is warranted.

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W P215

Dynamic Cerebral Autoregulation Is Impaired After Acute Intracerebral Hemorrhage

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Introduction: The understanding of cerebral autoregulation status after intracerebral hemorrhage (ICH) is important in maintaining optimal cerebral blood flow to the perihematoma penumbra. However, there are limited and conflicting data available on dynamic cerebral autoregulation after ICH. Hypothesis: We assessed the hypothesis that dynamic autoregulation is less effective in patients with acute ICH compared to community-dwelling healthy subjects by performing a case-control study. **Methods:** Twenty-one patients (66$\pm$15 years) with acute ($<$72 hours) lobar or basal ganglia ICH were prospectively studied and compared to twenty-three age-matched controls (65$\pm$9 years). Continuous measures of mean flow velocity (MFV) in the middle cerebral artery (MCA) and mean arterial blood pressure (MAP) were obtained over 5 min. Cerebrovascular resistance index (CVR_i) was calculated as the ratio of MAP to MFV. Dynamic autoregulation was assessed using transfer function analysis of spontaneous MAP and MFV oscillations in the very low (0.03-0.07 Hz) and low (0.07-0.15 Hz) frequency ranges. Inter-group differences in cerebrovascular hemodynamics were tested using *t*-test. Within the ICH group, intra-individual differences in MFV, transfer function coherence, gains, and phases between the ipsilateral and contralateral sides were tested using a repeated measures two-way ANOVA. An interaction between hemispheric differences and hematoma size was ascertained by using hematoma size as a covariate. **Results:** The ICH group demonstrated higher CVR_i compared to controls (ipsilateral: 1.91$\pm$1.01 mmHg·s·cm^{-1}, p=0.04; contralateral: 2.01$\pm$1.24 mmHg·s·cm^{-1}, p=0.04; vs. control: 1.42$\pm$0.45 mmHg·s·cm^{-1}). The ICH group had higher gains than controls in the very low (ipsilateral: 1.10$\pm$0.35 %^{2}/mmHg^2, p=0.03; contralateral: 1.20$\pm$0.85 %^{2}/mmHg^2, p=0.08; vs. control: 0.84$\pm$0.40 %^{2}/mmHg^2) and low (ipsilateral: 1.51$\pm$0.76 %^{2}/mmHg^2, p=0.0001; contralateral: 1.61$\pm$1.03 %^{2}/mmHg^2, p=0.001; vs. control: 0.78$\pm$0.32 %^{2}/mmHg^2) frequency ranges. The ICH group also demonstrated lower phases than controls in the low frequency range (ipsilateral: 20.0$\pm$35.5 degrees, p=0.03; contralateral: 24.4$\pm$32.8 degrees, p=0.07; control: 41.8$\pm$29.6 degrees). Within the ICH group, an interaction between inter-hemispheric differences in the very low frequency phase and hematoma size was observed ($P<0.05$). **Conclusions:** Dynamic cerebral autoregulation on both hemispheres are less effective in patients with acute ICH compared to healthy controls. Our findings also suggest that dynamic autoregulation may be further impaired in patients with larger hematomas.

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W P216

Hemicraniectomy And Craniotomy Have Similar Early Outcomes In Patients With Intracerebral Hemorrhage

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Background: Spontaneous intracerebral hemorrhage (ICH) accounts for 20% of all strokes and carries the highest morbidity and mortality. The role of surgery for ICH remains controversial. Craniotomy (C) with clot evacuation is the main reported surgical modality. There is little published data on decompressive hemicraniectomy (HC). We compared all cases of hemicraniectomy with craniotomy at our center for ICH patients. **Methods:** From our prospectively collected database from August 2004 until April 2010 we identified all patients with spontaneous ICH, excluding aneurysms, AVMs, and tumors. We compared two groups: patients with HC (+/- clot evacuation) versus craniotomy. We collected age, ethnicity, admission NIHSS and GCS, location of hemorrhage and volume of ICH (calculated using the AxBxC/2 formula). Primary outcome was (modified Rankin Scale) mRS$\leq$4 at discharge. Secondary outcomes included intensive care unit length of stay (LOS), total hospital length of stay, and in-hospital mortality. **Results:** We identified a total of 1330 spontaneous ICH. Less than 10% underwent surgical procedure. There were 64 HC patients (of which 8 had no clot evacuation), and 23 patients with craniotomy (Table 1). There was a trend to perform HC vs C on younger patients (52.5 years vs. 59 years; p= 0.055). Median NIHSS (19.5 vs. 19) and GCS (11 vs.7) at presentation were similar. The majority of patients were taken within 24hrs of symptom onset. The locations of the hemorrhages, whether lobar or basal ganglia were not significantly different. There was no significant difference in mRS $\leq$4 at discharge, intensive care LOS, or total hospital LOS. There was no significant difference in mRS scores, or mortality after adjustment for age and ICH volume. **Conclusion:** In our limited retrospective study, hemicraniectomy and craniotomy had similar hospital length of stay, mortality, and early clinical outcomes. We are now determining the 90 day outcome of survivors to further assess for possible differences between the surgical groups.

Table 1	Hemicraniectomy (n=64)	Craniotomy (n=23)	P value
Age:			
Range	19-80	36-76	0.055
Median	52.5	59	
Male/Female	61%/39%	61%/39%	0.99
Race:			
Caucasian	27 (42.2%)	10 (43.5%)	0.83
African American	21 (32.8%)	6 (26.1%)	
Hispanic	13 (20.3%)	5 (21.7%)	
Asian	3 (4.7%)	2 (8.7%)	
NIHSS Arrival:			
Range	0-40	2-41	0.81
Median	19.5	19	
GCS Arrival:			
Range	3-15	3-15	0.23
Median	11	7	
History of Diabetes	21 (32.8%)	10 (43.5%)	0.36
Time of Surgery:			
Within 24 hrs	54 (84.4%)	16 (69.6%)	0.12
Range (days)	0-14	0-13	
Location:			
Lobar	27 (42.2%)	15 (65.2%)	0.16
Basal Ganglia	32 (50.0%)	7 (30.4%)	
Both	5 (7.8%)	1 (4.3%)	
EVD Placement	37 (57.8%)	11 (47.8%)	0.41
Clot Volume (cm^3):			
Range	16.6-211.2	29.07-193.2	0.21
Median	72.3	62.7	
Length of Stay (days)			
Range	3-64	4-106	0.21
Median	16.5	21	
Days in ICU			
Range	0-28	2-23	0.79
Median	8	9	
mRS Discharge Median:	5	5	
The following outcome measures were controlled by age and ICH volume:			
mRS 0≤x≤4	21 (32.8%)	9 (39.1%)	0.75
Mortality	51 (79.7%)	20 (87.0%)	0.55

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W P217

Clinical Characteristics Stratify the Utility of Magnetic Resonance Imaging in Patients With Spontaneous Intracerebral Hemorrhage

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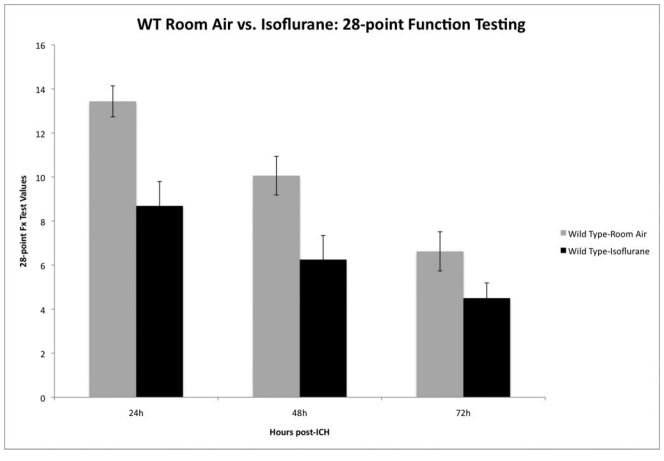
Background: The prevalence and predictors of underlying lesions on MRI in patients with spontaneous ICH are not well characterized. A prior study reported a low prevalence of structural lesions on conventional angiography in hypertensive patients older than 45 years of age with non-lobar ICH. We therefore investigated the performance of this clinical prediction model in a consecutive series of patients who underwent MRI for unexplained ICH. **Methods:** Using an administrative database, we identified all adults hospitalized at our institution with a diagnosis of ICH between January 1, 2006 and September 30, 2009. We included only patients with a head CT at baseline and a brain MRI within the following 6 months. We excluded patients with a clear cause of ICH, such as trauma, coagulopathy, or hemorrhagic infarction. Electronic medical records were used to collect information on demographic characteristics, medical history, blood pressure, and location of ICH. Hypertension was defined as a reported history of hypertension or blood pressure $>$ 140/90 mm Hg on admission. Non-lobar ICH included hemorrhage in the basal ganglia, thalami, or posterior fossa. Our primary outcome was a finding on MRI that changed the treating physicians' diagnosis of the cause of ICH. We applied Fisher's exact test to determine whether the yield of MRI was significantly lower in hypertensive patients older than 45 years of age with non-lobar ICH compared to the other patients. **Results:** Our cohort comprised 123 patients (mean age 64 $\pm$ 17 years, 55% male), of whom 109 (89%) had hypertension. In addition to non-contrast CT and MRI, 91 patients (74%) underwent CT angiography and 92 (75%) MRI with gadolinium. Findings on MRI changed the treating physicians' diagnosis of the cause of ICH in 30 cases (24%, 95% CI 17-32%); 10 of these patients (8% of the total cohort) were found to have vascular malformations, 10 (8%) amyloid angiopathy, 9 (7%) infarcts with hemorrhagic transformation, and 1 (1%) posterior reversible encephalopathy syndrome. None had a brain tumor. MRI findings that changed diagnosis were significantly less common in hypertensive patients older than 45 years of age who had non-lobar ICH (2 of 42 cases; 5%, 95% CI 0-11%) than in the rest of the cohort (28 of 81 cases; 35%, 95% 24-45%) ($p < 0.001$). **Discussion:** Our findings suggest that the diagnostic yield of MRI in the evaluation of spontaneous ICH varies significantly according to patient characteristics. We have validated a prior study's finding that hypertensive patients older than 45 years of age with non-lobar ICH seldom have clinically significant underlying lesions. On the other hand, MRI frequently changed the diagnosis in patients not meeting this profile. These results may help with determining appropriate indications for MRI in patients with spontaneous ICH.



Author Disclosures: H. Kamel: None. B.B. Navi: None. J. Hemphill: None.

W P218

Thrombin Triggers Angiogenesis In Rat Brains Following Intracerebral Hemorrhage

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Background and Purposes: Our recent studies have demonstrated that angiogenesis occurs in rat brains with intracerebral hemorrhage (ICH). Thrombin, a serine protease, is activated at the site of cellular injury, and experiments have confirmed that thrombin mediates mitogenesis and induce tumor angiogenesis. Accordingly, the purpose of the present study is to assess the hypothesis that thrombin triggers ICH-related angiogenesis. **Methods:** This study was divided into 2 parts. In the first part, rats (n=5 in each group at each time point) received 100 μL 0.9% sterile saline (sham) or 100 uL autologous blood with or without a thrombin inhibitor, hirudin (5 U) into right globus pallidus, and then received intraperitoneal injections of BrdU (50 mg/kg) at day 3, day 7 and day 14. In the second part, The rats (n=5 in each group at each time point) received either 1 U(50μL)thrombin or 50μL 0.9% sterile saline (sham) by direct infusion into the right globus pallidus, and then received intraperitoneal injections of 5-bromo-2-deoxyuridine (BrdU) (50 mg/kg) at day 1, day 3 and day 7. Brains were perfused to identify $BrdU^+/vWF^+$ cells and the expression of HIF-1á , VEGF, Ang-1 and Ang-2 was evaluated by immunohistochemistry or quantitative real time reverse transcription-polymerase chain reaction (Real time PCR). **Results:** In the sham-control group, little $BrdU^+/vWF^+$ cells or immunopositive vessels could be observed. After ICH induction, BrdU-labeled nuclei in cerebral endothelial cells (ECs) resided around the hematoma, and immunoreactivity of VEGF, Ang-1, HIF-1á and Ang-2 increased notably ($P<0.01$) compared with that of sham-operated animals. Real time PCR demonstrated that notable up-regulation of VEGF, Ang-1 and Ang-2 mRNA could be detected in the ipsilateral hemisphere ($P<0.01$) compared with that of sham-operated animals. However, after infusion of hirudin, the BrdU-labeled nuclei in ECs decreased significantly ($P<0.01$), and the HIF-1á, VEGF, Ang-1 and Ang-2 positive vessels reduced dramatically around the hematoma ($P<0.01$). Furthermore, the up-regulation of HIF-1á at protein level, VEGF, Ang-1 and Ang-2 at protein and mRNA level was inhibited ($P<0.05$). After infusion of thrombin, a few $BrdU^+$ nuclei in ECs were found in the affected globus pallidus, and VEGF, Ang-1, HIF-1á and Ang-2 immunoreactivity increased ($P<0.05$) compared with that of saline-infused animals. **Conclusions:** Our results demonstrated that thrombin could induce angiogenesis in rat brains and may be an important trigger for ICH-induced angiogenesis.

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W P219

The Role Of Iron In Brain Injury After Intraventricular Hemorrhage

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Background: Intraventricular extension of hemorrhage is a predictor of poor outcome in intracerebral hemorrhage (ICH) and iron overload contributes to brain injury after ICH. The current study investigated the role of iron in ventricular dilatation and neuronal death in a rat model of intraventricular hemorrhage (IVH). **Methods:** There were three parts in this study. First, male Sprague-Dawley rats had a 200-μl injection of either autologous blood or saline into the right lateral ventricle and were euthanized at day 1, 3, 7 and 28. Second, rats received intraventricular injection of iron or saline and were euthanized one day later. Third, rats had IVH and were treated with deferoxamine (DFX, 100 mg/kg, i.m. at 2 and 6 hours after IVH and then every 12 h for 7 days) or vehicle, and rats were euthanized 4 weeks later. All rats had magnetic resonance imaging (MRI) and brains were used for histology. **Results:** Intraventricular injection of autologous arterial blood resulted in marked enlargement of cerebral lateral ventricles. Lateral ventricular volumes in IVH rats were much larger than in rats receiving saline injection at 24 hours (61.7 $\pm$ 5.7 vs. 8.4 $\pm$ 1.3 mm3 in saline group, $P<0.01$) through 4 weeks (40.4$\pm$6.8 vs. 10.1$\pm$8.0 mm3, $P<0.01$). T2* lesions were mainly located in the lateral ventricle of the injection side at 1 day after blood injection. Thereafter, the T2* lesion volume progressively declined but lesions were still observable at day 28, when they were mainly at the edge of the lateral. Four weeks after IVH, hippocampal volumes were smaller in IVH rats compared to saline injected controls (87.0$\pm$2.6 vs. 102.2$\pm$5.1mm3 in the saline group, $P<0.01$). To examine the effect of iron on ventricular dilation, rats were injected with iron or saline into the right ventricle. At 24 hours, lateral ventricular volumes were significantly larger

in rats injected with iron (25.7±7.7 vs. 9.0±1.4 mm3 in the saline group, P<0.01). DFX was used as an iron chelator. DFX treatment reduced lateral ventricular volume significantly at 2 weeks (34.0 ±8.9 vs. 44.0±10.2 mm3 in vehicle-treated group, P<0.05) and 4 weeks (32.7±10.6 vs. 43.8 ±9.7 mm3 in vehicle-treated group, P<0.05) after IVH. There was a trend of decreasing of intraventricular T2* lesion volume in DFX- compared to vehicle-treated rats from the first week, but the difference only reached significance at 4 weeks after IVH (7.8±1.9 vs. 10.1±2.4 mm3, P<0.05). In addition, DFX reduced IVH-induced hippocampal tissue loss (89.0 ±2.7 vs. 85.2± 4.1 mm3 in the vehicle-treated group, P<0.05) and CA-1 neuronal loss (148 ± 23 vs. 120±29 cells/mm in the vehicle-treated group, P<0.05) at 4 weeks after IVH. **Conclusions:** Iron has a role in brain injury following IVH. DFX may be a therapy for patients with IVH or intraventricular extension after ICH.

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W P220

Improvement in Functional Outcome after Isoflurane Preconditioning in a Murine Model of Intracerebral Hemorrhage Involves an Inducible Nitric Oxide Mechanism

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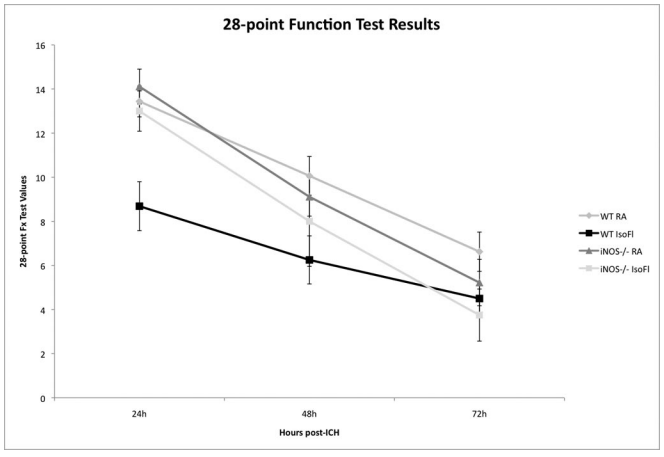
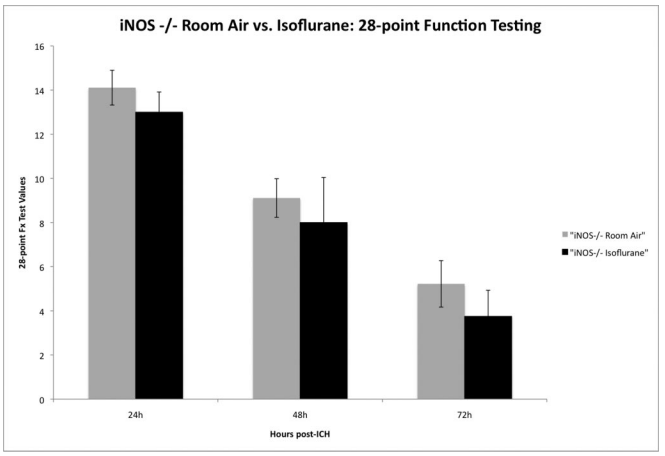
Introduction: Isofluorane preconditioning in ischemic stroke has been shown to be inducible nitric oxide synthase (iNOS) dependent. Mounting evidence suggests that ischemic and hemorrhagic stroke share many molecular mechanisms of cellular injury and death. Therefore we sought to investigate the impact of isoflurane preconditioning on outcome and the role of iNOS as a potential mediator of neuroprotection in a murine model of ICH. **Methods:** Wild-type C57b mice underwent a 4-hour exposure to 1% isoflurane anesthetic 24 hours prior to ICH and control C57b mice were exposed to room air and underwent ICH. Subsequently, iNOS-/- mice were similarly preconditioned and underwent ICH for a total sample size of 44 mice. Intracerebral hemorrhage was performed using a double autologous blood injection into the right striatum. Neurologic function was evaluated at 24, 48, and 72 hours using the 28-point test, which quantifies function based on seven categories of sensory and motor testing with a possible score of 0 to 4 in each. **Results:** Neurological function testing demonstrated that WT mice preconditioned with isoflurane performed significantly better at 24 hours (8.7 + 1.1 vs. 13.4 + 0.7, P<.00001) 48 hours (6.3 + 1.1 vs. 10.1 + 0.9, P<.001), and 72 hours (4.5 + 0.7 vs. 6.6 + 0.9, P<.05) as compared to the WT controls. We subsequently reproduced the same preconditioning setting in our iNOS KO mice. We did not observe a significant difference in neurological function between the room air WT and room air iNOS-/- mice, the room air WT and isoflurane iNOS-/- mice, or the room air iNOS-/- and isoflurane iNOS-/- groups. **Conclusions:** Cerebral preconditioning with isoflurane leads to improved neurological function in WT mice. Mitigation of this preconditioning effect in iNOS-/- mice strongly implicates the iNOS gene in the isoflurane preconditioning pathway in ICH.





Author Disclosures: S.E. Keesecker: None. P.R. Gigante: None. G. Appelboom: None. C.P. Kellner: None. B.Y. Hwang: None. M.L. Yeh: None. J. Gorski: None. E.S. Connolly: None.

W P221

Evaluation of Intraventricular Hemorrhage Assessment Methods for Predicting Outcome Following Intracerebral Hemorrhage

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Background and Purpose: Method for evaluating intraventricular extension of intracerebral hemorrhage (IVH) is not well established. We sought to prospectively evaluate IVH, LeRoux and Graeb Scores with regard to their abilities to predict outcome. Subacute IVH dynamics as well as the impact of EVD on IVH and outcome were also investigated. **Methods:** Sixty-five consecutive primary ICH patients were admitted to Columbia University Medical Center between February 2009 and March 2010. Baseline demographics, clinical characteristics, and EVD status were prospectively recorded. Admission CT scans performed within 24 hours of onset were reviewed for ICH location, hematoma volume, and presence of IVH. Scans with IVH were assigned IVH, Graeb, and LeRoux Scores. For each patient, the last scan performed within 6 days of ictus was similarly evaluated. Outcomes at discharge and 3-months were assessed using modified Rankin Scale (mRS). Receiver operating characteristic (ROC) analysis was used to determine the accuracies of the grading scales in predicting poor outcome (mRS ≥ 3). **Results:** Forty-two patients had evidence of IVH on admission. Mean ICH and IVH volumes were 25 ± 24 ml and 17 ± 22 ml, respectively. Poor outcome was seen in 81% and 67% of patients at discharge and 3-month, respectively. Within 6 days, 20 (47.6%), 2 (4.8%) and 20 (47.6%) patients had either increase, decrease, or no change in their IVH volume, respectively. Direction of volume change was not associated with outcome (p = 0.502). Areas under the ROC curve were similar among the IVH, Graeb, and LeRoux Scores when assessed at admission (0.809, 0.744, and 0.781, respectively) and within 6 days post-ictus (0.831, 0.774, 0.787, respectively). The IVH Score was associated with higher Youden Index than the Graeb and LeRoux Scores both at admission (0.522 vs. 0.412 vs. 0.515, respectively) and within 6 days post-ictus (0.559 vs. 0.522 vs. 0.493, respectively). Patients who received EVD had higher mean IVH volumes (28 ± 26 ml vs. 5.7 ± 6.9 ml, p = 0.001) and increased incidence of hydrocephalus (91% vs. 24%, p < 0.0001) at admission but had similar outcome at discharge and 3-month as those with no EVD. **Conclusions:** The IVH Score predicts outcome with good accuracy in ICH patients with IVH both at admission and within 6 days post-ictus. It may perform better than the Graeb and LeRoux Scores in this high-risk population. IVH growth is common even after the first 24 hours but its impact on clinical outcome remains to be elucidated. EVD improves outcome in patients with severe IVH with particularly poor prognosis at admission.

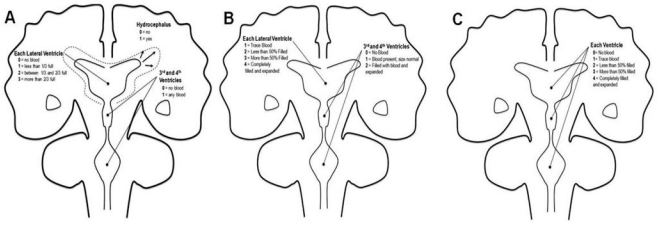

Figure . Grading scales for assessing IVH severity. A. The IVH Score (range 0-23). The IVH Score is calculated using the following equation: 3×(Right Lateral Ventricle Score + Left Lateral Ventricle Score + Hydrocephalus Score) + 3rd Ventricle Score + 4th Ventricle Score. B. The Graeb Score (range 0-12). C. The LeRoux Score (range 0-16).

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W P222

Plasma Levels Of Apolipoprotein E And Risk Of Intracranial Artery Stenosis In Acute Ischemic Stroke Patients

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Background and Object: Apolipoprotein E (apo E) is structural protein of triglyceride rich lipoprotein and has long been considered to be anti-atherogenic. But the data of plasma apo E level and intracranial artery stenosis (ICAS) is remarkably scarce. So we studied acute ischemic stroke patients with and without ICAS to identify the effect of plasma apo E levels on risk of ICAS. **Method:** Prospectively 188 patients with ICAS (ICAS group) and 116 patients without significant intra and extracranial stenosis (No stenosis group) from March, 2005 to May, 2010 were compared. All were acute ischemic stroke patients confirmed with brain MRI and admitted within 7 days of symptom onset. Blood sample was collected at fasting state within 3 days of admission. Plasma level of Apo E and total cholesterol, HDL and LDL cholesterol Apo A-1, B-100, C-III, lipoprotein (a) and Hs-CRP was obtained. The arterial segments were classified as normal, < 50 % stenosis or $\geq 50\%$ stenosis on MR angiography. Multiple logistic regression analysis was used to find out significant factors for ICAS. **Results:** ICAS group has significantly lower plasma level of apo E. (38.7 ± 15.9 vs 47.9 ± 21.04 ug/ml, $P<0.001$). Plasma level of apo A-1, B-100, C-III, hs-CRP showed no difference between ICAS and no stenosis group. Plasma level of lipoprotein (a) was higher in ICAS group(26.95 ± 21.99 vs 22.09 ± 18.81 mg/dl, $p=0.032$). But after adjusted age, history of hypertension, diabetes, smoking and previous stroke and plasma level of triglyceride and LDL cholesterol, only plasma level of apo E was significant for ICAS. (OR 0.968, 95% CI 0.952-0.985, $P<0.001$). **Conclusion:** Lower plasma level of apo E may be risk factors for ICAS in patients with acute ischemic stroke independently.

Author Disclosures: H. Cho: None. Y. Kim: None.

W P223

Effects of External Counterpulsation in Patients with Progressing Ischemic Stroke and Large Artery Occlusive Disease

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Background and Purpose: Progressive stroke is associated with poor outcome. External counterpulsation (ECP) increases cerebral blood flow non-invasively. We aim to investigate the therapeutic and hemodynamic effects of ECP in progressive stroke patients with large artery occlusive disease. **Methods:** Progressive stroke was defined as 2 or more NIHSS points worsening of motor function in the affected arm and leg within 7 days of symptom onset. In this retrospective cohort study, 29 consecutive progressive stroke patients admitted between 2005 and 2009 and received 35 one-hour sessions of ECP plus best medical therapy were recruited. Twenty-nine age and sex-matched patients from either FISS-tris trial (www.strokecenter.org/trials, number 493) or admitted to acute stroke unit whom developed further motor deterioration served as the controls. During the first session of ECP, cerebral blood flow velocity (CBFV) of middle cerebral artery (MCA) and mean blood pressure (BP) during ECP were recorded in 19 patients with good temporal window (Figure 1). **Results:** Mean NIHSS on admission was 8.7 for ECP group and 9.0 for the control group. Nine patients in the ECP group and 4 in the control group had a posterior circulation infarct. The proportion of patients with good outcome at 6 months (modified Rankin Scale dichotomized at 0-2) was 69.0% in the ECP group and 17.2% in the control group (OR=10.7, 95% CI=3.1 to 37.0; adjusted OR=15.6 for hypertension, diabetes and ischemic heart disease, 95% CI=3.4-66.8). Mean BP increased by 8.0% during ECP. Among 14 patients with MCA territory infarct, there was a 16.5% and 9.8% increase in mean CBFV in the relevant and irrelevant MCA, respectively ($p>0.05$). Although not statistically significant, the average increase in mean CBFV of bilateral MCAs was greater in patients with good functional outcome when compared with those with poor outcome (13.0% vs 11.1%). **Conclusions:** This study shows that ECP therapy increases mean CBFV in bilateral MCAs and might improve functional outcome of patients with progressing ischemic stroke. Further randomized studies are needed to demonstrate whether or not ECP may serve as an adjunctive therapy for patients with progressive ischemic stroke.

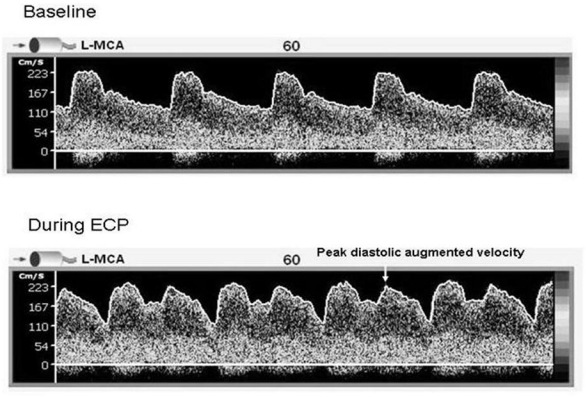

Figure 1. Normal Trancranial Doppler (TCD) waveform and ECP TCD waveform (white arrow indicates the peak diastolic augmented velocity, PDAV).

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W P224

Intracranial Stenosis in the Young Patients May Represent a Distinct Syndrome

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Background: Intracranial stenosis in the young patients from anecdotal experience appears to have different characteristics from that observed in the older population. **Objective:** To demonstrate that risk factor profile of young patients with intracranial stenosis is different when compared with older patients with intracranial stenosis using a case-control study. **Methods:** We reviewed data pertaining to clinical and angiographic characteristics of patients with intracranial stenosis (ICS) treated at three university affiliated tertiary care hospitals and identified their stroke risk factors. ICS patients were matched to a healthy population (without any history of stroke) using the National Health and Nutrition Examination Study (NHANES; 2003-04) by age, sex, and race/ethnicity. We stratified the population in two age groups (<45 and >45 years) and estimated the the relative risk (odds ratios) and attributable risk of known cardiovascular risk factors on the occurrence of angiographically confirmed intracranial stenosis. **Results:** A total of 17 (11%) patients from 153 patients with intracranial stenosis were aged 45 years or less in the study population. These patients were more likely to be women (53% versus 28%, $P<0.05$). The location of the lesion in the young patients was more likely to be in the internal carotid artery (65% versus 29%, $P<0.05$) and less likely to be in the vertebral or basilar artery (12% versus 45%, $P<0.05$). When compared with the control population from NHANES study group, it appears that the attributable risk of hypertension, diabetes mellitus, and coronary artery disease for intracranial stenosis was lower among patients $\leq$ 45 years than that for intracranial stenosis in patients $>$ 45 years of age (6.4% versus 13.1%, 19.9% versus 33.0% and 1.0% versus 10.8%, respectively). Attributable risk of cigarette smoking on intracranial stenosis did not differ between patients aged $\leq$ 45 and those $>$ 45 years old (11.9% versus 11.0%, respectively). Hyperlipidemia had a greater attributable risk of intracranial stenosis in patient $\leq$45 year old than those $>$ 45 year old (23.3% versus 9.3%). **Conclusions:** Intracranial stenosis in the young patients appears to be different when compared to older patients because of prominently lower contribution of known cardiovascular risk factors and different location of atherosclerosis.

Author Disclosures: F. Siddiq: None. G. Vazquez: None. A.I. Qureshi: None.

W P225

Delayed Absorption Of The Contrast Media In CT Angiography Indicates Plaque Stability In Carotid Stenosis

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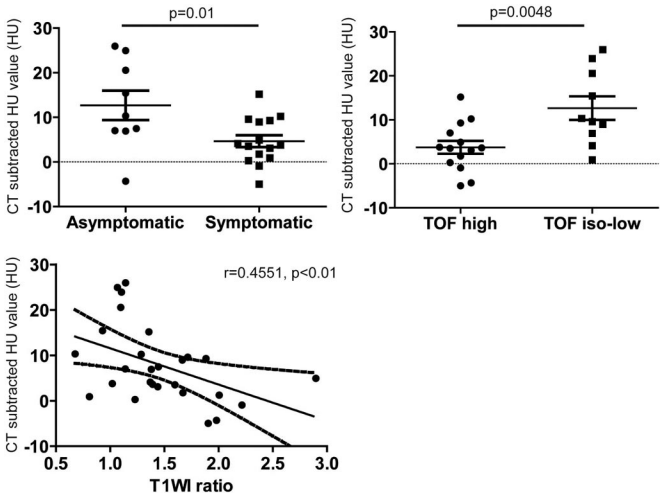
Background and Purpose: Plaque vulnerability is an important factor in the symptomatic carotid stenosis, and recent study focuses on the plaque morphology with some imaging modalities. Here, we prospectively evaluated plaque stability with subtraction method in CT angiography, and compared with MR imaging and histological findings. **Methods:** Fifty lesions in forty four patients (38 male, ages 71.7 ± 1.8) showing moderate to severe carotid stenosis ($>$50% in NASCET) were consecutively included in this study. Dynamic study with CT angiography (Aquilion Tsx-101A, TOSHIBA) was performed and images were obtained twice in the early and delayed phase with an interval of 2 minutes. Three equivalent axial slices were selected (thickest plaque and distal/proximal plaque with an interval of 3mm) in both phases and subtracted Hounsfield unit (HU) value in the plaque. The data was analyzed in association with plaque MR imaging (Black Blood method; Signa, GE Medical Systems) and pathological findings with surgical specimens. The reading of the images was analyzed by 2 experienced readers who were blinded. **Results:** Subtracted HU value was significantly associated with symptomatic presentation compared with the HU value in early phase ($p<0.01$), and negatively correlated with signal intensity on MRI T1WI and TOF. In terms of the histology, the plaques with fibrous tissue had higher subtracted HU value suggesting delayed absorption of the contrast media in the fibrous tissue. **Conclusions:** This study first shows functional plaque evaluation using new method in CT angiography. With this method, blooming effect due to calcification could be figured out and gives us more accurate information regarding plaque morphology. Delayed absorption of the contrast media could suggest plaque stability.



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W P226

Perfusion Images Can Enhance The Accuracy To Evaluate Intracranial Artery Stenosis.

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Background and Purpose: Although digital subtraction angiography (DSA) provides excellent and accurate visualization of the intracranial artery stenosis(ICAS), it has several limitations. Purfusion images are known to show the hypoperfused and critical brain areas in the hyperacute ischemic stroke patients. However, it remains unclear whether perfusion images can give additional information for ICAS in subacute or chronic stroke patients. Our purpose was to evaluate the ability of MR perfusion images to help detect and quantify intracranial stenosis and occlusion compared with DSA and MR angiography (MRA). **Methods:** From 2008, 83 patients underwent 3D time-of-flight (TOF) MRA, MR perfusion images and DSA for suspected cerebrovascular lesions like ICAS and intracranial aneurysm. All three studies were performed within a 14-day period. Four readers blinded to prior estimated or calculated stenoses, patient history and clinical information, examined 1079 vessel segments including basilar artery, PCA, M1,M2, A1,A2 and distal ICA. Lesions were categorized as normal (0-49%), moderate (50-69%), and severe (70-100%). DSA was the reference standard. Unblinded consensus readings were obtained for all discrepancies. First, we compared the only MRA with MRA combined with perfusion images(MRA/P). **Results:** A total of 73 diseased vessel segments were identified on DSA. After consensus interpretation, MRA/P revealed higher sensitivity and specificity than that of only MRA for intracranial stenosis (sensitivity, 68% versus 55%, $P = 0.02$;specificity, 85% versus 35%, $P < 0.01$). MRA/P had a higher positive predictive value than only MRA(88% versus 51%, $P < 0.01$) and a high interoperator reliability. All of five patients with false positive lesions on MRA/P had the large territorial infarction. Three false negative lesions on MRA/P were caused by the well developed collateral flows from ECA. **Conclusion:** Perfusion MR images enhanced the accuracy of diagnosis for ICAS, compared with only MRA and were recommended during evaluation of TOF MRA for detection of intracranial stenosis and occlusion. Perfusion images combined with MRA might reduce the frequency of unessential DSA in the patients without significant ICAS.

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W P227

Burden Of Symptomatic Steno-occlusion In Patients With Acute Cerebral Ischemia In Korea: Prevalence, Distribution And Functional Outcome

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Background: Symptomatic steno-occlusion (SSO) of cerebral arteries in patients with acute ischemic stroke has a great impact on their treatment options and prognosis. However, we do not know well about how prevalent it is, how it is treated, and what its outcome is, especially in the Korean stroke population, where intracranial cerebral atherosclerosis is a major cause of stroke and the fraction of cardioembolic stroke is increasing with rapid aging of society. **Method:** Between September, 2008 and March, 2010, a consecutive series of 5395 patients, who were hospitalized due to acute ischemic stroke to 9 centers that were scattered nationwide and participating in the 'Clinical Research Center for Stroke' program funded by the Korean government, were collected prospectively. 3181 patients were presented within 24 hours from symptom onset and had relevant lesions on diffusion weighted image (DWI). Among them, 3080 patients who underwent MR angiography (MRA) to evaluate cerebral vascular status were enrolled in this study. Demographics, clinical profiles, treatments, clinical outcomes, and imaging characteristics including vascular status on MRA were gathered prospectively. SSO was defined by stenosis or occlusion of cerebral arteries with relevant ischemic lesions on the corresponding arterial territory on DWI. **Result:** A total 1951 (63.3%) patients (mean age: 68.7 $\pm$ 12.0 years old, male 57.8%) of study subjects had SSO. Compared to those without SSO, they were older age, high glycosylated hemoglobin level and high cardioembolic sources (CE) with statistical significance. The median NIHSS score of patients with SSO was 6 (interquartile range: 2-14); those without SSO was 3 (1-6). Proportion of thrombolysis was 18.5% with SSO and 9.3% without SSO. The most affecting vessel was middle cerebral artery (34.6%), and followed by extracranial internal carotid artery (14%), vertebral artery (12.4%), basilar artery (8.7%) and intracranial internal carotid artery (8.7%). SSO were independent risk factor of poor functional outcome (mRS$>$2) at discharge adjusted by age, initial stroke severity,CE, thrombolysis and initial BP status (odds ratio: 1.72, 95% confidence interval: 1.42-2.09). Of patients with SSO, 559 (18.1%) presented multiple vessel involvement. Proportion of poor functional outcome of patient with multiple SSO (67.6%) was higher than those with single SSO (49.9%) and without SSO (29.6%). Patterns of multiple SSO were both anterior and posterior circulation (8.6%), unilateral anterior circulation (6.8%), posterior circulation only (2.7%) and bilateral anterior circulation (1.4%). Positioning of SSO in terms of anterior or posterior circulation was associated with age, hypertension history and CE. **Discussion:** About 63% of patients with acute ischemic stroke had SSO and 1/3 of them had multiple involvements. Distribution and patterns of SSO were associated with functional outcome.

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W P228

Prevalence Of Intracranial Atherosclerotic Disease Coexisting With Extracranial Atherosclerosis In The North Indian Population

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Background: Coexistent intracranial and extracranial atherosclerotic disease holds a worse prognosis than either disease alone. Data on this atherosclerotic burden is not available from India. **Objectives:** 1. To determine the prevalence of intracranial atherosclerotic disease(IAD) in patients with extracranial atherosclerotic disease(EAD)2. To study the association of risk factors with the intracranial and extracranial atherosclerosis. **Methods:** Patients 18 years and above with ischemic stroke or TIA in the anterior or posterior circulation were prospectively recruited.On confirming presence of extracranial atherosclerotic disease by ultrasound duplex,CT angiography (CTA)of the carotid and cerebral arteries was carried out within 3 months of the stroke.Risk factor assessment included hypertension, diabetes mellitus, hyperlipidemia, and cigarette smoking. **Results:** 60 patients were studies. Mean age was 64.65 years (45 -82 years). 78.33% were males.80% had anterior circulation symptoms,20% had posterior circulation. 13(21.67%) patients presented with TIAs. 78.33% were hypertensive,40% were diabetics,58.3% were dyslipidemic and 21.67% were smokers. Mean time period between stroke onset to CT angiography was 32 days (range:1 - 86 days). Duplex ultrasound revealed significant extracranial disease($\geq$50% stenosis or occlusion)in 41.67% patients. Prevalence of IAD on CTA was 88.33%. Males constituted 75.47 %.46.67% had anterior circulation disease alone, 5%posterior circulation and 36.6% had combined anterior and posterior circulation disease. 46.67% had significant IAD ($\geq$50% stenosis). 20% had significant disease in anterior circulation, 20 % in posterior circulation and 6.66% combined disease.Among the diseased segments, IAD was commonest in the carotid siphon (71.42%) followed by the intracranial portion of the vertebral artery (14.91%) and PCA (5.56%).Anterior and middle cerebral artery IAD was found in 2.5 and 3.1% segments, basilar in 2.5%. Significant combined EAD and IAD was present in 21.67% patients.15 patients had significant IAD without coexisting significant EAD. 30.78% patients of significant EAD had accompanying ipsilateral significant IAD in the carotid siphon or vertebral artery. 18.33% had extracranial disease alone corresponding to the involved side of stroke, 8.3% had significant IAD and combined significant IAD and EAD was present in 11.67%.None of the risk factors reached significance on comparing EAD with combined IAD and EAD. **Conclusion:** 1. IAD has a high prevalence in the north Indian ischemic stroke population.2. IAD is an important contributor to ischemic stroke etiology in this population accounting for $\sim$20% of ischemic strokes.3.IAD may be independent of EAD as a risk factor for ischemic stroke in this population.4.No specific risk factor is significantly associated with either coexistent disease or IAD alone in our study.

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W P229

High Levels of Apolipoprotein B/AI Ratio in Ischemic Stroke Patients with Intracranial Atherosclerosis

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Background & Objectives: Apolipoprotein B (apoB) level represents the small dense oxidized low-density lipoprotein (ox-LDL) particles and apolipoprotein AI (apoAI) level represents the

number of antiatherogenic [(high density lipoprotein (HDL)] particles. ApoB/apoAI ratio is a valid risk indicator of ischemic stroke. Insulin resistance, a basis of metabolic syndrome (MetS) is associated with small dense ox-LDL particles. Because intracranial large artery atherosclerosis (IC-LAA) is associated with the MetS and oxidation injury, we hypothesized that IC-LAA could be more associated with serum level of apoB/apoAI ratio than extracranial (EC)-LAA. **Methods:** We prospectively investigated demographic features and risk factors in ischemic stroke patients (≤7 days of onset) who underwent brain MRI/MRA from March 2008 through June 2010. Stenosis was diagnosed in cases showing a degree of luminal narrowing of ≥50%. The stroke subtypes were categorized as IC-LAA, EC-LAA, small artery occlusion (SAO), cardioembolism (CE), and stroke of undetermined etiology (SUE). MetS was diagnosed following the AHA/NHLBI criteria. We defined a high apoB/apoAI ratio as the highest gender-specific quartile (>75th percentile; >0.91 in male, >0.87 in female). We performed comparative studies of apoB/apoAI ratio based on angiographic findings and examined associations between quartiles of apoB/apoAI ratio and IC-LAA by controlling possible confounders. **Results:** We finally included a total of 388 patients (mean age 68.1±12.8; 210 males). One hundred and ninty-six patients (50.5%) were in the IC-LAA group, 34 patients (8.8%) were in the EC-LAA group, 77 patients (19.8%) were in the SAO group, 62 patients (16.0%) were in the CE group, and 19 patients (4.9%) were in the SUE group. The serum levels of apoB/apoAI ratio were higher in the IC-LAA than the other subtypes (P=0.014). Patients with a higher quartile of apoB/apoAI ratio showed increasing tendency to have higher MetS and its 5 components, stenosis, and apoB level, and lower level of apoAI (all P<0.05). The number of IC-LAA showed a tendency to increase in proportion to the quartile of apoB/apoAI ratio (P<0.0001) while the EC-LAA demonstrated no association. ApoB/apoAI ratio showed an independent predictor for IC-LAA, and a higher risk of IC-LAA in individuals with highest quartile of apoB/apoAI levels (OR 2.57; P=0.009) vs. patients with low apoB/apoAI levels. In terms of multiple(≥3) IC-LAAs, as compared with patients with 1st quartile, the adjusted ORs for IC-LAA increased from 3.90 for the 2nd quartile (P=0.025) to 4.94 for the 3rd quartile (P=0.009) and as high as 8.54 for the highest quartile (P<0.0001). **Conclusions:** High level of apoB with ox-LDL particle might be causal factor for IC-LAA. We suggest that apoB/apoAI ratio might be a useful biological marker for identifying patients likely to be harboring IC-LAA.

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W P230

Predictors of Neurologic Deterioriation in Large Vessel Strokes Presenting Outside the Traditional Treatment Window

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Background: Patients presenting with ischemic stroke in the setting of large vessel occlusions outside the established treatment time window for endovascular intervention present a therapeutic challenge. In this subacute stroke population, there is a lack of evidence to support which patients benefit from endovascular intervention to salvage remaining reversible ischemic tissue (penumbra) and which subgroups are at risk for further neurological deterioration from infarct progression. **Methods:** Retrospective cohort study of patients presenting with large vessel occlusion > 6 hours from symptom onset to Cleveland Clinic between 5/09 and 6/10. **Results:** 43 patients (mean age 63.5 ± 14.0, 41.9% female) met inclusion criteria. Mean NIHSS on admission was 13.7±8.3, median time from last known well to imaging was 21.0 hours. The majority (72.1%) had intracranial occlusions; these patients had higher NIHSS scores than those with extracranial occlusions only (mean NIHSS 16.5 vs 6.4, P<0.001). Neurological worsening or death during hospitalization occurred in 51.2% of patients overall, and was significantly more frequent in patients with intracranial occlusions (61.3%) than in those with extracranial occlusions (25%, p=0.03) and in patients with cardiac embolism (76.9%) compared to those with large vessel disease (40%, p=0.03). Patients who worsened had higher initial NIHSS (15.9 vs 11.4, p=0.08), were older (68 vs 59 years, p=0.03), had shorter times from last known well to imaging (21.6 vs 29.9 hours, p=0.11). 16 of 43 patients (37.2%) received endovascular therapy. Intervention was not associated with reduced rates of neurological worsening overall (62.5% intervention vs 44.4% no intervention, p=0.14) or within the following subgroups: intracranial occlusions [66.7% (8/12) intervention vs 57.9% (11/19) no intervention, p=0.62], NIHSS < 10 [75% (3/4) intervention vs 12.5% (1/8) no intervention, p=0.07], ASPECTS scores ≥ 8 (80% vs 20%, p=0.21), good collateral vessel grading score [20% (1/5) vs 12.5% (1/8), p=0.71]. **Conclusions:** Patients presenting with ischemic stroke and large vessel occlusions outside the traditional treatment time window for endovascular therapy represent a high risk population for neurological deterioration. In this analysis, patients with intracranial occlusions, higher initial NIHSS, cardioembolic disease, and older age had higher rates of neurological worsening. Although subject to selection bias, endovascular therapy in this patient population was not associated with reduced rates of neurological deterioration. Further study of this population is required to identify the predictors of neurological deterioration, and to determine the best medical or endovascular interventional strategies to salvage remaining ischemic penumbra and prevent infarct extension.

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W P231

Optimal Pressure of External Counterpulsation for Cerebral Blood Flow augmentation in Ischemic Stroke Patients

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Background: External counterpulsation (ECP) is a non-invasive method used to augment cerebral perfusion but the optimal pressure used has not been well documented. We aim to find the optimal pressure of ECP treatment in relation to the cerebral blood flow. **Methods:** We recruited 30 ischemic stroke patients with large artery occlusive disease. The mean time after symptom onset was 6.41 days. We monitored the blood flow velocities of bilateral MCAs before and during ECP therapy using TCD. We started ECP treatment pressure on the lower body from 0.02MPa (150mmHg), then gradually increased to 0.025MPa (187.5mmHg), 0.03MPa (225mmHg), 0.035MPa (262.5mmHg). TCD parameters, including peak systolic velocity PSV, end-diastolic velocity EDV, peak diastolic augmentation velocity PDAV and mean flow velocity MV were recorded for 3 minutes before and during each pressure increment. Monitoring data on MCA was analyzed based on whether it was ipsilateral or contralateral to the infarct. **Results:** The mean flow velocities on the symptomatic side under different ECP pressures, increased 18.49% (0.02MPa), 19.33% (0.025MPa), 19.16% (0.03MPa) and 18.46% (0.035MPa). All were significantly higher than baseline but did not differ among different pressures. Under increasing pressures, PDAV gradually increased (78.70%, 88.24%, 96.66%, 103.02% respectively compared with baseline EDV, P<0.001) while PSV decreased (3.60%, 2.64%, 1.02%, -1.88% compared with baseline PSV, p=0.001) and EDV decreased (-1.35%, -4.18%, -9.28%, -11.87% compared with baseline EDV, p=0.002). Contralateral MCA velocity change tendency showed similar picture. **Conclusion:** 150mmHg appears to be the optimal pressure to be used to increase cerebral blood flow. Further increase in pressure does not increase cerebral blood flow velocity.

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W P232

Predictors Of Outcome In Conservatively Treated Patients With Symptomatic Basilar Artery Occlusive Disease

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Purpose: To identify clinical and radiological predictors of outcome in patients with cerebral ischemia attributed to basilar artery occlusion that were treated conservatively with antiplatelets or anticoagulation. **Methods:** We retrospectively identified patients who were treated in the Acute Stroke Unit of Henry Ford Hospital with clinical and radiological evidence of cerebral ischemia attributed to basilar occlusive disease, and did not receive endovascular treatment because of delayed presentation or other contraindications. 18 patients were identified. Demographics, patterns of clinical presentation, parenchymal and vascular involvement as well as stroke etiology were reviewed and correlated with functional outcome at discharge. **Results:** Hypertension was the most prominent risk factor, with many patients sharing multiple vascular risk factors. Of the 18 patients included in this analysis, 11 had a modified Rankin Score (mRS) equal to or less than 3, and 7 had an mRS equal to or more than 4 upon discharge. Decreased level of consciousness upon presentation, tetraparesis/tetraplegia, bulbar/pseudobulbar manifestations, oculomotor findings, occlusion of the proximal 1/3 of the basilar artery, radiological evidence of brainstem ischemia and an acute pattern of onset (without preceding transient attacks) were associated with a poorer outcome. Patients with recurrent transient symptoms tended to do well, although some of them would progress to deteriorate clinically. Age, gender, presence of specific vascular risk factors, headache, demonstration of hyperdense vascular signs, and treatment with antiplatelets versus anticoagulation did not have a significant correlation with mRS upon discharge. **Discussion:** Basilar artery occlusive disease has a grave prognosis in the absence of endovascular intervention. No difference in outcomes with antiplatelets or anticoagulation treatment is observed in this study. Certain clinical and radiological parameters are noted to be significantly associated with functional outcome and can be used to guide management decisions. These parameters signify extensive brainstem ischemia that cannot be reversed with conservative measures.

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W P233

Prediction Of Asymptomatic Cerebrovascular Diseases Before Bypass Surgery For Peripheral Artery Disease

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Background & Purpose: Both cerebrovascular disease (CVD) and peripheral artery disease (PAD) are atherothrombotic disease and sometimes coexist with each other. We investigated predictive factors for CVD before bypass surgery for PAD. **Subjects & Methods:** For the present study, 102 consecutive PAD patients without a history of any stroke who were planned to undergo a bypass surgery were included. Before the surgery, all patients were studied by ankle brachial index (ABI), duplex carotid ultrasonography, magnetic resonance imaging (MRI) including diffusion weighted imaging (DWI), and MR angiography. A stenosis of ≥70% or occlusion of the major intracranial or extracranial cerebral arteries was defined as a severe vascular lesion. We also investigated the predictive factors for severe cerebrovascular lesions. **Results:** A severe vascular lesion of the intracranial and extracranial cerebral arteries was observed in 15 (15%) and 19 (19%) patients respectively. There were asymptomatic ischemic lesions on MRI in 62 (61%) patients. Among them, 9 (9%) patients had asymptomatic high-intense lesions on DWI. Severe carotid stenosis (44% vs 16%, p=0.0372), low echoic plaques (89% vs 30%, P<0.0001), or ulcerative plaques (44% vs 7%, p=0.0003) were more frequent in patients with than without high-intense lesions on DWI. Eight patients were diagnosed as having an indication for cerebral revascularization before the bypass surgery for PAD: carotid endarterectomy in 7 and extracranial-intracranial bypass in 1. In patients with severe vascular lesions of the intracranial cerebral arteries, female was more frequent (53% vs 24%, p=0.0138) and ABI value was relatively lower (0.29±0.22 vs 0.42±0.28, p=0.0772) in comparison to patients without severe vascular lesions. ABI value was relatively lower in

patients with than without severe vascular lesions of the extracranial cerebral arteries (0.26±0.21 vs 0.42±0.27, p=0.0667). Female was more frequent (43% vs 24%, p=0.0464), ABI value was lower (0.29±0.28 vs 0.44±0.28, p=0.0199), and hypercholesterolemia and ischemic heart disease were relatively more frequent in patients with than without severe vascular lesions of the intracranial or extracranial cerebral arteries. On multivariate analysis, ABI was a significant predictor for a severe vascular lesion of any cerebral arteries. With regard to the sensitivity-specificity curve analysis, the ABI cut-off value of 0.40 or less yielded the highest diagnostic accuracy (sensitivity, 68%; specificity, 66%) for severe cerebrovascular lesions. The ABI cut-off value of 0.67 or less yielded a complete sensitivity. **Conclusions:** ABI value was a significant predictor for severe cerebrovascular lesions before the bypass surgery for PAD. Asymptomatic high-intense lesions on DWI could be observed in PAD patients with severe carotid stenosis, low echoic plaques, or ulcerative plaques.

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W P234

The Triglyceride:High-Density Lipoprotein Cholesterol Ratio and Intracranial Arterial Stenosis

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Background: The extent of carotid artery atherosclerosis correlates with increased plasma concentrations of total cholesterol (TC) and low-density lipoprotein cholesterol (LDL) and with a decreased plasma concentration of high-density lipoprotein cholesterol (HDL). Emerging data suggest that a triglyceride (TG):HDL ratio may be a better predictor of vascular risk than the traditional lipid measures such as TC and LDL. However, there have been few reports on the association between serum lipid indices and steno-occlusive disease of the intracranial arteries. **Objective:** The purpose of this study was to directly compare the clinical utility of TC, LDL, TG, HDL, and the TG:HDL ratio as predictors of intracranial arterial stenosis in stroke-free Korean adults using brain magnetic resonance angiography (MRA). **Methods:** We retrospectively analyzed the records of 361 stroke-free subjects who consecutively visited a general health promotion center in a university-affiliated hospital from February 2006 through April 2009. Included subjects underwent brain 3D time of flight MRA as part of their voluntary health checks. The presence of stenosis (≥25%) in the basilar artery (BA) and in the horizontal portion of the middle cerebral artery (MCA) was assessed using brain MRA. All patients had fasting lipid panels drawn. We categorized serum lipid indices into quartiles and logistic regression analyses were performed. **Results:** The subjects were 183 men and 178 women, and their mean age was 52 ± 10 years. Eight subjects were using lipid-lowering medication. One hundred thirty-seven subjects (38%) had MCA stenosis, and 105 subjects (29%) had BA stenosis. Univariate analyses of the correlations between clinical parameters and BA stenosis and between clinical parameters and MCA stenosis were performed. Patients with MCA stenosis were older and more likely to be on antihypertensive medication than patients without MCA stenosis. Systolic blood pressures were significantly higher in patients with BA stenosis than in patients without BA stenosis. None of the serum lipid indices was associated with prevalence of MCA stenosis. None of the traditional lipid measures was associated with prevalence of BA stenosis. However, the TG:HDL ratios in the upper three quartiles compared with the lowest quartile were associated with increased prevalence of BA stenosis with odds ratios of 2.4 (95% CI 1.2-5.0), 3.3 (95% CI 1.6-6.8), and 2.5 (95% CI 1.2-5.2), respectively. Adjustment for age, systolic and diastolic blood pressure, and the prior use of antihypertensive medication did not substantially change the associations. **Conclusion:** The TG:HDL ratio is a better predictor of the intracranial stenosis, especially BA stenosis than any standard lipid measure in stroke-free Korean adults.

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W P235

Collaterals Determine the Hemodynamic Impact of Atherosclerotic Intracranial Stenosis

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Background: Degree of luminal stenosis is the principal variable used to guide potential therapeutic strategies for symptomatic intracranial atherosclerosis (SIA) but the role of hypoperfusion remains unclear. Collaterals have recently been shown to dramatically alter risk of recurrent stroke in intracranial stenosis. Our aim was to characterize the association of delay and dispersion on CT/MR perfusion (CTP/MRP) imaging with type of perfusion (antegrade versus collateral) on digital subtraction angiography (DSA) in patients with SIA. **Methods:** Consecutive cases of SIA with concurrent CTP/MRP and DSA were analyzed. CTP/MRP measures of cerebral blood volume (CBV) and Tmax>4s were calculated. DSA features including degree of luminal stenosis, length and irregularity were assessed in blinded fashion. Antegrade perfusion on DSA was measured by Thrombolysis in Cerebral Infarction (TICI) grade and collaterals were scored by ASITN/SIR grade. CTP/MRP lesion volumes were analyzed with respect to all DSA parameters. **Results:** 28 cases (mean age 62.8±14.1 years; 16 men, 12 women) of recent SIA and concurrent CTP/MRP and DSA were analyzed. Stenoses ranged from 50-99%, with lesion length ranging from 1.0-12.9 mm and irregularity noted in 10/28 (36%). CBV lesion volumes included ischemia (mean 0.9%±0.9), penumbra (mean 3.4%±2.6), and hyperemia (mean 20.3%±5.3). Tmax>4s lesions indicative of abnormal delay included mean 17.3%±8.8. DSA measures were evenly distributed across the full range of scores for antegrade perfusion (TICI) and collaterals. Extensive variability was also noted between the extent of delay on Tmax>4s and dispersion of hyperemia on CBV across the full range in degree of luminal stenosis. Antegrade perfusion measured on DSA (TICI) was inversely correlated with compensatory collateral grade ($p<0.01$). Such DSA measures of antegrade flow beyond the lesion and downstream collaterals provided distinct information from CTP/MRP measures of delay and dispersion. **Conclusions:** The hemodynamic impact of intracranial atherosclerosis on antegrade flow reflects collateral perfusion, not just degree of stenosis. Downstream hyperemia or elevated CBV may balance delayed perfusion yet these parameters appear distinct from DSA measures. Noninvasive imaging may therefore complement conventional angiographic characterization of SIA.

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W P236

Individual Vessel and Regional Blood Flow Measurements: Implications for Flow and Collateral Assessment in Cerebrovascular Occlusive Disease

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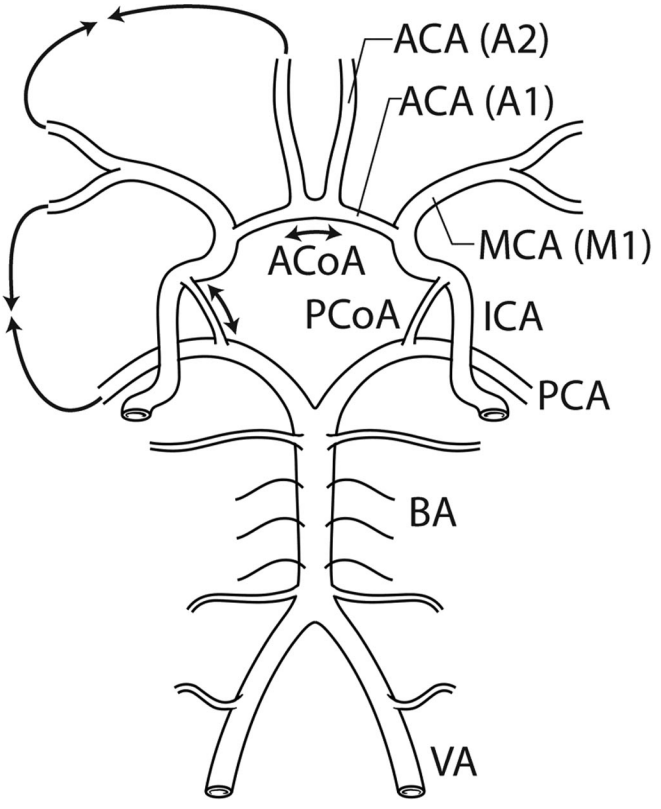
Objective: We sought to analyze blood flow rates in individual major cerebral arteries and vessel territories, using quantitative magnetic resonance angiography (QMRA). **Methods:** 326 healthy adult volunteers with no history of cerebrovascular disease underwent QMRA of head and neck vessels using commercially available software, NOVA (Vasol, Inc.). Individual vessel flows were measured in the internal carotid artery (ICA), middle cerebral artery (MCA), anterior cerebral artery (ACA) A1 and A2 segments, posterior cerebral artery (PCA), basilar artery (BA), and vertebral artery (VA). In a subset (n=192) with a full complement of vessel flows (including A2s), regional distal territory flows, incorporating primary (Willisian) and secondary (leptomeningeal) collaterals were calculated (see figure). Specifically, for MCA or ICA territory we examined flows for the anterior circulation left region (LR) and right region (RR) = MCA + A2 + PCA; for VA or BA territory, we looked at the posterior region (PR) = BA + PCAs. **Results:** In the full cohort, mean age was 48 (18-84) years old, with 48% females; the subset cohort was not demographically different. For individual vessels, the range of blood flows, as reflected by the coefficient of variation (CV) was larger for paired vessels with potential for anatomic variability* (hypoplasia or dominance), such as VAs or A1 segments compared to MCA and PCAs. The BA flows also showed larger variability **, likely reflecting the wider range of flows given distal anatomic variants such as fetal PCA, and posterior communicating artery (PcoA) anatomy. For regional territory flows, LR and RR have a lower CV, than their individual vessel counterparts, ICA and MCA. Similarly the PR has a lower CV than its individual vessel counterparts, the BAs and VAs. **Conclusions:** In evaluating the flow effects of cerebrovascular occlusive disease, comparison to normative distal territory flows, rather than individual vessel normative flows, may provide a more robust measure of flow compromise, as the former is less susceptible to anatomic variants. Furthermore, territorial flows provide a more global measure of hemodynamic status, incorporating both primary and secondary collaterals.



	LICA	RICA	LMCA	RMCA	LA1*	RA1*	LR	RR
Flow (ml/min)	257±50	255±53	158±28	146±28	85±27	91±30	298±49	281±51
CV	19%	21%	18%	19%	32%	33%	**16%**	**18%**
	LPCA	RPCA	BA**	LVA*	RVA*	PR		
Flow (ml/min)	68±14	65±15	138±40	99±38	89±31	270±59		
CV	21%	23%	27%	38%	35%	**22%**		

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W P237

Validation of 'Reversed Robin Hood Syndrome' by Acetazolamide-Challenged HMPA-SPECT in Patients with Severe Steno-occlusive Disease of Intracranial Carotid or Middle Cerebral Artery

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Background: Intracranial stenosis is the commonest causes of stroke among Asian patients. An association exists between the degree of stenosis and stroke recurrence. In severe intracranial steno-occlusive disease, perfusion is maintained by collateral pathways and cerebral autoregulation (CA). CA may be impaired due to inadequate cerebral vasodilatory reserve (CVR) & intracranial steal phenomenon, so-called the 'reversed-Robin Hood (RRH) syndrome'. Identification of patients with inadequate CVR may help in selecting high-risk patients who could benefit from various revascularization procedures. **Methods:** We prospectively included patients with symptomatic and severe intracranial steno-occlusive disease (intracranial carotid artery and middle cerebral artery). Severe intracranial stenosis was defined according to validated transcranial Doppler (TCD) velocity criteria and blunted flow in distal segments. CVR was evaluated with TCD and breath-holding index (BHI) <0.69 determined inadequate reserve. RRH was detected as transient velocity reduction in affected artery at the time of velocity increase in the reference normal artery. Intracranial steal magnitude was calculated in these cases. Patients with RRH were further evaluated with acetazolamide-challenged HMPAO-SPECT and net deficit in metabolic perfusion was calculated. **Results:** 101 patients (73 males, mean age 56yrs; range 23-78yrs) with severe intracranial stenosis fulfilled our TCD criteria of inadequate CVR on TCD. RRH phenomenon was observed in 33 (33%) patients with a median steal magnitude of 17% (inter-quartile range, IQR 10). Acetazolamide-challenged HMPAO-SPECT demonstrated significant metabolic perfusion deficit (median 8%; IQR 13%) in 31 out of these 33 cases (sensitivity 77%, specificity 97% with positive predictive value 97%). A strong relationship between RRH on TCD and acetazolamide-challenged HMPAO-SPECT was noted on ROC curve analysis (area under curve 0.93; 95% confidence interval 0.88-0.98;petazolamide-challenged HMPAO-SPECT (Pearson correlation coefficient, $r=0.643$;pchemia ($p=0.04$; RR 1.7, 95%CI 1.2-3.6). **Conclusions:** Reversed Robin Hood syndrome in patients with severe intracranial stenosis is associated with very high risk of cerebral ischemic events. Acetazolamide-challenged HMPAO-SPECT is reliable in the diagnosis of reversed Robin Hood syndrome in patients with severe steno-occlusive disease of intracranial carotid and middle cerebral artery. Identification and quantification of intracranial steal magnitude helps in identifying a target group of patients for possible revascularization procedures.

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W P238

Increased Hemorrhagic Risk of Thrombolysis in Acute Ischemic Stroke Patient with Malignancy

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Background and Purpose: As the prevalence of malignancy increased, there is increased chance of thrombolysis in ischemic stroke patient with malignancy. However, it is not well known about the hemorrhagic risk of thrombolysis in these patients. We evaluated the risk of symptomatic and asymptomatic hemorrhage after thrombolysis in acute ischemic stroke with current or remote malignancy. **Methods:** We retrospectively reviewed stroke database from five university hospitals and selected patient who received thrombolytic treatment with current or remote malignancy. Symptomatic and asymptomatic intracranial hemorrhage was evaluated by the 24 hour brain CT after thrombolysis and clinical symptom. Risk of hemorrhage according to the malignancy status and type of thrombolysis was also analyzed. **Results:** Of 843 patient who treated by thrombolytic therapy, 40 (4.7%) patients had a malignancy. Twenty patients had current malignancy and remaining had remote malignancy. Twenty-four patients received intravenous (IV) tPA only, 3 received IV tPA plus intra-arterial urokinase (IAU), 8 received IAU only, 2 received stent insertion, and 3 received IV tPA plus IAU plus stent insertion. Intracranial hemorrhage occurred in 19 (47.5%) patients (symptomatic 6, asymptomatic 13). Nine hemorrhages (symptomatic 3, asymptomatic 6) occurred in current malignancy and 10 hemorrhages (symptomatic 3, asymptomatic 7) occurred in remote malignancy. Intracranial hemorrhage occurred 37.5% in IV tPA, 62.5% in IAU, 66.7% in IV tPA plus IAU, 0% in stent insertion, and 100% in IV tPA plus IAU plus stent insertion. **Conclusions:** Intracranial hemorrhagic risk after thrombolysis is high in patient with malignancy when we consider reported risk of hemorrhage of the previous clinical trials. Status of malignancy does not affect the risk of intracranial hemorrhage. Further study is needed to verify this finding.

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W P239

C-Arm CT Cerebral Blood Volume, MR Diffusion-Weighted Imaging, and Histology in a Canine Model of Acute Ischemic Stroke

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Although MR perfusion-diffusion mismatch is well validated, emergency MR imaging is not widely available. Increasingly, CT based perfusion-cerebral blood volume mismatch is employed to triage patients. We hypothesize that C-arm CT cerebral blood volume (CBV) will correlate well with MR diffusion weighted imaging (DWI) and histopathology in an experimental model of acute ischemic stroke. **Methods:** Seven purpose-bred dogs were anesthetized as per the procedures approved by our IACUC. Autologous blood clot was prepared by mixing whole blood with thrombin and barium, and allowed to age for 24 hours. Following baseline MR imaging, a 5F catheter was placed in either internal carotid artery and a 1cm clot fragment was delivered. MRI was performed on a 3.0 Tesla system using an 8 channel receive only knee coil and serial diffusion and perfusion sequences were acquired. Within 10 minutes following the last diffusion scan (at 4 hours post stroke), the animals were transferred to the angiography suite, where non-contrast and contrast enhanced flat-panel cone-beam CT sequences were acquired. Animals were then euthanized and the coronal brain sections were stained with 2% 2,3,5-triphenyltetrazolium chloride (TTC). Apparent Diffusion Coefficient (ADC) maps were generated and imported into Matlab for image processing. ADC values below $0.53 * 10^{-3}$ mm^2/s were identified and segmented. The CBV was determined by dividing the difference of the change in HU of the brain by that of the in-flowing blood between the contrast enhanced and non-contrast CT. A brain mask was generated from T2 weighted MRI and registered to the CT data for analysis. For all subjects mean CBV values and standard deviation (SD) were determined in a volume of interest ($5\times5\times5$ voxels, 0.12 ml) in healthy and ischemic tissue. CBV lesion volumes were calculated using various thresholds based on the SD measured in healthy brain and resulting volumes were compared to infarct volumes measured with histology by a linear regression analysis. Time-to-peak perfusion images were analyzed using commercial software. **Results:** Complete occlusion was successfully induced with an embolus lodged in the middle cerebral artery in all animals. The perfusion imaging revealed hypoperfused brain with heterogeneous severity due to the variability of collateral circulation. The final ADC lesion volume was $4,385\pm1,930mm^3$ (mean$\pm$ standard error of the mean) and the mean perfusion lesion was $6,483 \pm 1,515mm^3$. The TTC infarct volume was $4,408 \pm 1,805mm^3$. The mean CBV lesion with an optimized threshold of 2.5xSD was $3,567\pm1,010$ mm^3. As compared with the correlation between DWI and TTC ($R^2=0.99$), the correlation between the CBV lesion volume and TTC was not as strong ($R^2=0.84$). **Conclusion:** Our preliminary results indicate that there a fair correlation between histologically defined infarct and optimized C-arm CT CBV volumes.

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W P240

Variability in the Relationship Between Diffusion and Perfusion Volumes in Acute Stroke Patients

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Background: Multimodal MRI is often used to triage acute ischemic stroke (AIS) patients for intervention. Perfusion weighted imaging (PWI) is thought to identify deficits in blood flow. Reduced apparent diffusion coefficients (ADC) on diffusion weighted imaging (DWI) is thought to reflect densely ischemic tissue which in most cases of human stroke will progress to infarction. Areas of reduced cerebral blood volume (CBV) (derived from PWI) are sometimes also used as a surrogate for DWI while Time-to-peak (TTP) is a PWI measure sometimes used to identify non-infarcted at-risk tissue. Hypothesis: The tissue damage characterized by DWI is directly related to the CBV in a relationship that is similar between patients. Conversely TTP maps should be less likely to reflect ischemia. **Methods:** Twenty AIS patients with a diffusion-perfusion mismatch were retrospectively identified from our stroke database. Lesion volumes over a range of thresholds were calculated from DWI using ADC maps and from PWI using CBV maps and TTP maps. Varying the threshold which defines the lesion determines its volume. For a given volume, the ADC threshold was plotted against the corresponding PWI threshold. **Results:** Figure 1 shows the relationships between ADC value and CBV expressed

as a percent of normal. Although all curves showed a similar sigmoidal shape with an abrupt change in slope, the ADC threshold at which this occurred varied considerably. Figure 1b shows the relationships between ADC and TTP which were less heterogeneous but still variable. **Conclusions:** The relationship between PWI and DWI lesions in our cohort varied considerably. It is likely that this relationship is complex and involves more variables than those considered in this study. CBV should not be used as a surrogate for ADC.

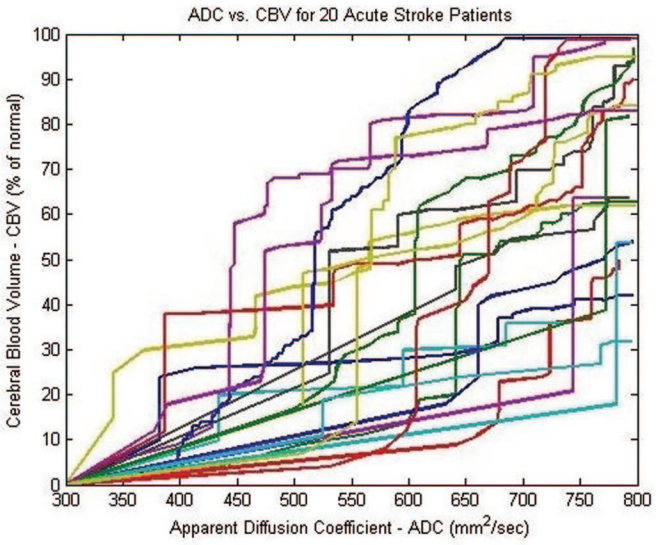

Figure 1

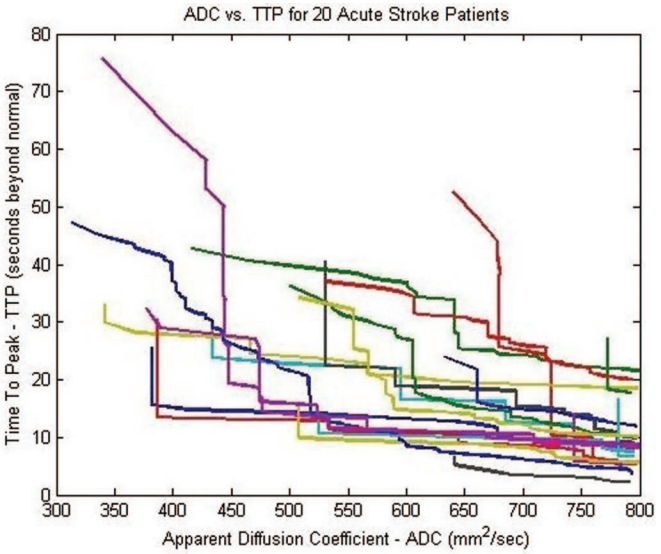

Figure 2

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W P241

Persistent contrast is a Predictor of Poor Clinical Outcome in Acute Stroke Patients Treated with Intrarterial Therapy

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Background: The *persistence of contrast sign (PCS)* in the artery during an angiogram is a radiological sign that may be observed in some patients with an arterial occlusion. We aimed to evaluate if the presence of *PCS* in patients with acute stroke who underwent endovascular procedures may influence recanalization, clinical outcome and mortality as a surrogate marker of poor collateral circulation. **Methods:** Acute stroke patients (<8h) who underwent endovascular procedures were prospectively studied. Location of vascular occlusion was confirmed by angiography, and the presence of *PCS* was considered if after the complete angiography sequence (>8seconds) the contrast remained at the location of occlusion. Patients were evaluated using NIHSS and c*linical improvement* was considered if decrease ≥4 points from the baseline to discharge was observed. **Results:** 115 consecutive patients were included, mean age was 70.8 (±11.8), 42.7% were female (n=50) and median baseline NIHSS was 19 (IQR 17-21). Fifty-four patients (51.4%) showed recanalization after endovascular treatment (TIMI ≥2). Distribution of occlusion location was: ICA 39 (33.3 %), MCA 56 (48%), Basilar 14 (12 %). The *PCS* was observed in 40 patients (34.2%): ICA 30 (88.2%), MCA 4 (9%), Basilar 6 (66.7%). Patients with positive *PCS* had lower recanalization rate (41% vs 61.2%) (p<0.034), lower clinical improvement (23.8%vs 76.2%) (p<0.001) and a trend to a high mortality rate (43.2%vs24%) (p=0.058). Other clinical variables are included in table 1. A logistic regression model showed that only TICA occlusion (OR 6.08 (1.05-35.17) p=0.044)) and *PCS* (OR 3.60 (1.04-12.40) (p=0.043)) were independent predictors of lack of clinical improvement after endovascular treatment. **Conclusions:** *PCS* is strongly associated to TICA occlusion; PCS is an independent predictor of lower clinical improvement after endovascular treatment in acute stroke patients.

Variable	Pc sign positive	Pc sign negative	P
Age, mean (SD)	68.5 (54-83)	72.4 (62-82)	0.145
Women, No. (%)	20 (51.3)	26 (53.1)	0.52
Smoker, No. (%)	7 (19.4%)	3 (6.5%)	0.076
Hypertension, No. (%)	25 (73.5%)	27 (60%)	0.21
Diabetes, No. (%)	3 (8.6%)	7 (15.6%)	0.28
Atrial Fibrillation, No. (%)	16 (44.4%)	26 (56.5%)	0.278
Endovenous thrombolysis, No. (%)	20 (51.3%)	28 (57.1%)	0.583
TICA occlusion No. (%)	*19 (51.4%)*	*1 (2.1%)*	*0.0001*
Ischemic changes on Acute CT, No. (%)	15 (43%)	11(24.4%)	0.081
Mortality No. (%)	*16 (43.2%)*	*12 (24%)*	*0.058*
Collateral circulation, No. (%)	6 (25%)	7 (39%)	0.33
Recanalization No. (%)	*16 (41%)*	*30 (61.2%)*	*0.034*
Baseline NIHSS (median, IR)	20 (18-22)	19 (16-21)	0.097
Time to recanalization (minutes) (median) (SD)	362 (193-531)	329 (221-437)	0.36

Table 1. Clinical variables of both groups.

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W P242

Effect of Transcranial Doppler Ultrasound on Combined rt-PA and Eptifibatide Thrombolysis in an in-vitro Human Clot Model

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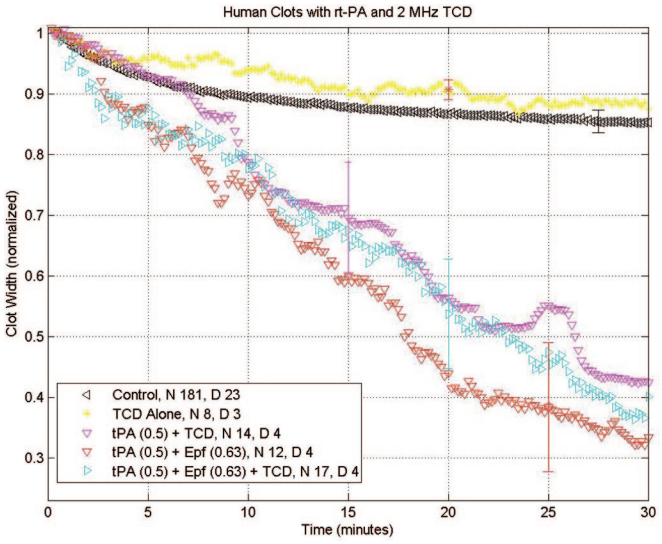
Background: Recombinant tissue plasminogen activator (rt-PA) is the only FDA approved thrombolytic therapy for acute ischemic stroke. Interest in improving the lytic efficacy and reducing the bleeding complication of rt-PA thrombolysis has led to the study of adjunctive therapies such as GP IIb-IIIa inhibitors and ultrasound enhanced thrombolysis (UET). The ideal acoustic parameters for UET are unknown at this time. Previous studies looking at low frequency ultrasound (~ kHz) showed increased initial lytic rates with ultrasound exposure. However, while ultrasound increased the overall lytic efficacy of single agent thrombolytic therapy, it did not increase the efficacy of combined rt-PA and eptifibatide thrombolysis. **Objective:** We determined the effects of high frequency 2 MHz transcranial Doppler ultrasound (TCD) on the thrombolytic efficacy of combined rt-PA and eptifibatide thrombolysis in an in-vitro human clot model. **Methods:** Human whole blood clots were made from blood obtained from volunteers, after appropriate institutional approval. Clots were incubated at 37°C for 3 hours and aged for 3 days at 4°C to maximize lytic resistance. Sample clots were exposed to human fresh-frozen plasma (hFFP) alone (control), and rt-PA and eptifibatide (rt-PA+Epf) in hFFP at a concentration of 0.5 and 0.63 ìg/ml respectively. Exposures were for 30 minutes at 37° with (+US) and without ultrasound (-US) with a 2 MHz TCD. Clot width was measured using a microscopic imaging technique and mean percent fractional clot loss (FCL) at 30 minutes was used to determine thrombolytic efficacy. Data were analyzed using Matlab (Version 6.5R13, Natick, MA). **Results:** Each of 4 treatment groups had a minimum of 8 clots (range: 8-181) from 3 different donors (range: 3-23), for a total of 218 clots. In control groups, FCL was 14.7 ± 3.7% (mean ± standard deviation; -US) and 12.5 ± 3.4% (+US). FCLs for the rt-PA+Epf groups were 66.6 ± 21.2% (-US) and 59.9 ± 18.0% (+US) (Figure 1). **Conclusion:** Unlike low frequency ultrasound enhanced single agent thrombolytic therapy, the use of high frequency 2 MHz transcranial Doppler does not affect thrombolytic efficacy of combination therapy with rt-PA and eptifibatide in an in-vitro human clot model.



Author Disclosures: W.W. Chang: None. J.M. Meunier: None. G.J. Shaw: None.

W P243

Agreement and Variability in the Interpretation of Presenting Computed Tomographic and Computed Tomographic Perfusion Imaging Changes in Ischemic Stroke Patients Qualifying for Endovascular Thrombolysis

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Background: Computed tomography (CT) is the current gold standard in evaluation of stroke patients for acute thrombolysis. The relative mismatch between regional cerebral perfusion and blood volume on computed tomography perfusion (CT-P) scan in acute ischemic stroke patients has been used to identify presence of salvageable tissue. However, insecurity and conflicting data exist over the ability of clinicians to correctly recognize and interpret these changes. **Objective:** To evaluate the agreement and variability in interpreting CT and CT-P imaging between stroke specialists in stroke patients qualifying for endovascular treatment. **Methods:** All endovascular treated acute ischemic stroke patients were identified through a prospective database maintained from two comprehensive stroke centers. 25 consecutively treated patients were used for this analysis. Their emergency department presentation, initial CT images, and CT-P data were independently read and classified by 5 board eligible/certified vascular neurologists with additional subspecialty training to decide whether or not to select for endovascular treatment. The CT images and CT-P images were evaluated separately and used as the sole decision making criteria, two weeks apart from each other (memory wash-out period). For each set of imaging, inter-rater and intra-rater reliability scores were obtained using Coneh's Kappa statistic to assess the proportion of agreement beyond chance. **Results:** Kappa-values for the CT images was 0.43 (ranged from 0.14, 0.8) (moderate agreement), and for the CTP images was 0.29 (ranged from 0.07, 0.67) (fair agreement) among the 5 reviewers. There was substantial variability within the group and between images. Observed agreement was found to be 75% with CT images and 59% with CTP images (with no adjustment for chance). Kappa-Values for intra-rater reliability was -0.14 (ranged from -0.27, 0.27) (poor agreement). **Conclusion:** There is considerable lack of agreement, even among stroke specialists, in recognizing and quantifying early CT changes and CTP identified salvageable tissue. This mandates a careful evaluation of CT and CT-P methods of recognizing and quantifying early ischemic changes prior to widespread adoption as an exclusion or inclusion criteria.

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W P244

Head-to-Head Comparison of Combination tPA Thrombolysis in an in-vitro Human Clot Model

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Introduction: Incidence of hemorrhage linked to treatment of ischemic stroke with tissue plasminogen activator (tPA) has led to interest in combination therapies such as ultrasound (US) enhanced thrombolysis (UET) or plasminogen (Plg), with the goal of decreasing the administered volume of tPA. High-frequency US (~MHz) such as 2 MHz transcranial Doppler (TCD) has demonstrated increased recanalization *in-situ*, but long-term benefits may not be significant. Low-frequency US (~kHz) has demonstrated higher lysis capabilities but has been associated with a high incidence of hemorrhage. *In-vitro* studies using plasminogen have shown enhancement of lysis while minimizing bleed-outs. This study compared the enhancement of tPA-induced lysis using combination therapy, with US at low or high frequency, or with Plg, in an *in-vitro* clot model. **Methods:** Blood was drawn from 30 subjects after local Institutional Review Board approval. Clots were made in 20-μL pipettes and placed in a water tank for microscopic visualization during treatment. Sample clots were exposed to tPA in human fresh-frozen plasma (hFFP) at concentrations of 0, 0.5, 1.00, and 3.15 ìg/ml. Clots were exposed to tPA alone, tPA and Plg (+Plg), tPA and 120 kHz US (+US), or tPA and 2 MHz TCD (+TCD) for 30 minutes. The extent of thrombolysis was determined by assessing clot width as a function of time, using a time-lapse microscopic imaging technique; the fractional clot loss (FCL) at 30 minutes was used to determine thrombolytic efficacy. **Results:** Each of 16 treatment groups had a minimum of 8 clots (range: 8-158) from 3 different donors (range: 3-24). There was no enhancement of lysis for any combination therapy with a tPA concentration of 0 ìg/ml; lysis for all groups increased when tPA (0.50 ìg/ml) is added. As tPA concentration increased from 0.50 to 3.15 ìg/ml, lysis increased for the +US and +Plg groups (increasing the FCL from 50.3% to 70.2%, +US; 65.2% to 82.5%, +Plg) but remained constant for the +TCD group (57.6% to 54.6%). Thrombolytic efficacy was similar for +US and +Plg groups at all concentrations. **Conclusions:** Improvement of lytic efficacy in combination therapy is dependent on tPA concentration.

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W P245

Telestroke Facilitates Access to Fibrinolytic Treatment for Patients with Ischemic Stroke.

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Both TELE-STROKE and rtPA have been demonstrated to improve the outcome of patients with acute ischemic stroke in health centres without Stroke Units or a specialized team on stroke care. In the framework of a competitive research project, TELE-STROKE was developed to manage the treatment of acute ischemic stroke with rtPA within the first 4.5 hours of symptom onset. The study was carried out in an urban reference hospital (RH) serving a population of 1,000,000 inhabitants; and two community hospitals (CH-1, CH-2) with different demographic and geographic characteristics. We analysed the results of patients treated with TELE-STROKE between January 2009 and May 2010. CH-1 serves a metropolitan population of over 200,000 inhabitants and CH-2, which is located in a hill area, provides health care coverage for 80,000. They are 10 and 68 miles from the RH respectively. 12 patients were treated, 6 between January and May 2010. CH-1: 9 out of 52 potentially treatable patients (excluding hemorrhagic stroke and those over 80 years old); initial median NIHSS score was 15.7 (range 8 to 24) and 10.7 (0-22) at discharge; time for fibrinolysis from symptom onset (TF) 149 (120-210) and door-to-needle (DN) time 65 (33-119), in minutes. CH-2: 3 out of 18 potentially treatable patients; NIHSS 16.7 (11-23) and 14.7 (10-18); TF 160 (130-205) and DN 100 (40-118). CH-1+CH-2: 12 patients; NIHSS 15.7 (8-24) and 10.7 (0-22); TF 154.5 (120-210) and DN 69 (33-119). No hemorrhagic complications occurred within the first 36 hours after rtPA. Intrahospital mortality 1/12 (initial NIHSS 16, malignant cerebral edema, CH-2); 5/10 Rankin < 3 at hospital discharge with a mean length of hospital stay of 1 week (2/10 Rankin=0) without variations after 6 months (2 remain unevaluated); mortality at 6 months after hospitalization 3/11 (2 CH-1: 1 for new stroke, 1 CH-2, residual pseudobulbar syndrome and aspiration pneumonia) and 1/12 protocol violation with no complications (platelet antiaggregant therapy and prevention of thromboembolic disease during 24 hours after fibrinolysis). In our pilot project, TELE-STROKE demonstrates improved access to safe and efficient treatment for patients with acute ischemic stroke supervised by stroke experts. At present, we are implementing TELE-STROKE in new health centres to provide coverage for a larger population.

Author Disclosures: A. Palomino: None.

W P246

Sedation Practice Patterns in Acute Stroke Endovascular Therapy: The IMS III Trial Experience

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Background: General anesthesia (GA) use is correlated with worse clinical outcomes and increased mortality in retrospective studies of patients undergoing endovascular therapy for acute ischemic stroke. We sought to quantify sedation practice patterns and better characterize the decision to use GA versus conscious sedation (CS) among sites in the ongoing Interventional Management of Stroke (IMS) III trial. **Methods:** The IMS III trial is a randomized study of IV rtPA versus combined IV/intra-arterial (IA) therapy for ischemic strokes (NIHSS>/=8). Specific sedation practices are not mandated. To capture sedation practice patterns, we surveyed stroke (neurology/emergency medicine) and neurointerventional local principal investigators at the 55 IMS III sites in the United States, Canada, and Australia using a multiple-choice questionnaire. Questions pertained to use of GA, CS, and sedation logistics. For the summary statistics, data are provided based on site except when local clinical and neurointerventional

PIs gave discordant answers, in which case both answers are included. **Results:** Respondents included neurointerventionalists (53.7%), stroke clinicians (39.0%), and emergency physicians (7.3%). Among 33 sites (60% response rate) and 41 surveys, 40.5% electively sedate (GA or CS) most patients prior to IA treatment, 8.1% sedate only cases planned for mechanical thrombectomy, 37.8% electively sedate cases based on individual clinical factors, and 13.5% do not electively sedate patients. Among those who perform elective sedation for any reason, approximately half start with GA and half start with CS, and the majority sedate patients prior to performing the diagnostic angiogram. Among those who electively sedate with GA first, 46.7% extubate immediately after the procedure while 26.7% typically extubate between 12-24 hours. Elective GA use is driven primarily by personal experience with unsedated patients (73.3%), but institutional standards guide the decision for some (20.0%). Although 52.9% reported that GA contributed to <15-minute delay in initiating IA therapy, 29.4% reported a 30-45 minute delay. Among those who use GA routinely, 28.6% reported not treating brief decreases in blood pressure during GA induction. Among those that electively sedate and use CS first, most noted that switching to GA due to respiratory depression (84.2%) or inadequate pain control (68.4%) was rarely or never needed. Among those that do not electively sedate patients by any method, 71.4% use CS as their initial method when it becomes clinically necessary. **Conclusions:** Sedation practices are highly variable among clinical sites in the IMS III trial. Half of sites electively sedate most patients, and half of those who sedate use GA as the standard approach. Whether the risks of GA (intubation, induction-related hypotension, and treatment delay) are justified requires further study.

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W P247

Manual Aspiration Thrombectomy, A Novel Approach To Endovascular Therapy For Acute Stroke

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Introduction: Manual aspiration thrombectomy (MAT) is an endovascular recanalization modality that is frequently used in acute coronary artery syndromes. In intracranial vessels however, there is little experience to date with this method . We aimed to evaluate recanalization rates, clinical outcomes and safety with this method in a consecutive case series treated at our center. **Methods:** Retrospective review of a prospectively acquired acute endovascular stroke database comprising 560 patients to date, from which patients treated with MAT were identified.MAT was carried out with the Distal Access Catheter (DAC) 0.54 and 0.43 French and Penumbra Reperfusion Catheter 0.52 and 0.41 French placved in the thrombus and attached to a syringe. Collected data include baseline demographics, risk factors, clinical and imaging characteristics. Successfully recanalization was defined as TIMI 2 and 3, Outcome (available in all patients analyzed) was considered favorable if mRS at 90 days was ≤ 2. **Results:** Between 11/2008 (date of first use of MAT) and 07/ 2010, 186 patients were treated. Of those, 126 patients underwent MAT and were included in the analysis. Median age: 65, median NIHSS: 16, occlusion location M1 MCA 67- 53 %, ICA terminus 36- 28%, M2 MCA 4- 3.2%, vertebrobasilar 19-15%, tandem extracranial carotid- intracranial carotid occlusion 23-18.5%. Median ASPECTS score 8. tPA administered in 44-35% (iv) and 50- 40.6% (ia). MERCI device used in 115-92%, Penumbra device used in 51- 41%.Median time from stroke onset to procedure start - 390 minutes. Median treatment duration- 118 minutes, TIMI 2 and 3 recanalization was achieved in 114/90.5% of patients, with TIMI 3 recanalization noted in 31/24.6%, Parenchymal hematoma was noted in 16-15.5% of patients. Favorable outcome was achieved in 53- 42.% of patients. When compared to all patients in our data base (n=560), MAT was associated with higher recanalization rates then patients treated without MAT, 90% vs 71%, p tivariate logistic regression analyses, admission NIHSS (OR 0.85, 95%CI 0.75-0.97, p=0.018), age (OR 0.88, 95% CI 0.82-0.94 P< 0.0001), intubation (OR 0.12, 95% CI 0.02-0.63, P=0.012) and baseline ASPECT scores (OR 2.45, 95% CI 1.36-4.41, P= 0.003), but not TIMI 2-3 recanalization were found to be significant predictors of outcome. The latter was attributed to the high overall recanalization rate observed. **Conclusion:** MAT is a useful addition to the armamentarium of endovascular treatment modalities for acute stroke. When used as part of multimodal recanalization strategies it appears to enhance the recanalization rate and possibly to improve outcome. In addition, when used in substitution to other treatment modalites it may significantly reduce procedural cost.

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Midterm Clinical and Angiographic Follow Up for the First FDA-approved Prospective, Single-arm Trial of Primary Stenting for Stroke: SARIS (Stent-Assisted Recanalization for acute Ischemic Stroke)

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Background and Purpose: Although early data demonstrate encouraging angiographic results following intracranial stent deployment for acute ischemic stroke, longer-term follow-up is necessary to evaluate clinical outcomes, as well as durability of angiographic results. We report 6-month clinical and radiologic follow-up data of the 20 patients prospectively enrolled in the Stent-Assisted Recanalization in acute Ischemic Stroke (SARIS) trial. **Methods:** Twenty patients were prospectively enrolled to receive self-expanding intra-arterial stents as first-line therapy for acute ischemic stroke treatment. Patients were scheduled for follow-up 6-months after treatment for clinical evaluation (modified Rankin Scale [mRS] score obtained by a trained certified research nurse/nurse practitioner) and repeat cerebral angiography. Angiographic interpretation was performed by an independent adjudicator. **Results:** At 6 months, mRS score was ≤3 in 60% of patients (n=12) and was ≤2 in 55% of patients (n=11). Mortality at 6-month follow-up was 35% (n=7). Follow-up angiography was performed for 85% (11 of 13) of surviving patients. All patients undergoing angiographic follow-up demonstrated Thrombolysis in Myocardial Infarction 3 flow on digital subtraction angiography or stent patency on computed tomographic angiography. None of the patients demonstrated evidence of in-stent stenosis (≥50% vessel narrowing). **Conclusion:** The midterm angiographic and clinical results following intracranial stent deployment for acute ischemic stroke are encouraging. Further study of primary stent-for-stroke treatment is warranted.

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W P249

Solitaire Device for Immediate Flow Restoration and Revascularization in Acute Stroke. Geneva experience

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Introduction: Acute revascularization improves outcomes after large vessel acute ischemic strokes (AIS). We now describe the angiographic and clinical results of the use of a novel mechanical clot retriever (Solitaire device). **Methods:** Patients presenting with AIS were treated at the Geneva University Hospital. We work under a bridging stroke protocol where patients arriving until 4h30min start IV thrombolysis and, at 30 minutes, if no clinical improvement or transcranial Doppler initial recanalization (TIBI 3), a bridge to IA therapy is performed. Patients with any contraindication to IV rtPA or arriving later than 4h30min are treated direct with IA therapy. **Results:** From March to December 2009, twenty-five cases of acute stroke due to occlusion of the intracranial internal carotid (n=5) or middle cerebral (n=20) arteries were treated using the Solitaire AB or FR device as the first line treatment modality. Fifteen patients were men (60%). The mean age was 66,3 years (range, 20-85) and the mean baseline NIHSS score was 18,7 (range, 8-30). Twelve (48%) patients had IV treatment before endovascular procedure and thirteen (52%) patients went directly to intra-arterial mechanical therapy. The mean time from the onset of symptoms to treatment was 250 minutes. The mean time from first angiogram to reperfusion (TICI ≥2) was 42 minutes. A final satisfactory angiographic result (TICI 2b and 3) was obtained in all patients. In twenty-two patients, the device was used exclusively with a mean of 2,3 attempts to get final result. The overall hemorrhagic complication rate was 20% but only 12% symptomatic. One subarachnoid hemorrhage with no clinical significance was also observed. One patient developed malignant edema in spite of an angiographic result of TICI 2b. Good outcomes at 90 days (mRS ≤2) were achieved in 16/25 (64%) patients. The group with previous IV treatment had 66% favorable outcome (8/12) and group direct mechanical IA had 61% favorable outcome (8/13) there were no statistical difference between these two groups. The best predictor of a favorable outcome at 3 months (mRS 0-2) was time to recanalization. Logistic regression model and comparison with age, NIH at admission, final TICI and time to recanalization (OR 0.94 95% CI 0.9 to 0.99) demonstrated a statistical significance (p>0.036). **Conclusion:** Mechanical thrombectomy with the Solitaire device appears to be safe and effective and may result in faster recanalization.

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W P251

Medical Complications of Systemic Thrombolysis, Primary Intra-Arterial Reperfusion and IV-IA Bridging Procedures

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Background & Purpose: Prior safety analyses focused on symptomatic intracerebral hemorrhage (sICH) rates comparing intravenous (IV) tPA, primary intra-arterial (IA), and IV-IA bridging procedures while data are generally lacking comparing medical complications of these treatment strategies. Subjects&Methods: Consecutive patients with acute ischemic stroke and a proximal intracranial arterial occlusion undergoing IV tPA, primary IA or IV-IA bridging treatment at a tertiary care center were analyzed. Neurological deficits were scored with the NIH Stroke Scale. Identified medical complications were classified as serious adverse events (SAEs) and adverse events (AEs). sICH was defined as parenchymal ICH (PH1 and 2 types) that was temporarily and causatively associated with an NIHSS increase of 4+ points. Outcome variables also included mortality, length of hospital stay (LOS), and modified Rankin scores at 3 months. **Results:** A total of 213 acute stroke patients received reperfusion treatment for a proximal intracranial occlusion (104 IV tPA, 73 primary IA, and 36 IV-IA). Apart from symptom onset-to-treatment time differences and median pre-treatment NIHSS scores (12, 15, 17 respectively, p=0.01), all groups were similar with respect to average age (63, 60, 60 yrs, p=0.28). Captured in-hospital SAEs included pulmonary embolism, MI, cardiac arrest, respiratory failure, sepsis, and sICH (Figure). AEs included seizures, pneumonia, DVT, pulmonary edema, UTI, and asymptomatic ICH (Figure). After adjustment for baseline stroke severity, age, and sICH, SAEs decreased the chance of recovery to mRS 0-2 at 3 month with IA or IV-IA (OR 4.0, 95%CI 1.2-13.2, p=0.025) but not with IV (OR 2.7, 95%CI 0.5-13, p=0.24). SAEs increased the risk of poor outcomes (mRS 4-6 at 3 month) after IA or IV-IA (OR 3.5, 95%CI 1.2-10.2, p=0.02), but not with IV alone (OR 3.1, 95%CI 0.8-12, p=0.11). Despite SAEs, mRS 0-2 at 3 month was achieved by 35% IV, 34% IA and 44% IV-IA patients, p=0.52. **Conclusions:** SAEs frequently occur frequently after reperfusion (in 1/5 patients with IV, 1/3 with primary IA and 1/2 with IV-IA). These events, independent of sICH, lead to a 3.5-fold increased risk of poor outcomes after IA or IV-IA procedures. More vigilant medical management may be preventative against SAEs, thus resulting in more patients achieving good functional outcomes after reperfusion treatment.

	IV only	IAT only	IV + IAT	p value 3x2, $\chi 2$
Age, median (range)	64.5(21-93)	61(22-85)	65(27-84)	0.283
Gender, % male	54.8	55.5	50	0.758
Race, % African American Caucasian Other	 44.2 53.8 1.9	 28.8 69.9 1.4	 41.7 58.3 0	0.255
Admission NIHSS, median (range)	12(0-29)	15(0-30)	17.5(0-30)	0.01
Time from onset to IV t-PA in hours, median (range)			1.9(0.5-3)	
Time from onset to IAT in hours, median (range)		6(1.4-48)	4.5(2-24)	0.008
Vessel, % ICA MCA ACA BA VA PCA	 0 89.4 1 9.6 0 0	 28.8 53.4 0 15.1 2.7 0	 33.3 38.9 0 13.9 8.3 2.8	<0.0001
Any adverse event, %	51	69.9	66.7	0.028
Any serious adverse event, %	20.2	38.4	50	0.001
PNA, %	7.7	28.8	22.7	0.001
UTI, %	14.4	37	13.9	0.001
Sepsis, %	3.8	12.3	13.9	0.059
Pulmonary edema, %	22.3	30.1	36.1	0.225
MI, %	2.9	1.4	2.8	0.793
DVT, %	3.8	8.2	2.8	0.336
PE, %	6.7	1.4	2.8	0.195
Respiratory Failure, %	9.6	28.8	50	<0.0001
Code, %	0	2.7	2.8	0.234
Seizure, %	2.9	2.7	2.8	0.998
Symptomatic ICH, %	4.8	8.2	8.3	0.597
Asymptomatic ICH, %	12.5	24.7	25	0.072
Other bleed, %	1.9	1.4	0	0.706
LOS, median (range)	5(1-29)	7(1-60)	6(1-36)	0.001
mRS at 3 mo, median (range)	3(0-6)	4(0-6)	3(0-6)	0.621
mRS at 3 mo 0-2, %	34.6	34.2	44.4	0.524
mRS at 3 mo 4-6, %	46.2	53.4	47.2	0.621
Death, %	9.6	20.5	33.3	0.004

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W P252

M5, a Thrombolytic Which Induced Significant Functional Recovery and Less ICH than tPA in Rat Stroke Models

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M5 is a mutant of the fibrin-specific proenzyme, single-chain urokinase-type plasminogen activator. M5 has the unusual property that its non-specific two-chain enzymatic form (tcM5) is inhibited rapidly by plasma C1-inhibitor (C1I). As a result, non-specific plasminogen activation, responsible for the hemorrhagic complications of plasminogen activators, can be prevented by C1I. Exceptionally, the rat endogenous C1I does not significantly inhibit tcM5, making rats unusually sensitive both to the side effects of M5 and to the salutary effects of added C1I. Two stroke models were used in a proof of concept study: (I) irreversible ischemia by ligation of the ICA and cauterization of the MCA in order to evaluate ICH. Thrombolytic infusions (30 min) were administered 4h later ; (II) reversible ischemia by thromboembolic occlusion of the MCA and infusions 2h later. Rats were given either tPA (10mg/Kg) or M5 (15mg/Kg) +/- an adjunctive bolus of C1I or saline +/- C1I. In model I, ICH mortality was high with both tPA (57%) and M5 (75%) but was reduced significantly by C1I to 25% and 17% respectively. In model II, M5+C1I induced the lowest infarct volume and caused the least non-lethal ICH (17%) and was the only group among the six to achieve significant reduction in functional neuroscore between pretreatment (3.30.2) and 24h later (2.00.4). The infarct volumes of tPA alone and M5+C1 were comparable (9221 and 8815 mm^3 respectively), indicating a comparable fibrinolytic effect. However, tPA alone caused much more ICH and was accompanied by the greatest edema volume (64mm^3 or 70% of the infarct volume), consistent with tPA's known disruption of the blood brain barrier. Adjunctive C1I increased the tPA infarct volume to 14215 mm^3, making it no longer significantly less than controls (21328 and 22713). However, C1I also reduced the tPA edema volume significantly to 24% of infarct volume. Activation of the complement pathway by tPA has been previously described by others, which may explain this C1I effect. In conclusion, the combination M5+C1I was as effective as tPA alone and more effective than tPA+C1I, causing significantly less ICH, edema volume, and the most functional improvement. These in vivo findings with M5 validate the in vitro data with C1I and provide a promising development for a new, effective and safer treatment of ischemic stroke.

	M5+C1I	tPA	M5	tPA+C1
Neuroscore reduction	Yes	NS	NS	NS
% with ICH	+	+++	++++	++
Edema vol.	++	+++	++	+
Infarct vol.	+	+	+	+++

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W P253

Comparison of Acute Medical Treatments in Ischemic Stroke Patients Aged 80 Years or Older

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Objectives: To compare the clinical outcomes of acute ischemic stroke patients aged ≥80 years treated with either intravenous recombinant tissue plasminogen activator (IV rt-PA), endovascular intervention with or without IV rt-PA, and non-thrombolytic medical treatment. **Methods:** A retrospective, non-randomized, observational study of patients, admitted within 9 hours of symptom onset, at three academic, University affiliated hospitals. The main outcome measures were neurological improvement, defined by improvement in National Institute of Health Stroke scale (NIHSS) score at 7 days or discharge of >=4 or achieving a score of 0, symptomatic and asymptomatic intracerebral hemorrhage, favorable outcome (discharge modified Rankin score 0-2), and in-hospital mortality. **Results:** A total of 44 patients received IV rt-PA, 46 received endovascular intervention with or without IV rt-PA, and 66 received non-thrombolytic medical treatment. IV rt-PA treated patients had a significantly clinically higher chance of favorable outcome [OR (odds ratio) 5.6; 95% CI (confidence interval) (1.8-17.5)], when compared with non-thrombolytic medical treatment. A significantly higher rate of neurological improvement was observed among the IV rt-PA [OR 7.2; 95% CI (2.7-19.5)] and endovascularly treated patients [OR 5.8; 95% CI (2-16.8)] when compared with non-thrombolytic medical treatment. **Conclusions:** A prominently higher rate of neurological

improvement and favorable clinical outcome was observed among acute ischemic stroke patients ≥80 years treated with IV rt-PA or endovascular intervention when compared with non-thrombolytic medical treatment; supporting the use of acute thrombolytic therapies in this patient population when contraindications are not present.

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W P254

In Vivo Thrombolytic Efficacy of Tissue Plasminogen Activator-Loaded Echogenic Liposomes

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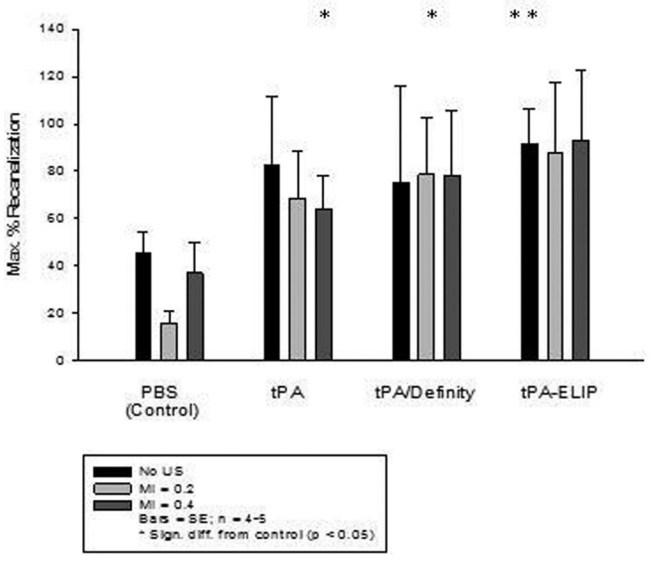
Background: Clinical studies have shown that pulsed Doppler ultrasound (US) can enhance the thrombolytic efficacy of tissue plasminogen activator (tPA) administered to acute ischemic stroke patients. We previously demonstrated that tPA-loaded echogenic liposomes (ELIP) enhanced thrombolysis in a rabbit aorta thrombus model in the presence of color Doppler US. We also demonstrated that tPA-loaded ELIP retain their acoustic reflectivity and tPA affinity for fibrin. This study aimed to compare tPA-loaded ELIP to other US-enhanced thrombolytic protocols. **Methods:** Clots were induced in the abdominal aortas of male New Zealand white rabbits (2-3 kg) using thrombin and a sclerosing agent (sodium ricinoleate) after aortic denudation with a balloon catheter. Treatment (200 μg of tPA alone, tPA mixed with 50 μl Definity, or tPA-loaded ELIP) was given proximal to the clot through a catheter introduced into the abdominal aorta from the carotid artery. The clot within the aorta was visualized and color Doppler US (6 MHz) was applied externally over the clot for 30 minutes at low MI (0.2) to induce acoustically-driven diffusion or for 2 minutes at high MI (0.4) to cause fragmentation of microbubbles and ELIP. Degree of recanalization was determined by Doppler flow measurements distal to the clots. **Results:** All treatments showed thrombolysis, measured as % recanalization at 2-minute intervals, maximum % recanalization in a 30 minute period (Fig. 1), and rate of total recanalization within 30 minutes. However, tPA-loaded ELIP appeared to be the most efficacious regimen. Enhancement of the thrombolytic effect by the addition of US at these settings was not observed for any of the treatments, but we confirmed that high MI color Doppler US increased tPA exposure at the liposomal surface. **Conclusions:** We have demonstrated that tPA-loaded ELIP thrombolytic efficacy is comparable to other previously described effective treatment protocols, while offering the advantage of US monitoring. Future studies will focus on optimization of US-induced thrombolytic efficacy.

Figure 1. Comparison of Thrombolytic Treatments in Rabbits



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W P255

THR-18 Peptide, a Modulator of tPA action: A Summary of Preclinical and Clinical Studies

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A synthetic PAI-1-derived 18-mer peptide, consisting of an amino acid structure of Ac-MAPEEIIMDRPFLYVVR-amide, was shown to be a modulator of tPA activity in two rat stroke models. In one model, embolic stroke was induced by intra-carotid injection of micro-clots to rats, while in the other model, mechanical stroke was induced by transient occlusion of the middle cerebral artery (tMCAO). tPA (6 mg/kg) was administered IV with or without THR-18 (1 mg/kg) at 2 or 4h post occlusion. In the embolic stroke model, addition of THR-18 to tPA led to an improvement in vessel patency post reperfusion. In both the embolic and mechanical models, the combination of tPA and THR-18 resulted in reduced mortality and a lower frequency (10% versus 30-45%) of tPA-induced intracranial hemorrhage, as well as dramatic reductions of infarct size and brain edema as compared to the control and tPA-treated rats. THR-18 alone was without effect. Comprehensive toxicological studies were performed in rats and dogs, utilizing doses of 5 to 50 mg/kg of THR-18. At doses of 15 mg/kg or higher, some insoluble test material was deposited in the lungs of rats, but not in the dogs. In dogs, a significant decrease in blood pressure, which persisted for 30 -60 min, was seen following administration of 10 and 30 mg/kg of THR-18, but not following the 5 mg/kg dose. No other drug-related adverse effects were found. A First-In-Human Phase 1 dose-escalation study was conducted in healthy volunteers. THR-18 was administered intravenously at doses of 0.25 - 1 mg/kg during 15min. No adverse effects were found noted following administration of the 0.25 and 0.5 mg/kg doses. At higher doses (0.75 and 1 mg/kg), several instances of orthostatic hypotension were noted during the first 1.5 hours post drug administration. No clinically significant changes in blood pressure were noted at any dose in the supine position. No serious or severe adverse events were reported throughout the study. Following these encouraging phase I safety data , we plan to further evaluate THR-18 in stroke patients receiving tPA in a multinational Phase IIa clinical study. This study is expected to commence in 2011.

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W P256

The SPEED Trial: A Study of the Penumbra Early Evacuation Device

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Introduction: The Penumbra System is an aspiration-based mechanical thrombectomy device indicated for the revascularization of large vessel occlusion in acute ischemic stroke. Reported herein are results of a proof of concept study to assess the extent to which a reperfusion catheter with a larger internal diameter (0.054 inch) affects on-the-table aspiration efficiency/speed, accessibility and safety of the System. **Methods:** This was a retrospective case review of 53 consecutive patients with large vessel occlusion in the brain who were treated with the larger Penumbra System 054 catheter at 9 centers in the U.S.. Main inclusion criteria were presentation within 8 hours of symptom onset and an occlusion of a treatable cerebral vessel. The primary endpoints were time of aspiration and rate of complete revascularization as measured by the TIMI scale. Results from the Penumbra Pivotal* trial that utilized the smaller catheters (0.026 to 0.041 inch) were used as the historical control. **Results:**

	PIVOTAL* (N=125)	054 (N=53)
Age (mean)(years)	64	63
Female	49%	60%
Baseline NIHSS (median)(range)	18(8-34)	18(4-31)
Time from Symptom Onset to Groin Puncture (median)(hrs)	4.1	4.8**
Time from Groin Puncture to End of Aspiration (median)	97 min	52min**
Time Required for Aspiration (median)	45 min	14 min**
Pre-Procedure TIMI 0-1	100%	98%
Post Procedure TIMI 0-1	18%	11%
Post Procedure TIMI 2	54%	47%
Post Procedure TIMI 3	27%	42%**
Symptomatic ICH	11.2%	9.4%
Number of Patients with Procedural Serious Adverse Events	3	3

*Stroke 2009;40:2761-2768 **P< 0.05 vs. PIVOTAL* **Conclusion:** Increasing the internal diameter of the Penumbra Reperfusion Catheter to 0.054 inch can enhance aspiration efficiency and speed, leading to a shorter aspiration time and a more complete revascularization without affecting accessibility or safety.

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Intra-arterial Thrombolysis Initiated Greater than 24 Hours after Stroke Onset

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There is growing evidence to support the hypothesis that vessel recanalization is the strongest determinant of outcome in patients with acute ischemic stroke due to large vessel occlusion.

Current selection criteria for recanalization therapy utilizes rigid time windows. However the evolution from ischemia to infarction occurs at variable rates. We assessed the hypothesis that it is safe to treat patients by endovascular means beyond the 24 hour time window in highly selected patients based on the presence of a small ischemic core and large ischemic penumbra (substantial mismatch-SM). **Methods:** Retrospective review of a prospectively acquired clinical database of all patients treated at the University of Pittsburgh Medical Center between 2004 and 2009. Patients were included if they presented with a symptomatic intracranial large vessel occlusion that was treated by intra-arterial thrombolysis greater than 24 hours after stroke onset. Wake-up strokes were included if above criteria were met. Presence of SM was determined by MRI or CT perfusion. **Results:** We identified 34 patients out of a total of 385 patients (8.8%). Mean and median times from symptoms onset to groin puncture were 63 and 48 hours respectively. Median age: 67. Median presenting NIHSS was 13. Distribution of vessel occlusion: vertebrobasilar 16/47%, internal carotid terminus 5/14%, M1 MCA 9/26.47%, M2 MCA 4/12.12% Recanalization rates: 24/70.5% TIMI score of 2 or 3, and 10/29.4% TIMI 3. PH1/PH2 parenchymal hematoma occurred in 3% and HT1/HT2 hemorrhagic transformation occurred in 21%. Follow-up was available in all patients. Mortality rate was 9/27.7%. A good outcome (mRS of 0,1,2) was achieved in 16/47.6% of patients. **Conclusions:** Our results indicate that intra-arterial therapy initiated beyond 24 hours after ictus can be performed with a safety profile that is no different compared to treatment within conventional time windows. Due to lack of a control group clinical efficacy of this approach cannot be evaluated. Prospective randomized controlled are needed to adequately answer this question.

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W P258

General Anesthesia during Mechanical Thrombectomy Negatively Impacts Functional Independence and Mortality in Only Less Severe Ischemic Stroke

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Background: Use of general anesthesia (GA) during mechanical thrombectomy for acute ischemic stroke has been correlated with worsened outcomes. In this prospective, multicenter registry, we evaluated use of GA during thrombectomy as a predictor of 90-day morbidity and mortality and examined whether this effect was dependent on stroke severity at onset. **Methods:** Prospectively collected data including demographics, baseline clinical variables, and procedural characteristics were obtained from the Merci Registry. Univariate and multivariable analyses were performed to assess the relationship between these variables and primary outcome measures of morbidity (mRS 0-2) and mortality at 90 days. Mixed logistic models with facility as random effect were used to adjust for variance between study centers. Using ROC curves to determine the appropriate cutoffs for NIHSS, regression analyses were again performed for dichotomized strata of NIHSS to elucidate a differential effect of GA depending on stroke severity. **Results:** Data for 761 patients from 34 centers were included in the analyses. Median age was 69.4 years, and median initial NIHSS was 18. Sixty-three percent of all patients were intubated and placed under GA for thrombectomy with wide variability in the proportion of intubated patients by center (5.9-100%). GA status, recanalization, age, history of congestive heart failure, procedure duration, and baseline NIHSS were all independent determinants of morbidity and mortality in univariate analyses. In addition, prior TIA and IA thrombolysis were determinants of morbidity, while diabetes was predictive of mortality in univariate analyses. In a multivariable model, GA remained significantly associated with lower likelihood of good outcome (OR 0.51; $p=0.003$) and higher risk of mortality (1.84; $p=0.008$). Use of GA in patients with more severe stroke (NIHSS$>=$20) was not associated with good outcome (OR 0.73; $p=0.43$) or mortality (OR 1.38; $p=0.27$). However, for those with less severe stroke (NIHSS$<$20), the effect of GA remained independently associated with poor outcome (OR 0.40 for mRS 0-2; $P<0.001$) and mortality (OR 2.40; $p=0.005$). **Conclusion:** Use of GA during mechanical thrombectomy for ischemic stroke correlates with mortality and worsened functional outcomes in those with less severe stroke (NIHSS$<$20) but not in those with more severe stroke (NIHSS$>=$20). Treating physicians should consider using alternative sedation modalities for patients with less severe stroke, but need not avoid tracheal intubation in patients with more severe stroke.

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W P259

Intra-Arterial Thrombolysis Demonstrates Better Clinical Outcome than Intra-Arterial Thrombectomy

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Background: A recent meta-analysis suggested that intra-arterial (IA) thrombolysis substantially improves clinical outcomes in acute ischemic stroke. Due to lack of concurrent controls in study design, similar data is not available for IA thrombectomy. We hypothesized that IA thrombolysis would demonstrate improved clinical outcomes compared with IA thrombectomy. **Methods:** From our prospectively collected stroke registry, we identified all patients who underwent IA therapy from November 1996 to January 2010. Patients were divided into two treatment groups: IA thrombolysis only (Group A, with/without mechanical clot disruption with the guidewire) or IA thrombectomy (Group B, MERCI or PENUMBRA with/without thrombolysis). The primary outcome measure was good clinical outcome at discharge defined as modified Rankin Scale (mRS) 0-2. Secondary outcome measures included recanalization (TICI $\geq$2b), need for hemicraniectomy, symptomatic intracranial hemorrhage (sICH), and length of stay (LOS). Statistical analysis for treatment effect included chi square, fisher's exact and multivariate logistic regression. **Results:** A total of 257 patients underwent IA therapy (147 Group A, 110 Group B). The two groups were similar in age (63 yrs. vs. 61 yrs., $p=0.26$), gender (55% male vs. 50% male, $p=0.45$) and median NIHSS (17 vs. 19, $p=0.17$). Despite lower rates of recanalization in Group A (51.4% vs. 74.0%, $p=0.0003$), a higher proportion of patients in Group A had a good outcome (21.7% vs. 12.7%, $p=0.07$). There was no difference between groups in the occurrence of sICH (4.8% Group A vs. 7.3% Group B, $p=0.43$) or any other secondary outcome measure. Our multivariate model adjusted for baseline NIHSS, age, and recanalization demonstrated that patients in Group A were more likely to have a good outcome (OR 2.24, 95% CI 1.002-5.000, $p=0.0496$). **Conclusions:** In our population, IA thrombolysis was associated with better clinical outcomes despite lower recanalization rates when compared with IA thrombectomy. This analysis is limited by its retrospective nature, but suggests the possibility that a group of patients less likely to benefit may be driving the results or, more concerning, the possibility of harm (not related to sICH) with IA thrombectomy. Given the cost associated with thrombectomy and lack of data supporting its clinical efficacy, current and future randomized controlled trials evaluating IA thrombectomy are imperative to clarify these issues since IA thrombectomy is quickly becoming 'usual care' for acute ischemic stroke.

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W P260

Failure of Conscious Sedation Among Patients Undergoing Neuro-Endovascular Procedures

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Background: Neuro-endovascular procedures are performed under conscious sedation (local anesthesia) in varying proportion of patients in various institutions. It is known that in certain patients conscious sedation may be inadequate during the procedure and an unplanned conversion to general anesthesia may be necessary. **Objective:** To ascertain the rate of failure of conscious sedation in patients undergoing neuro-endovascular procedures and compare the prognosis of patients that were converted from conscious sedation to general anesthesia to those initiated with general anesthesia. **Methods:** All 1971 endovascular treated patients were identified through a prospective database maintained from two comprehensive stroke centers between 2006-2009. Favorable outcome (modified Rankin score of 0-2), death, and patients' clinical and procedural characteristics were obtained and reviewed. **Results:** The rate of failure of conscious sedation in 265 patients (387 procedures) undergoing neuro-endovascular procedures under conscious sedation was 2.3%. Demographics, risk factors, outcomes and procedure type are provided in the tables below. (Tables 1 and 2)

Table 1

Per patient analysis (N=265)

Characteristics	N (%)	Failure of local anesthesia (n=8)
Mean Age± SD	56±18	53±16
Female	134 (51%)	1 (13%)
Clinical outcome		
Favorable outcome (mRS 0-2)	111 (42%)	4 (50%)
Death	46 (17%)	1 (13%)

Table 2

Per procedure analysis (n=387)

Characteristic	Frequency Distribution	Local to General conversion rate
Procedures	387	9 (2.3%)
Type of procedure		
IA vasospasm	88 (23%)	2 (2.3%)
Extracranial Carotid Stent Placement	11 (3%)	1 (9.1%)
Intracranial Carotid Stent Placement	30 (8%)	1 (3.3%)
Embolization ruptured aneurysm	86 (22%)	1 (1.2%)
Embolization unruptured aneurysm	53 (14%)	1 (1.9%)
Endovascular treatment-acute ischemic stroke	50 (13%)	3 (6.0%)
AVM/epitaxis	69 (18%)	0 (0%)
Number of procedures per patient		
1	199 (75%)	
2	38 (14%)	
3+	28 (11%)	

Conclusions: There is a minimal rate of conscious sedation failure among patients undergoing neuro-endovascular procedures with minimal rates of adverse outcomes. Such observations support broader use of local anesthesia in neuro-endovascular practice.

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W P261

The Hyperdense Vessel Sign on CT is Predictive of Successful Recanalization Using the Merci Device in Acute Ischemic Stroke

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Introduction: The physical characteristics of the occlusive thrombus in acute stroke may have therapeutic implications. Specifically, clot with high fibrin content may be more adhesive and difficult to retrieve by endovascular techniques. Ideally, the interventional strategy should be based on information about the physical characteristics of the clot that could be ascertained during non-invasive imaging before treatment. Thrombus with a high erythrocyte content is hyperdense on CT, whereas fibrin-rich clot may be isodense. We hypothesized that the physical clot characteristics that determine CT density may also determine likelihood of retrieval with the Merci device. **Methods:** We reviewed all acute stroke cases treated with the Merci device at UCLA between 2006 and 2007 that underwent pretreatment non-contrast CT. Each CT was assessed for the presence or absence of the hyperdense vessel sign (HVS) by a neuroradiologist (PV) who was blinded to treatment outcome. Angiographic outcome after treatment with the Merci device was assessed using the Thrombolysis in Cerebral Infarction scale (TICI) by a neuro-interventionalist (MTF) who was blinded to CT findings. **Results:** We identified 22 patients that had a non-contrast CT before attempted Merci thrombectomy (mean age 69; median NIHSS 18), 20 of whom had MCA occlusion, 5 also involved the ICA, and 2 presented with basilar occlusion. Fifteen patients exhibited the HVS, of whom 13 had successful revascularization (TICI 2a or better) after Merci thrombectomy. In contrast, 7 patients did not exhibit the HVS, of whom only 1 experienced successful revascularization with the Merci device. This difference was highly significant ($p=0.0023$; Fisher's exact test). **Conclusion:** The absence of the HVS on non-contrast CT in acute ischemic stroke was strongly predictive of failure of revascularization using the Merci device. In contrast to the erythrocyte-rich thrombi that are associated with the HVS, the occlusive thrombus in these cases may have a higher proportion of platelets and fibrin, which may create a more resistant clot. The absence of HVS on pre-treatment CT may serve as an indicator of adhesive clot which may require a more aggressive or alternative therapeutic approach.

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W P262

Gasometric Analysis Of Blood Samples Directly Obtained Beyond Arterial Mca Occlusion During Endovascular Procedures Predicts Response To Revascularization

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Background: Endovasclar procedures for acute stroke may last several hours until final recanalization is achieved. During this time, measures offering information about the degree of ischemic damage of the affected brain tissue may help the physician taking decisions about whether to pursue or not efforts to achieve recanalization. We studied gasometric parameters of blood samples drawn through the microcatheter. **Methods:** Acute stroke patients undergoing endovascular procedures were studied. After clot was crossed with the 2.3 French microcatheter a 3-4 ml. blood sample was obtained from the arterial segment distal to the occlusion (Post). Simultaneously another sample was obtained from femoral artery (Pre). A gasometric study was immediately performed. We defined clinical improvement as NIHSS decrease ≥ 4 points at discharge or 7 days. Infarct volumes were measured on 24 hour CT scan. **Results:** Post-occlusion blood sampling was performed in 12 patients with an acute middle cerebral artery occlusion. No complications related to the procedure were observed. The gasometric analysis showed differences between Pre and Post blood samples in mean oxygen partial pressure (Post-paO2 73.2 Vs Pre-paO2 79.3; $p=0.007$), mean oxygen saturation (Post-Sat O2 93.08% Vs Pre-Sat O2 94.4%: $p=0.006$) and mean anion GAP (Post-Gap 12.00 Vs Pre-Gap 13.02: $p= 0.04$). Despite that neither Post-paO2 ($r=0.07$;$p=0.8$) nor Post-SatO2 ($r=0.1$; $p=0.8$) were correlated with time from symptom onset to gasometry, the final infarct volume was inversely correlated with Post-paO2 ($r=-0.722$, $p=0.018$) and Post-SatO2 ($r=-0.664$, $p=0.036$). We identified a cut point value of Post-paO2$>$70 mmHg that better predicted differences in final infarct volume (386 Vs 69 cc; $p=0.032$) and discharge NIHSS (27 Vs 12; $p=0.011$). The only variables associated with clinical improvement were Post-paO2$>$70 ($p=0.014$) and dyastolic blood pressure ($p=0.03$). In the logistic regression model adjusted for time to recanalization Post-paO2$>$70 emerged as the only independent predictor of clinical improvement (OR:27 95%CI:1,043-689,790; $p=0.047$). **Conclusion:** Direct local blood sampling from the ischemic brain is feasible during endovascular procedures in acute stroke patients. A gradient in oxygenation parameters was demonstrated between Pre and Post occlusion blood samples. This information may be used to predict clinical outcome and help in decision making in the angio-suite.

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W P263

Persistent Penumbra in a Rabbit Stroke Model at 24 Hours: Incidence and Histologic Characteristics

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Background: Occlusion of cerebral vessels which leads to stroke may also induce significant hypoxia in regions adjacent to infarction, penumbra. The duration and extent of penumbra is clinically important, as it determines the window and brain volume in which interventions may save hypoxic but viable tissue. Understanding the development and duration of the penumbra in animal models is necessary in order to design meaningful models that translate to effective clinical therapies. In this study, we demonstrate incidence and characteristics of penumbra at 24 hours post infarction in a rabbit thromboembolic model with and without thrombolytic therapy. **Methods:** New Zealand White rabbits (5.2 ± 0.03 kg, $n=51$) were assigned to one of three groups: stroke induced by aged autologous clot ($n=23$), stroke induced by insoluble microspheres ($n=14$), and sphere-stroked animals treated with 3μm microbubbles plus ultrasound ($n=14$). Stroke rabbits were embolized with 3 to 5 hr autologous cylindrical blood clots or 700-900μm diameter insoluble microspheres using selection of the internal carotid artery. Rabbits were euthanized at 24 hr and infarct volume was measured following triphenyltetrazolium chloride (TTC) staining of brain sections. Penumbra was visualized using immunostaining of pimonidazole injected fifteen minutes prior to euthanasia. Penumbra was defined as strong staining adjacent to and contiguous with infarcted regions. Morphometric analysis of the stained slides was used to measure infarct area and penumbra area in each brain section. Brain sections from unstroked animals were used as a negative staining control. **Results:** Penumbra was present in 8/51 (15.7%) stroked rabbits. Penumbra incidence did not vary by model ($p=0.62$) or with treatment ($p=0.65$). There was no relationship of penumbra size to stroke volume ($p=0.64$). Average size of penumbra as a percentage of total lesion (infarct plus penumbra) was 14% $\pm$4% (range 0.96% to 35%). **Conclusions:** Potentially reversible penumbra is present in 15.7% of rabbits at 24 hours after embolic stroke. At this time point, penumbra can represent as much as 35% of the total lost brain tissue. Intervention at this time point may be of benefit to a significant patient population, and could potentially result in significant clinical improvement.

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W P264

A Novel Dimension Changing Distal Access Aspiration Catheter For Acute Stroke Treatment

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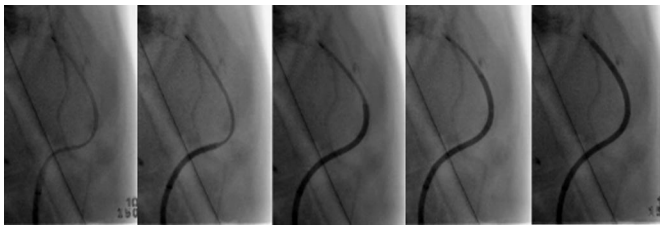
Objective: To test the feasibility use of a novel dimension changing distal access aspiration guide catheter in an in vivo vasculature setting. **Methods:** Two Swine were utilized to assess intracranial access, thrombus aspiration ability, and safety of a novel dimension changing distal access aspiration guide catheter compared to another commercially available neuro guide catheter. In this study, thrombi were prepared in such a way to represent characteristics of those found in acute stroke patients. The thrombi were injected into target maxillary arteries, via a 6Fr guiding catheter. The thrombi were allowed to set up in situ for at least 15 minutes until complete localized occlusion of the target vessels were confirmed by angiography. Once the occlusion was confirmed, the novel guide would be positioned adjacent to the target occlusion, then expanded to a larger ID and used to aspirate thrombus focally with or without the aid of a mechanical thrombectomy device positioned through the lumen in a coaxial fashion; additionally a histological safety study was conducted in the renal arteries to assess vasculature damage when this novel device is positioned and expanded. Parameters collected for this assessment study were navigational assessment, vessel straightening, clot aspiration, and vessel trauma. A commercially available neuro vasculature indicated guide catheter was used as a control. **Results:** Deeper, more distal access was achieved with the novel dimension changing aspiration guide catheter, which conformed much better to the vessel tortousity, and with much less vessel straightening than the commercially available control. Insofar as the renal artery safety study, histopathology revealed no differences in vascular damage between the novel guide and the control. Distal clot was aspirated with the novel guide, whereas the commercially available guide catheter could not reach the target occlusions. **Conclusions:** The novel dimension changing distal access aspiration guide catheter appears feasible for distal access and thrombus aspiration in the swine neurovascular model with much less vessel straightening when compared to a guide catheter control.



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W P265

Clinical-Diffusion Mismatch Better Discriminates Infarct Growth than MTT-DWI Mismatch in Patients with MCA-M1 Occlusion and Limited Infarct Core

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Background and Purpose: Previous studies have suggested that the Perfusion-Diffusion Mismatch (PDM) model is more accurate than the Clinical-Diffusion Mismatch (CDM) model for selecting patients who are likely to benefit from reperfusion therapy. However, these studies have not accounted for site of occlusion. Our purpose is to compare CDM and MTT-DWI mismatch in patients with proximal MCA occlusion and small infarct core on presentation. **Methods:** Single institution, retrospective study of consecutive AIS patients admitted between 01/05-03/08 fulfilling the following criteria: (1) MCA-M1 Occlusion on admission CTA; (2) MRI performed $\leq$10 hours from stroke onset; (3) Stroke Volume $\leq$25cc on admission MRI-DWI. CDM was defined as baseline NIHSS $\geq$8 and DWI volume $\leq$25cc (as proposed by Davalos et al). MTT-DWI mismatch was defined as a MTT lesion ([MTT-DWI])/DWI) volume $\geq$ 20% and $\geq$10cc larger than the DWI lesion volume. Significant infarct growth was defined as $>$5cc (at least 20%) increase in infarct volume on follow-up imaging. Univariate and multivariate analysis were performed to define the predictors of significant infarct growth. **Results:** A total of 43 patients were identified (mean age, 75.8$\pm$16.4 years; 62% females; median/IQR baseline NIHSS 13/8-17; median/IQR time from symptoms to DWI, 5/3-6 hours; median/IQR glucose: 125/111-153 mg/dL; 65% right-sided lesions; median/IQR baseline DWI volume, 6.5/1.8-12.5). Nine patients underwent IV thrombolysis, six endovascular treatment, and six combined therapy. On univariate analysis, larger admission DWI volume ($p<0.0001$), baseline NIHSS $\geq$8 ($p=0.001$), lack of IV and/or endovascular treatment ($p=0.021$), glucose levels $>$125mg/dL ($p=0.024$), CTA-collaterals equal or less than contralateral hemisphere ($p=0.046$), and lower admission ASPECTS ($p=0.049$) predicted infarct growth. Baseline NIHSS $\geq$8 was the only independent predictor of stroke growth in the multivariate analysis ($p=0.001$). All patients had MTT-DWI mismatch greater than 20%. There was no significant association between the amount of MTT-DWI mismatch and infarct growth ($p=0.33$). **Conclusions:** CDM is the most powerful predictor of infarct growth in patients with MCA-M1 occlusion and small infarct core. All M1-occlusion patients with a small stroke on presentation will have a significant oligemic MTT lesion regardless of NIHSS on presentation and the intensity of the mismatch does not necessarily predicts infarct growth. Therefore, MTT-DWI oligemic mismatch is patients with proximal MCA occlusions is not an accurate measurement of clinical meaningful penumbra. The degree to which these results may be generalizable to other, more strictly defined surrogates of penumbra, including thresholded transit time and CBF measures, is currently under investigation.

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W P266

Collateral Circulation as a Prognostic Factor in the Selection of Patients for Endovascular Treatment of Acute Ischemic Stroke

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Background: Endovascular treatment (ET) showed to be safe for acute ischemic stroke (AIS), but uncertainty remains about which patients mainly benefit from this treatment. Preclinical and neuroimaging studies suggest that collateral circulation (CC) could preserve ischemic penumbra, reducing infarct size and improving clinical outcome. We aim to evaluate the role of CC on functional outcome in patients treated with ET. **Methods:** We analyzed consecutive patients treated with ET for AIS due to proximal middle cerebral artery (M1) and internal carotid artery (ICA) occlusion from 2004 to 2009. We prospectively collected clinical data and retrospectively reviewed neuroimaging data. Early ischemic changes and extension of infarction were evaluated with ASPECTS on baseline and 24h CT scans. Collaterals were scored on pretreatment coronal section angiograms using the Collateral Circulation Score (CCS). Based on extent of collaterals in Anterior (ACA) and Middle (MCA) Cerebral Artery territory, this score identifies 5 grades of collateralization: 0=no flow in both ACA and MCA; 1=flow in ACA; 2=flow in MCA above insular region; 3=flow in MCA including insular region; 4=flow in MCA-M1. We dichotomized CCS in good (2-4) and poor CC (0-1). We defined good outcome in the presence of mRS$\leq$ 2 at 90 days. Hemorrhage was considered symptomatic in the presence of $\geq$1 point increase on NIHSS. **Results:** Out of 67 patients with anterior circulation AIS, we identified 44 patients with proximal occlusion (29 ICA, 15 M1); 23 patients were excluded from analysis (17 with distal occlusion and 6 for low quality imaging). There were 29/44 (66%) patients with good (mean age 67.5+/-14.3; M 69%) and 15/44 (34%) patients with poor CC (mean age 67.9+/-12.4, M 33%). Poor CC patients had larger size lesions (24h ASPECTS mean+/-DS=2.9+/-2.9 vs 4.8+/-2.1; $p=0.037$) and higher rate of symptomatic hemorrhage (27% vs 10%, $p=0.161$) compared to good CC patients. Good outcome was observed in no patients with CCS 0, 10% with CCS 1, 50% with CCS 2 and 40% with CCS$\geq$ 3 ($p=0.048$ ÷2 for trend). A synergic effect between recanalization and collaterals was also observed, with good outcome in 10% of patients with recanalization/CCS 0-1 and 80% of patients with recanalization/CCS 2-4 (OR 0.090, CI 0.016-0.506; $p=0.006$) **Discussion:** In our series the absence of CC is associated with increased size lesion and worse outcome. We suggest the evaluation of CC could be used as a tool for the selection of patients for ET.

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W P267

Facing The Clot: Angiographic Appearance Predicts Recanalization And Clinical Outcome In Acute Ischemic Stroke

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Background: Previous studies have suggested that the angiographic appearance of an occlusion during acute stroke may offer some predictive value of endovascular thrombolysis outcomes. Various methods of describing such occlusions have been utilized. We evaluated different methods of grading angiographic clot margins to assess thrombolytic outcomes in patients with acute cerebral ischemia undergoing endovascular recanalization. **Methods:** We identified a cohort of consecutive patients admitted between January 1, 2007 and July 31, 2010 who presented with acute stroke symptoms from internal carotid artery (ICA) or middle cerebral artery (MCA) occlusions and underwent endovascular recanalization therapy (ERT) with intra-arterial tissue plasminogen activator (IA-tPA) or mechanical thrombectomy. Patients were included regardless of whether intravenous tissue plasminogen activator (IV-tPA) was infused before ERT. Contrast opacification proximal to the angiographic occlusion was categorized as blurred or sharp. The target lesion was also described as tram track if any flow was observed around the clot, complete cutoff if no contrast flow was present around the clot, and tandem if multiple occlusions were identified along the vessel. Assignments were based on consensus opinion by two investigators. Analyzed outcomes included revascularization graded on the Acute Occlusive Lesion (AOL) and Thrombolysis in Cerebral Infarction (TICI) scales and global disability at discharge (modified Rankin Scale - mRS). **Results:** Among the 65 patients, median age was 73 (range 22 - 95) and 65% were female. Occlusion sites were: ICA - 19; M1 MCA - 40; distal MCA - 6. The average time to endovascular recanalization was 390 $\pm$ 154 minutes and 10 patients (15.4%) received IV-tPA prior to angiography. ERT techniques included IA-tPA in 7 and mechanical thrombectomy in 58. Sharp vs blurred clot margins did not predict recanalization, with median AOL of 3 vs 2, $p = 0.121$, and median TICI of 2b vs 2a, $p = 0.118$. Patients with sharp clot margins had better discharge functional outcome, median mRS 3 vs 5, $p= 0.001$. Patients with a tram track morphology clot appearance had better recanalization outcomes than those with complete clot cutoffs: median AOL 2 vs 3, $P<0.05$, and median TICI 2a vs 2b, $p=0.057$. Only two patients demonstrated tandem lesions. Differences in discharge disability score for clot morphology groups did not reach significance: mRS median 4 vs 5, $p = 0.151$. **Conclusions:** The initial angiographic appearance of the clot face predicts recanalization and clinical outcomes after endovascular therapy. These features may guide future revascularization approaches.

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W P268

Admission DWI Infarct Volume May Be A Stronger Predictor of Clinical Outcome than The Presence of Proximal Arterial Occlusion in Acute Stroke Patients Undergoing Reperfusion Therapy

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Purpose: To determine independent predictors of good outcome (3-month modified Rankin Scale (mRS)$\leq$2) in acute ischemic stroke patients who received thrombolysis. **Methods:** We retrospectively reviewed the imaging and clinical data of consecutive patients admitted with acute stroke symptoms to our institution, between May 2008 and May 2010. We included all 56 patients who received IV and/or IA therapy and had CTA and MRI-DWI within 9 hours of stroke onset. DWI lesion volumes were manually segmented and CT angiographies were accessed for the presence of a proximal arterial occlusion (i.e. ICA, M1 or M2 occlusion). We dichotomized patients into two groups based on 3-month clinical outcome: those with mRS$\leq$2, and those with mRS $>$2. Appropriate univariate analysis was used to compare admission NIHSS, Age, DWI volume, stroke laterality, and the presence of proximal arterial occlusion

between the two study groups. Binary logistic regression was used to find the independent predictors of good outcome. **Results:** The univariate analysis showed that admission NIHSS (11 ± 6 vs. 15 ± 5, p=0.005), age (63.2 ± 19.5 years vs. 43.4 ± 13.0 years, p=0.019), and DWI admission volume (23.0 ± 6.1 ml vs. 60.6 ± 10.5 ml, p=0.004) were significantly lower in those patients with 3-month mRS≤2. The laterality of stroke (p=0.785) and the presence of proximal arterial occlusion (p=0.496) were not different between two outcome groups. The stepwise logistic regression showed that admission DWI infarct volume (p=0.007) and patients' age at the time of stroke (p=0.031) were the only independent predictors of clinical outcome (3-month mRS). **Conclusion:** In the subgroup of acute stroke patients receiving thrombolytic therapy, admission DWI lesion volume and patients' age best predict clinical outcome at 3 months, and are stronger predictors of clinical outcome than the presence of proximal arterial occlusion on admission CTA.

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W P269

Long-term Angiographic Follow-up Following Stenting For Chronic Total Occlusion Older Than Three Months Of The Proximal Subclavian Artery

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Background and Purpose: The purpose of our retrospective study was to investigate success rate, safety and long-term angiographic outcome following stenting for chronic total occlusion (CTO) older than three months of the subclavian artery (SA). **Materials and Methods:** Chronic total occlusion (CTO) was defined as total occlusion older than three months since initial documentation by conventional angiography, CT angiography or MR angiography. Among 12 patients who underwent stenting of subclavian artery lesions from Jan 2006 to Dec 2009, 5 patients (3 male, mean age 71 years) had CTOs of the left SA and estimated occlusion length was about 40 mm. The five patients presented subclavian steal phenomenon and their brachial systolic blood pressure difference was 42mmHg (median).[Results]Successful recanalization was achieved in all five patients and the Palmatz stents were implanted. Left vertebral artery flowed antegradely after stenting and their brachial systolic blood pressure difference was reduced to 2 mmHg (median). No complications occurred except pseudoaneurysm at puncture site in one case. Angiography at 3-6 months after stenting demonstrated neither restenosis nor re-occlusion, which was defined as diameter stenosis of more than 50%. **Conclusion:** Stenting for CTO older than three months of the subclavian artery was feasible and safe. Long-term angiographic outcome was favorable.

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W P270

Title: No Risk of Increased Risk of Symptomatic Intracerebral Hemorrhage among Sub-therapeutic Warfarin Patients Treated with Tissue Plasminogen Activator

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Background: Intravenous tissue plasminogen activator (tPA) is an effective treatment for ischemic stroke. While tpa increases the likelihood of a favorable outcome, it also poses and increased risk of symptomatic intracerebral hemorrhages (SICH). Know factors that increase the risk of a SICH occurring include, increased age, higher National Institutes of Health Stroke Scale (NIHSS) scores, increased international normalized ratios (INR), history of atrial fibrillation, diabetes mellitus, and hypertension. A recent study suggests that patients taking Warfarin with INRs of 1.7 or less, might have an increased risk of SICH post tpa. Patients taking Warfarin are determined to be therapeutic when their INR is between 2.0 and 3.0. The objective of this study is to determine if Warfarin correlates with an increased risk of patients developing a SICH post tpa treatment in spite of a non-therapeutic INR. **Methods:** This is a retrospective study investigating patients with ischemic strokes all of which received tpa treatment between February 2004 to April 2010 at a large Primary Stroke Certified hospital with over 700 ischemic stroke discharges last year. One hundred twenty nine patients were reviewed in this study. All patients who received additional endovascular treatments, such as a thrombectomy, or intra-arterial lytics were excluded. For the purpose of this study SCIH was defined using CT scans, a decline in clinical status (based on a chart review of the nurse's comprehensive neurological assessments and progress notes and discharge status. Descriptive statistics and logistic regression were used in the analyses. **Results:** The population consisted of 74 males, 55 females, ages ranged from 24 to 97 with a mean of 67.57. The NIHSS ranged from 2 to 31 with a mean of 12.47. INR values ranged from 0.8 to 1.9 with a mean of 1.06. Onset till treatment time ranged from 76 to 255 min with a mean of 155.71 min. Of the 129 patients 10 (7.75 %) were taking Warfarin prior to treatment, with an INR range of 0.8 to 1.6 and a mean of 1.19. Out of the 129 patients treated with tpa 6 (4.69%) developed SICHs. None of the 10 patients taking Warfarin prior to treatment developed a SICH. It was determined that the risk of developing a SICH was not statistically different between patients taking Warfarin prior to treatment and those not taking Warfarin (p=0.999). **Conclusion:** The findings of this study suggest that taking Warfarin prior to treatment with tpa does not increase the risk of developing a symptomatic intracerebral hemorrhage in patients with INRs below therapeutic values. This conclusion differs from previous reports. One limitation of this study is the sample size, as was the case with the other referenced study. Further study on the incidence of SICH in this patient population are needed, with larger numbers of SICHs and patients taking Warfarin receiving tPA.

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W P271

Does Cognitive Function Improve After Intracranial Artery Angioplasty And Stenting?: A Prospective, Controlled Study

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Background: The purpose of our study was to evaluate changes in cognitive function after stent placement in patients with intracranial atherosclerotic stenosis (ICAS). **Method:** Eleven consecutive patients who underwent stent placement for symptomatic ICAS were studied. Patients with significant language and motor dysfunction that may hamper them to perform cognitive tests were excluded. Control subjects were sex and age matched patients with moderate/severe ICAS who were advised for but refused stenting due to various reasons. Cognitive function was assessed with following neuropsychological tests at baseline and 12 months after stenting: the Mini Mental State Examination, verbal learning test, Rey complex figure test, digit span, digit symbol test, Trail making test, verbal fluency, clock drawing and grooved pegboard test. **Results:** Eleven patients (male 73%, age 48-73, mean 57.3) with distal internal carotid artery (n=3), middle cerebral artery (MCA) (n=4), basilar artery (BA) (n=2) and distal vertebral artery (n=2) stenosis, and 11 control (male 64%, age 49-72, mean 60.7) subjects with MCA (n=8) and BA (n=3) stenosis were enrolled. As compared to controls, stent group patients showed tendency for improved score in verbal memory, visual memory, working memory and fine motor control (Table). However, the difference was not statistically significant. In stent group, 6 of 11 underwent brain SPECT before and after stenting, which showed improved perfusion after stenting in all the patients. **Conclusions:** Our preliminary study suggests that stenting may improve cognitive function in patients with ICAS. Further studies with a larger number of patients are required to prove our findings.

	Control group (n=11)		Difference score	Stent group (n=11)		Difference score
	Baseline	1 year		Baseline	1 year	
MMSE	26.6±2.4	27.0±2.7	0.72	25.4±5.3	25.8±6.3	2.36
Attention						
Forward digit span[a]	7.7±1.4	6.5±1.5	-1.00	7.2±1.4	6.0±2.0	-1.18
Psychomotor speed						
Trail making test part A (time)[b]	68.3±28.5	59.8±30.3	-1.27	61.0±40.4	76.9±51.9	15.90
Digit symbol test[a]	30.2±10.7	39.1±16.5	3.45	36.9±20.4	39.6±23.6	2.74
Mental flexibility						
Trail making test part B (time)[b]	143.6±60.3	136.4±63.8	7.54	149.4±80.1	163.8±136.4	14.32
Verbal fluency						
Phonemic category[a]	11.4±3.9	11.1±4.1	-0.91	12.5±6.9	12.5±5.9	0.00
Verbal memory						
Total score[a]	15.8±4.6	16.9±7.0	0.72	16.6±6.0	18.2±6.1	2.36
Delayed recall[a]	4.0±2.4	5.1±3.8	0.64	4.4±3.3	4.4±3.1	0.45
Recognition score[a]	19.8±2.3	18.8±3.3	-0.91	18.2±4.6	19.4±3.4	1.64
Visual memory						
Rey complex figure score[a]	30.7±3.6	30.6±7.5	0.50	24.7±14.2	31.4±5.1	6.77
Delayed recall[a]	12.4±6.8	16.9±9.5	3.27	9.8±9.6	17.6±7.2	7.75
Recognition score[a]	20.4±1.9	19.5±3.4	-0.90	18.8±3.9	19.8±2.0	0.98
Working memory						
Backward digit span[a]	3.9±1.2	3.5±1.5	-0.18	3.5±1.2	3.8±1.8	0.27
Visuospatial function						
Clock drawing[a]	6.7±0.6	6.2±1.9	-0.55	5.8±1.8	5.4±2.7	-0.45
Fine motor control						
Grooved pegboard (time)[b]	104.2±29.5	71.3±8.9	-31.75	223.2±237.7	110.5±63.2	-112.72

[a] Positive values of the difference score indicate improvement.
[b] Negative values of the difference score indicate improvement.

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W P272

Utility Of Final Infarct Volume As Predictor Of Functional Outcome After Endovascular Stroke Treatment

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Background: Previous studies investigating outcomes after endovascular therapy for acute ischemic stroke have established age, recanalization and baseline stroke severity as main

predictors of clinical outcomes. However these studies did not take final infarct volume into consideration. We aimed to analyze predictors of clinical outcomes considering final infarct burden assessed by magnetic resonant diffusion weighted imaging (MR DWI) following endovascular treatment for patients with acute ischemic stroke with similar territory at risk (M1 MCA occlusion). **Methods:** Retrospective review of a prospectively acquired database of endovascular acute stroke therapy at University of Pittsburgh Medical Center was performed. Patients with M1 MCA occlusion and available DWI MRI on follow-up were selected. Data abstracted included baseline risk factors, national institute of health stroke scale (NIHSS) and Alberta Stroke Program Early CT (ASPECT) scores, time to treatment and type of endovasuclar treatment (mechanical and/or pharmacologic). Patient outcome data including Thrombolysis in Myocardial Infarction (TIMI) recanalization grade, post treatment DWI volumes obtained by a blinded investigator using a semiautomated method, and 90 day modified Rankin scores (mRS) were reviewed. Successful recanalization was defined as TIMI grade 2 & 3. Clinical outcome was considered favorable if 90 day mRS was ≤ 2. **Results:** Between November 2002 and April 2010, we identified 178 patients. Ninety day functional outcomes were available in 168 patients. TIMI grade 2 & 3 recanalization was achieved in 144 (80.9%) patients. Overall 76 (45.8%) patients had favorable outcomes. Patients with favorable outcomes had lower final infarct burden as compared to the unfavorable outcome cohort (55.2 ml versus 127.8 ml, $P<0.01$). Also patients achieving successful TIMI 2 & 3 recanalization had lower final infarct volumes than patients who failed recanalization attempt (77.1 ml versus 152.9 ml, $p < 0.01$). While in univariate analysis baseline NIHSS (OR 0.91, CI 0.85-0.97, $P<0.01$) and successful recanalization (OR 2.75, CI 1.14-6.6, $p=0.02$) along with higher pretreatment ASPECT scores (OR 1.34, CI 1.03-1.73, $p=0.02$) were found to be significantly associated with favorable outcomes, multivariate analysis identified only age (OR 0.88, CI 0.83-0.93, $P<0.01$), and post treatment DWI infarct volume (OR 0.98, CI 0.97-0.99, $P<0.01$) as significant predictors of favorable outcome. **Conclusion:** Our study findings indicate that amongst a homogenous patient population with intracranial MCA M1 occlusion, age and final infarct volume rather than recanalization or baseline stroke severity appear to be the only predictors of clinical outcome following endovascular therapy for acute ischemic stroke.

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W P273

Stenting Angioplasty In The Treatment Of Venous Sinus Stenoses:clinical And Angiographic Outcome In 34 Patients

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Object: Cerebral venous sinus stenoses have been considered as a mechanism responsible for raised intracranial pressure without a mass lesion or cerebral edema. Very few studies have been carried out on venous sinus stenosis treatment with stenting . As an invasive treatment, the safety and efficacy has been controversial. The purpose of present study was to evaluate the clinical and neuroimaging-based results in 34 venous sinus stenosis patients treated with stent angioplasty. **Methods:** 34 consecutive patients (twenty-three women and eleven men, age range 18 to 56 years) who had presented with isolated intracranial hypertension with venous sinus stenoses underwent examination with magnetic resonance venography (MRV), digital subtraction angiography (DSA), direct retrograde cerebral venography and manometry to confirm morphologic features and venous pressures. All patients demonstrated irregular filling defect in venous sinuses and the pressure gradients across stenoses over 15cmH_2O were treated with intrasinus stenting placement with or without auxiliary balloon angioplasty and intrasinus pressures and correlated with clinical outcome were recorded before and after the procedure. During the follow-up period of more than 6 months, symptoms, fundus examination, intracranial pressures, stent patency rates and complications were assessed. **Results:** All 34 patients were treated with sinus stenting angioplasty. In the 33 patients stenotic cerebral sinus were improved by stenting and a reduction in intrasinus pressure was achieved (the pressure gradient $<$3.5cmH_2O). During the mean follow-up 22.5months (range 6$\sim$84months), 31 patients (91.2%) were improved or asymptomatic and the follow-up DSA or MRV demonstrated absence of stent thrombosis and restenosis. Out of 34, only one patient had been confirmed intraparenchymal hematoma after procedure and died of brain hernia. In 2 patients, the intracranial hypertension did not improved after procedure. During follow-up period, DSA showed dural arteriovenous fistula (DAVF) involving the transverse sinus in these two patients, thus embolism treatment were performed. **Conclusions:** Our result indicates that Stenting angioplasty is a save and effective treatment in Venous sinus stenosis, suggesting that endoluminal stenotic lesions with a distinct pressure gradients across the stenoses lead to raised intracranial pressure and that endovascular treatment in this type of stenoses is a promising treatment.

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W P274

Usability Testing the Self-Management TO Prevent Stroke Tool

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Background: Paper-based clinical practice guidelines are difficult to integrate with clinicians' real time workflow and documentation needs. Decision support tools incorporated into the electronic medical record may enhance implementation of best practices for secondary stroke prevention. The STOP Stroke Tool is a clinical decision support application that prompts clinicians on guidelines for secondary stroke prevention, and provides simultaneously access to patient education materials and self-management plans for stroke risk factors. **Methods:** Usability-engineering methods were applied to develop and test the STOP Stroke Tool. Iterative prototype testing sessions with end-users were completed to evaluate the functionality and usability of multiple renditions of a STOP Stroke Tool prototype. End-users included physicians and nurses involved in the follow-up care of Veterans with ischemic stroke or transient ischemic attack. During each testing session, clinicians provided feedback to guide design strategies and to identify usability barriers and facilitators. Multiple testing methods were applied. Documentation of guidelines was compared among multidisciplinary clinicians ($N=15$) using test case scenarios. Usability was evaluated with Think-Aloud protocols, questionnaires and open-ended survey questions. Most recently, ($N=12$) clinicians viewed a demonstration video of a newer web-based prototype and provided feedback on barriers and facilitators to implementing the tool in practice. Nonparametric, descriptive statistics and direct content analysis were applied to analyze the data. Results The initial template-based prototype prompted a significant increase ($p \leq .05$) in provider documentation for 6 of 11 guidelines as compared to baseline documentation while using the standard system. Out of a possible 56 points, usability was scored high ($M = 48.9$, $SD = 6.8$). Themes around implementation barriers were related to 'time constraints', 'lack of interoperability with the current system', 'learning how to use the tool', and 'access to the tool'. Themes around implementation facilitators were focused on the tool providing 'reminders for best practices' 'automated documentation', 'systematic care processes' and 'comprehensive stroke follow-up'. **Conclusions:** Results support that usability-engineering strategies can be successfully applied to produce guideline prompting and clinical decision support for secondary stroke prevention in the electronic medical record. Current testing is focused on describing provider and patient collaborative management of stroke risk factors while using the STOP Stroke Tool.

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W P275

Stroke Patient Education Tools Increase Nursing Compliance and Documentation of Stroke Patient Education

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Background: Annually 795,000 people experience a new or recurrent stroke. Approximately 185,000 are recurrent strokes. The incidence of Transient Ischemic Attack (TIA) in the United States is estimated to be 200,000 to 500,000 per year. After TIA, the 90 day risk factor of stroke is 3.0% to 17.3% and is highest within the first 30 days. Several studies revealed a lack of knowledge regarding stroke/TIA risk factors and symptoms. **Purpose:** The purpose was to increase patient, family and caregiver awareness to the signs and symptoms of stroke/TIA and secondary stroke prevention, while giving nurses the tools for complete and consistent education according to the Stroke Get With The Guidelines (GWTG) recommendations. **Methods:** A 97 page comprehensive stroke patient education workbook was given to each stroke and TIA patient to review their personal risk factors and stroke etiology. In 9/2008, a stroke patient education form was implemented. This form addresses stroke signs, symptoms, 911, stroke risk factors, cholesterol levels, secondary stroke prevention medications, healthy lifestyle modifications, neurology and rehab follow-up. The nurse uses the tool each shift upon admission and requires patient/caregiver initials for each topic discussed. Stroke GWTG core measures are documented in the electronic charting. Patient educational videos and Stroke Smart magazines are also provided. **Results:** Analysis of stroke patient education for 956 patients from 1/1/2008 through 6/30/2010 with ischemic, TIA, or hemorrhagic stroke revealed a significant improvement. The quarter prior to implementation of our tool results were 90.6% (96/106).The quarter after increased to 98% (96/98). We have maintained at least 97% each quarter since then. **Conclusions:** The combination of these tools ensures that all required stroke education is completed. As a result of the multiple educational interactions, tools and documentation, there is increased awareness by nurses of the need for patient stroke education. Starting education upon admission has eased the discharge process. Further follow-up is warranted to validate increased awareness of stroke symptoms and secondary stroke prevention by the patient and caregiver.

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W P276

Cerebrovascular Risk Factors are Different in Patients with Ischemic and Hemorrhagic Stroke in Northeastern Brazil

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Introduction: Risk factors for ischemic and hemorrhagic strokes are similar but not exactly the same. Our objective was to compare the prevalence of classic stroke risk factors of patients admitted with stroke or transient ischemic attack (TIA) in Fortaleza, Ceará, Brazil. Fortaleza is the state capital of Ceará (Northeastern Brazil), has a population of over 2.5 million, and is the 5th largest city in Brazil. Hypothesis: We hypothesized that patients admitted with hemorrhagic and ischemic stroke in Fortaleza have similar but not identical risk factors. **Methods:** Data were prospectively collected from patients admitted to the EDs of 19 hospitals in Fortaleza with a diagnosis of stroke or TIA by trained research coordinators from June-2009 to May-2010. In 2008, 90% of the patients admitted with stroke in Fortaleza were evaluated in either one of the 19 hospitals studied. Daily visits to EDs of the selected hospital were performed and all patients admitted with a diagnosis of stroke or TIA were prospectively evaluated. A dedicated nurse coordinator reviewed all the patients. Controversies were discussed with two stroke neurologists. **Results:** We evaluated 1510 patients: 1084 had ischemic stroke (IS) (71,8%), 303 hemorrhagic strokes (ICH) (20%), 82 subarachnoid hemorrhage (SAH) (5,4%) and 41 TIA (2,7%). Mean age was 67.9 $\pm$ 14.5 yo (50.2% males). Patients with ICH (including SAH) were younger (61 $\pm$ 15.2 years- versus 69 $\pm$ 13.6 years- IS patients, $P<0.01$). The two groups

were similar in gender, prevalence of hypertension, hyperlipidemia, smoking and previous myocardial infarction. Patients with ICH had more frequently a history of alcohol abuse (IS 24.2% versus ICH 31.5%, p=0.03), and patients with IS had a higher frequency history of previous stroke (IS 46.1% versus ICH 26.4%, P<0.01) and diabetes (IS 46,5% versus ICH 37. 4%, p=0.01). **Conclusion:** Although risk factors for IS and ICH are similar, diabetes and previous stroke seem to be more frequent in patients with IS; conversely, alcohol abuse is more frequent in patients with ICH. A more focused approach for primary and secondary prophylaxis in patients with IS and ICH should be based in the knowledge of the differential risk factors for distinct stroke subtypes.

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W P277

Stroke: Bridging the Gap Between Knowledge and Practice

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Background and Issues: The implementation of evidence-based treatment guidelines into clinical practice has been shown to improve stroke outcomes. Although evidenced-based guidelines have been developed along with improved treatment and diagnostic capabilities, there are many inconsistencies with how these guidelines are applied in clinical practice. Bedside nurses were left trying to recall the ten stroke performance measures while caring for multiple patients with varying diagnoses and co-morbidities. As a result, there were repetitive oversights which created a gap between recommendations and actual clinical practice. This became a pattern, continued from shift to shift and resulted in inconsistencies in care provided. Internal observations revealed that the utilization of interdisciplinary resources, such as dietitians and diabetic educators, were being underutilized. **Purpose:** A tool was developed to assist the nursing staff in tracking compliance with each of the ten Performance Measures. The tool also promoted an organized approach to the interdisciplinary management of each stroke patient. The goal of the implementation of the tool was to increase the compliance with each performance measure to levels above the national benchmark as well as increased utilization of dietitians and diabetic educators within the organization. **Methods:** The tool is initiated upon admission and is used throughout the hospital stay. The charge nurse oversees the completion of the tool by obtaining updates from the interdisciplinary team each shift. Data entered onto the tool guides the charge nurse to obtain appropriate medical orders to ensure compliance with each performance measure. In addition, consults are generated to the diabetic educator and dietitian based upon lab results and basic admission data. **Results:** Since implementation of the tool in early 2008, we have seen great improvement with adherence to the Performance Measures. Of the ten Performance Measures, seven have shown a consistent increase and three have remained within statistical control and are significantly higher than the national benchmark. Based upon recommendations from the nursing staff, changes were made to the tool to include spaces for actual lab results (LDL and A1C). In addition, critical elements specific to required discharge medications along with contraindications were added to the tool. The tool is continuously reviewed and recommendations for changes and additions are closely evaluated. As a result of the increased compliance with the Performance Measures, Aultman Hospital was recently awarded the Gold Plus award for exemplary stroke care from the American Heart Association and received the Gold award in both 2008 and 2009.

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W P278

System Standardization of Dysphagia Assessment Education Increases Compliance with Acute Stroke Patients

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Introduction: Dysphagia may occur in up to 65% of stroke patients per the American Stroke Association. One of the most common complications of a stroke is aspiration pneumonia caused by dysphagia. The University Hospitals Stroke and Cerebrovascular Center (UHSCC) developed an educational module to teach nurses caring for stroke patients how to assess for dysphagia. **Methods:** The UHSCC developed a bedside dysphagia protocol to standardize dysphagia assessments across the health system. Nurses caring for stroke patients were educated on the protocol requirement. The director of the UHSCC and a speech therapist created a DVD that demonstrated dysphagia assessments performed on real patients to aid in the education of the nurses. In the initial pilot, 100 nurses viewed the video and were given a pre and post test to assess the effectiveness of the teaching mechanism. The DVD is now available to all nurses on an electronic learning management system. Compliance with dysphagia assessments for stroke patients is monitored using the Get With the Guidelines program. **Results:** Of the 100 nurses who viewed the DVD in the pilot, 67 had no prior dysphagia assessment education. The average pre test score of these nurses was 80% and the average post test score was 90% (p value < 0.0001). Forty three nurses in the pilot had prior dysphagia education. This group's average pre test score was 87% and the average post test score was 96% (p value $= 0.0003$). The DVD competency requirement for the system was rolled out in 2009 and 96% of the nurses caring for stroke patients throughout the UH health system have been educated using the video presentation. Compliance with dysphagia assessments for stroke patients across the UH health system has increased from 40% in Q1 2009 to 82% in Q1 2010. **Conclusions:** Standardization of dysphagia education across the UH Health system through the use of this educational tool has resulted in a significant increase in dysphagia assessment compliance for stroke patients. This DVD is now used as an annual competency throughout the health system for nurses caring for stroke patients with plans for all medical-surgical nurses to complete in 2011.

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W P279

Initial NIHSS and Timely t-PA Predicts 3 Month Disability

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The effectiveness of intravenous alteplase (IV t-PA) in the treatment of acute ischemic stroke has been proven in multiple trials. The long term outcome of treatment however, depends on multiple factors that can influence clinical decision making. The purpose of this study was to explore the effect of initial stroke severity and initial response to treatment on the 90-day outcome of patients with acute ischemic stroke (IS) treated with IV t-PA. **Methods:** As part of an on-going study 38 consecutive patients treated with IV t-PA for acute IS at four community Primary Stroke Centers were followed prospectively for 3 months. Demographics, initial and post-procedure NIHSS score and post-hospital disposition were abstracted from the *ASA Get With The Guidelines Database*. A 90-day modified Rankin Scale (mRS) score was obtained by phone interview by a trained stroke coordinator. **Results:** Thirty-eight patients received IV t-PA and a mRS at 90 days. Mean age was 72 yrs±15. Mean NIHSS on admission was 10±7 and post-procedure NIHSS was 4±7, for a net treatment effect (NIHSS delta) of -5±7. NIHSS on admission and discharge correlated positively with patients mRS (*rho* = .741 & *rho* = .583, *P*<.0005, respectively). In-hospital NIHSS delta did not correlate with mRS (*p*=.286). Timely IV t-PA treatment was associated with greater in-hospital NIHSS delta (*rho* = -.349, *p*=.047), but timely IV t-PA did not show significant association to mRS (*p*=.378). **Conclusion:** We demonstrate that 90-day outcome post IS is predicted by stroke severity, measured by the NIHSS on admission and discharge. Timely administration of IV t-PA was not directly correlated with 90-day outcome, but is associated with improved in-hospital NIHSS score and therefore functioning on discharge, which is correlated with 90-day outcome. These findings lend empirical support to public health initiatives to increase early presentation and shorten door to needle times in patients with acute IS.

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W P280

Community-acquired Pneumonia In Acute Ischemic Stroke

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Background and Purpose: Pneumonia is an important complication of ischemic stroke and increases mortality 3-fold. We aimed to determine key characteristics associated with community-acquired pneumonia in admission of acute ischemic stroke patients. **Methods:** We studied a series of consecutive patients with acute ischemic stroke who were admitted to hospital from January 2006 to June 2008. The evaluation included patients's clinical status, NIHSS and Glasgow Coma Scale, laboratory and radiological data. The diagnosis of pneumonia was defined if the patient had an infiltrate on chest radiograph that was new or progressive, along with clinical findings suggesting infection, which include the new onset of fever, purulent sputum, leukocytosis, and decline in oxygenation in the first 48 hours of admission (according American Thoracic Society 2005 consensus). **Results:** We studied 554 patients with acute ischemic stroke; 52 (9.38%) met the study criteria for community-acquired pneumonia. Subjects who developed pneumonia were older (69.4±15.22 vs 64.3 ± 14.3 years); had higher modified NIHSS scores: 17 (IR 10-24) vs 9 (IR 4-17); lower Glasgow Coma Scale scores 12 (IR 9-14) vs 14 (IR 12-15); higher level of glycemia (141±53.7 vs 131±59.2mg/dL) and lower mean arterial blood pressure (102.5±23 vs 113.24 ± 21.6mmHg) on admission. These patients had higher mean length of hospital stay (22.3±29 vs 13.47±20 days) and higher mean of in-hospital mortality (50% vs 14.9%). In logistic-regression analysis, independent predictors (P < 0.05) associated with pneumonia were age (OR=1.04;IC=1.02-1.05); NIHSS (OR=1.06; IC1.03-1.09) and glycemia at admission(OR=1.01;IC=1.01-1.02). **Conclusions:** Community-acquired pneumonia after acute ischemic stroke is frequent and is associated with older age, severity of stroke deficits (NIHSS) and glycemia at hospital admission. Patients who developed community-acquired pneumonia had higher length of hospital stay and higher in-hospital mortality.

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W P281

Maximizing Subject Follow-Up by Minimizing the Number of Cooks in the Kitchen

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Background: Accurate collection of follow-up data in clinical trials is critical for reliable interpretation of study results. We hypothesized that direct involvement of a primary contact with study patients would improve protocol compliance with follow-up visits (FUVs) as opposed to contact with multiple people on the study team. **Methods:** The *S*afety of Pioglitazone for *H*ematoma *R*esolution in *IN*tra*C*erebral Hemorrhage (SHRINC) study is a randomized, placebo-

controlled trial designed to assess the safety of pioglitazone (PIO) in patients with intracerebral hemorrhage (ICH). Objectives are to determine the maximal tolerated dose of PIO and to evaluate the rate of ICH and edema resolution with MRI. Patients are seen every 2 weeks for 8 weeks, day 90 and 6 months for FUVs. FUVs evaluate safety and functional measures, glucose logs, drug accountability, and MRI. Initially, our primary study coordinator (PSC) conducted data collection during the acute hospitalization and subsequent outpatient FUVs were to occur in a Clinical Research Unit (CRU) which provided different coordinator support. We determined the number of missed FUVs that occurred when our PSC was not involved in the FUV process. We considered a FUV 'missed' by the CRU if the patient did not show or if our PSC had to collect the data by means other than a CRU visit (e.g. site visit or phone follow-up). **Results:** A total of 36 patients have been enrolled. Four patients have died and their data are not included. FUVs for the first 21 subjects were conducted by the CRU. FUVs for subjects 22-34 were conducted by the PSC. The proportion of FUVs missed by the CRU was 33% (39/120 possible FUVs) compared with only 2% (1/60 possible FUVs, $P<0.0001$) when the PSC communicated directly with patients. A total of 45% of patients followed by the CRU had more than 1 missed FUV compared to 0% when followed by the PSC ($p<0.01$). **Conclusion:** In our cohort of patients with ICH, protocol compliance with FUVs was better with one primary contact than when multiple people were involved in FUVs. Possible reasons include non-familiarity with the study population and their needs, lack of flexibility in scheduling in a busy CRU and no other method for data collection if the patient no-shows. As a result of our findings, data collection has significantly improved thus ensuring internal validity of the study.

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W P282

The Effectiveness of Four Translation Strategies on Nurses' Adoption of an Evidence-Based Bladder Protocol

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The Effectiveness of Four Translation Strategies on Nurses' Adoption of an Evidence-Based Bladder Protocol Background: Mixed evidence exists regarding the effective use of the four translation strategies of educational materials, educational meetings, reminders, and audit and feedback on the adoption and implementation of interventions by nurses. Many clinical practice guidelines for the care of the stroke patient advocate for bladder training, but evidence-based bladder protocols for the stroke patient are not available. The best available bladder protocol identified was a prompted voiding algorithm from the Registered Nurses' Association of Ontario. Review of the literature reported 32-79% of hospitalized stroke patients suffer from urinary incontinence. Strong support for prompted voiding demonstrated reduction of urinary incontinence in patients with cognitive deficits. **Purpose:** The primary purpose of this study was to examine the effects of an intervention consisting of four translation strategies: educational materials (clinical practice guideline), educational meetings, reminders, and audit and feedback on nurses' adoption of an evidence-based bladder program for stroke patients in an acute care setting. The second purpose was to evaluate the difference in incontinence episodes of patients before and after nurses received the intervention. The third purpose of the protocol was to evaluate the influence of nurses' attitudes on adoption and use of the evidence-based bladder program after receiving the intervention. **Methods:** A time-series design, using 8 one-week time points before the intervention and 16 one-week time points after the intervention, was used to obtain the required sample, $n = 29$. The nurse and medical record samples were convenience samples from a 40-bed neuroscience acute care unit affiliated with a 695-bed academic medical center. The purpose of the intervention was to teach and encourage nurses to adopt a prompted voiding algorithm for stroke patients. The Research Utilization Survey was used to evaluate the influence of nurses' attitudes on the adoption and the use of the evidence-based bladder program after receiving the intervention. **Results:** Data supported the degree of change as a two-fold increase in the nurses' adoption of an evidence-based bladder protocol, but there was no statistical difference in the incontinence episodes pre- and post-intervention. The increased research utilization and attitude scores were not statistically significant. Nurses' level of basic nursing education was positively associated with the adoption and the use of the evidence-based bladder protocol. **Conclusions:** This study was the first to provide empirical support for the influence of the combination of these four translation strategies and nurses' attitudes toward research on adoption of evidence-based practice in a time-series design study.

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W P283

Preserving Patient Safety During Handoffs for Acute Stroke Patients that Receive Alteplase.

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Background and issues: Patients receiving IV tissue plasminogen activator (tPA) for acute ischemic stroke (AIS) are at risk for bleeding and other complications. Recommendations for vital signs and neurological checks during and after administration are very strict and must be retrievable in the medical record, with accurate nursing documentation. Transportation from the location where tPA was administered to an ICU creates opportunities for delay in or missed documentation as a result of handoffs between care providers. **Purpose:** To improve documentation and safety measures for tPA patients in a new electronic medical record (EMR). **Methods:** With a change to a new EMR in 10/09, our Stroke Collaborative Practice Team created a new order set and visible reminders to enhance safety for tPA patients. Retrospective chart review noted vitals and neurochecks were not consistently documented in the medical record according to treatment guidelines. Emergency Department and inpatient acute stroke admission packets were updated with a paper tPA flowsheet. The flowsheet outlines the 24-hour requirements for vital signs and neurochecks, and contains several patient precautions and monitoring requirements. Additionally, a 'head of the bed' tPA precaution sign was also placed in the ED and ICU admission packets to become a visible in-room reminder that the patient is at risk for post-tPA complications. Both items were placed on our hospital's intranet to allow printing from any patient care area. Education of nursing staff on use of the flowsheet, a review of the expectations for vitals and neuro checks in tPA patients, and the head of the bed sign was completed by 100% of ED staff in 9/09. The ICU nursing staff was also educated on these changes. An order to place the head of the bed sign was revised in the AIS departmental order set. **Results:** All tPA patient charts were reviewed from 10/09 to 2/10. Six patients received IV tPA for AIS during the review period; in all instances the patients had appropriate, consistent documentation using the flowsheet. Spot checks were completed to ensure the head of the bed sign was posted in the patients' rooms (100% compliance). **Conclusion:** A formalized documentation tool specifically for AIS patients receiving tPA, as well as a precaution sign with visible reminders for caregivers, has helped to ensure that patients are monitored according to evidence-based guidelines and protected from potential complications after receiving a high risk, but infrequently used, medication.

Author Disclosures: K. Gray: None. S. Hickenbottom: None.

W P284

Implementation of the American Stroke Association Sharegiver Program (Peer Support)

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As part of a post stroke intervention study, we have locally adapted the American Stroke Association Sharegiver program and implemented at two Veteran Administration Medical Centers located in Indianapolis and Houston. The program entails training stroke survivors to serve as peer support for current hospitalized patients with stroke and supervising the peers as they deliver the support. We describe the program contents and administration. We recruited and trained 13 stroke peer sharegivers over 18 months across 2 sites. A coordinator at each facility assigned new patients to each stroke peer based upon availability. The stroke peers reported their frequency of interactions with their assigned patients to the coordinator. The supportive interactions were made in person at the medical center or by telephone. To understand the motivation behind the stroke peer volunteerism and to understand the barriers that arose and how they were resolved, we conducted focus groups of the stroke peers at both medical centers and are analyzing the transcripts for common themes. Our data demonstrates the feasibility of implementing a stroke peer support program for stroke survivors alongside traditional care. We plan to create an implementation toolkit to disseminate to clinical programs. This project was supported by a grant from the Veterans Health Administration IAB 05-297.

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W P285

Early Mobilization of Ischemic Stroke Patients post-Intravenous TPA Infusion

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Background and Purpose: To examine safety of early mobilization of IV tissue plasminogen activator (TPA) treated acute ischemic stroke patients by Physical Therapy (PT) and Occupational Therapy (OT) before 24hours. **Methods:** We conducted a prospective study between February to June 2010 of early mobilization (i.e., PT/OT initiated between 12 and 24 hrs post TPA) of all IV TPA-treated patients at a single, academic medical center, Mayo Clinic, Jacksonville, FL. A safety screen was performed before mobilization occurred in acute stroke patients who received IV TPA. Safety screen included hemodynamic and neurologic stability including orthostatic blood pressure, absence of adverse symptoms, and no active bleeding. If safety screen failed, the patient mobilization was postponed and rescreened later by nursing until stable for subsequent PT/OT. Secondary analysis was review of hospital length of stay (LOS) by two-tailed unpaired t-test for the prospective group of patients compared to a control group, which was mobilized per standard 24 hrs post TPA infusion (AHA guidelines). **Results:** 12 patients were identified in the study period (6 female, 4 males, mean age, 66, range 52-91 years). Mean admission NIHSS was 12 (range 2-29). One patient was not screened before mobilization, and another screened after 24hrs, both being excluded from analysis. Of the remaining 10 patients screened, 90% (9/10) of screened patients met safety screen criteria. One patient failed orthostatic blood pressure screening on two occasions by 24hrs. Compared to the historical controls, the average LOS (ALOS) for the prospective group which passed safety screen ($n=9$) was 3.1 days (range 1 -9, SD = 2.4), compared to the control group ($n=9$) ALOS was 3.6 days (range; 2-9, SD= 2.9), which did not meet statistical significance ($p=0.7$). **Conclusions:** Early mobilization of ischemic stroke patients between 12 and 24 hours after IV-TPA infusion appears safe for 90% of patients, whereas but one patient failed due to orthostatic hypotension but was of advanced age (91 years). There was no difference in average length of stay compared to the control population which is mobilized patients 24hrs after TPA infusion. Further, larger powered studies are needed to provide guidelines about safety and factors which shorten length of stay for stroke patients and provide best outcomes

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W P286

Efficacy of Health Education

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Background & Purpose: Stroke knowledge in general population is very poor in all countries around the world. It is necessary to provide health education with information about the risk factors to prevent it, and its warning signs to reach an early recognition and treatment. The aim of this study is to evaluate the increase of knowledge about stroke warning signs and risk factors, after an educative intervention addressed to hospitalized stroke patients and their relatives. **Methods:** pre-post prospective study by interviewing patients and their relatives with close-ended questions about their knowledge of stroke, before and after an educative intervention. The study was conducted from the 1st of March 2010 to the 1st of June 2010 in the University Hospital of Girona (Spain). Pre-post comparisons were made using parametric T student analysis. **Results:** We interviewed a total of 50 people (8 stroke patients and 42 relatives) with a mean age of 47.12 $\pm$ 16.6 years old. 62 % were women. Differences between pre and post scores were statistically significant when comparing the number of stroke symptoms and risk factors known before and after the educative intervention, with a p-value of 0.01 and 0.00 respectively. Pre-test interview showed that subgroups like: patients, women, higher level of studies and younger people had a higher previous knowledge of stroke than the rest. Otherwise the post test scores were very similar in all groups. Hypertension, identified previously by a 90% of the participants, was the most known risk factor, followed by Hypercholesterolemia (78%) and Smoking (72%). Warning signs most commonly recognized were weakness and (96%) slurred speech (88%). After receiving the information, 92% of the participants considered changing their life habits into a healthier lifestyle, and more than an 80% could identify the key-factors to recover and prevent new events. The educational program was very well appreciated by the participants with an overall score of 9.96 out of 10. **Conclusion:** An educational intervention can improve people's knowledge of stroke which is necessary to prevent it, helps to recover from it, and to seek urgent medical attention in case of recurrences. Nurses have a key role doing these educational programs due to being an important part of the patient's treatment, and changing patient's and family's lifestyles. The effects of the intervention are temporary so it is necessary to reevaluate it in a mid-long period.

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W P287

Can Clinical Presentation Provide Clues to Conversion Disorder in Code Stroke Patients? A Descriptive Analysis of Clinical Findings

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Background: Stroke mimics are well described in the literature, and include seizure with Todd's paralysis, complicated migraine, hypertensive encephalopathy, hypoglycemia, and conversion disorder. While conversion disorder is often described as inconsistent clinical findings, few papers detail conversion disorder presentations mimicking acute stroke. We aimed to describe common features of conversion disorder to enable improved detection of this disorder. **Methods:** Presenting clinical findings in consecutive code stroke patients that ultimately were diagnosed with conversion disorder were analyzed to determine if trends in clinical presentation could be identified. **Results:** During a 12 month period, 23 code stroke patients were assigned a diagnosis of conversion disorder at discharge. Mean age was 45 (range 15 to 63); 78% were women. Admission NIHSS scores ranged from 0-18, with a median of 8; only 5 patients presented with an NIHSS $<$ 5 points. Distribution of NIHSS findings demonstrated a higher prevalence of motor findings affecting the non-dominant left arm (57%), and the left leg (61%), as compared to the right arm (22%) and right leg (30%). In patients presenting with left hemiparesis, 46% exhibited aphasia (mild-moderate) as well as dysarthria (mild-moderate). Left arm and bilateral lower extremity weakness was found in 3 (13%) patients, with 2 of these also presenting with aphasia and dysarthria. Of patients presenting with right motor weakness, only 9% were scored as aphasic (mild-moderate), while 80% were dysarthric (mild-moderate). No patients presented as mute or demonstrated a receptive component to their aphasia. One patient in the series was treated with IV tPA on 2 separate admissions with resolution of symptoms; 2 patients were discharged home from the ED and the remaining 21 were admitted to the hospital for a complete stroke work-up. **Conclusion:** Conversion disorder patients may exhibit a higher prevalence of motor findings affecting the non-dominant side, with a disproportionate increase in lower extremity weakness and preservation of language fluency and reception. These findings may indicate a subconscious need to maintain control despite significant underlying stress and anxiety.

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W P288

Reducing Urinary Tract Infections in Stroke Patients Using Bladder Scanning technology and Nurse Managed Algorithms

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Effective measures to prevent urinary infection are generally lacking in stroke patient populations. Our research team developed innovative strategies to reduce urinary tract infections (UTIs) in our ischemic and hemorrhagic stroke patients. Routine insertion of indwelling urethral catheters and intermittent catheterization protocols every 6-8 hours have been standard care for our patients. Following discovery of a significant percentage of UTIs in our patients, we realized a correlation with GI based organisms, female gender and prolonged length of stay in these patients We designed pathways to address both incontinence and urinary retention for the neuroscience patient to decrease hospital length of stay, as well as readmissions. Bladder scan technology and mobilization for toileting has not been evaluated in a comprehensive, evidence-based protocol driven methodology. The average adult urine production is 60 mL per hour and a risk for urinary tract infections increases with a bladder volume of 180-300 mL. However, most bladder management protocols only evaluate urinary status every 6-8 hours. Our research team has developed and validated urinary management algorithms for stroke patients in five different clinical applications. We will feature these essential state of the art evidence-based algorithms to evaluate urinary elimination in defined patient conditions every four hours, using non-invasive technology, which ultimately reduces the potential risk for infection, and outline a statistically significant reduction in UTIs for our patients.We will also discuss challenges as well as solutions for changing current paradigms in nursing and physician care, physician order sets and application in practice at the bedside.

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W P289

Intensive Nursing Education and Monitoring Significantly Improve Compliance to Vital Sign and Neuro-check Documentation After Intravenous Thrombolysis in Acute Ischemic Stroke

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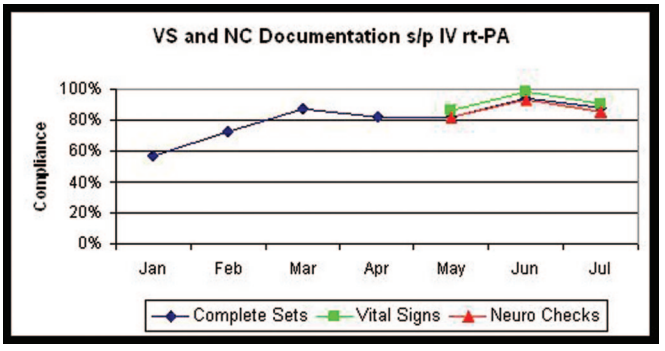
Background: Compliance with standardized guidelines for sequential vital signs (VS) monitoring and neurological assessments after administration of intravenous rt-PA for acute ischemic stroke may vary depending on patient location, duration of pre and post procedure transportation and off-unit staff awareness during diagnostic testing. **Purpose:** To examine our institution's compliance with VS and neuro-check (NC) documentation after IV tPA administration including drip-and-ship (DAS) cases, identify barriers to compliance and implement solutions. **Methods:** A baseline retrospective review of cases in January 2010 was conducted in patients who had IV rt-PA initiated at our center or by a transferring facility (DAS). The evaluation focused on the 24 hour period following administration of IV rt-PA. We identified 36 complete set "opportunities" (denominator) per patient in which VS and neuro-checks (defined as pupillary response, motor strength and GCS) were to be assessed and documented per protocol: q 15 mins x 8, q 30 mins x 12, q 60 mins x 16. Opportunities were prorated based on time of patient arrival with respect to initiation of IV rt-PA in the DAS group. Compliance was calculated as the number of fully documented VS and NC sets divided by eligible opportunities. In February 2010, an IV rt-PA monitoring form was introduced as was direct bedside nurse coaching to facilitate increased compliance. Comparisons of total compliance between institution initiated IV rt-PA VS vs DAS treated patients and VS Only vs NC Only was conducted for the last 3-month period of the study. **Results:** Thirty-seven patients over a 7 month period were included and analyzed, with 43.2% (16/37) arriving via DAS. Baseline compliance was 56.7% (76/134) of opportunities in 4 patients and incremental improvement was noted in subsequent months with a compliance peak of 92.9%. Overall compliance (May to July 2010) for institution initiated IV rt-PA (88.8%) was higher than DAS (81.2%) and a variance was observed in the VS Only group (91.4%) vs the NC Only group (86.4%). Peak monthly compliance was 97.9% in the VS Only group.



Conclusions: High compliance to documentation of VS/NC monitoring in IV rt-PA treated patients is achievable and sustainable through aggressive education across the continuum of acute patient care areas, including testing and transport. Further opportunity to educate staff exists specific to drip-and-ship cases and sequential neurologic assessments.

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W P290

The Impact of Concurrent Review on Stroke Center Measures at The Miriam Hospital

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Background and issues: Little research has been published about which interventions impact practice patterns such that quality measures have been impacted. Evidence is presented in support of concurrent review in stroke patient management by examining overall performance

over time on quality indicators for The Miriam Hospital (TMH), a hospital certified as a primary stroke center by The Joint Commission (TJC) and a participating hospital of the American Heart Association and American Stroke Association (AHA/ASA) Get with the Guidelines program. TMH tracks a number of indices, one called a composite index. The defect-free measure is used to evaluate how well the hospital did in providing all appropriate interventions to every patient. The hospital's proportion of patients who received interventions they were eligible, is calculated. The data time period is January 2006 to December 2009. A concurrent review process was implemented at TMH in June of 2008. **Purpose:** To evaluate the effectiveness of concurrent review on stroke center measures. **Method:** A dedicated quality improvement nurse coordinator launched the pilot June 2008. The design included: concurrent review plan, paper & electronic data collection tools, process for evaluating data, strategies to communicate with clinicians. The primary method for concurrent review is the daily examination of admitted patients using a combination of paper and electronic records. Information is transferred to a data collection tool to form a patient profile and to use to communicate with the responsible clinicians and nurses. This strategy was implemented beginning in June 2008. Data was reviewed regularly from the Outcome Science Database repository. Reports were generated and results were trended. Changes in composite scores over time were compared using a generalized estimating equation with a logit link function to fit a piecewise regression with an inflection point at the time TMH implemented concurrent review. **Results:** Composite scores for TMH overall showed significantly increasing trends in the composite scores for the time period January 2006 and April 2008 ($p<.0001$). TMH increased at a faster rate ($p=0.0013$) and these trends further increased significantly between May 2008 and August 2009 for TMH, following implementation of concurrent review ($p<.0001$). The difference between these increases was statistically significant ($p<.0001$). **Conclusions:** Concurrent review at TMH provides an advantage and improves stroke center measures over time.

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W P291

In-house Stroke Code Team Leads To Quicker Assessment, Evaluation And Treatment Of Acute Strokes

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Background and Purpose: After researching best practice it was decided a unit specific to the care and treatment of the acute stroke patient would greatly improve outcomes and help in the prevention of secondary stroke. Sharp Grossmont Hospital designated a stroke specific unit in 2005; February 2006 the hospital obtained Joint Commission (JC) certification as a stroke center. During the establishment of the unit research was also found that indicated 6.5 to 15% of first time strokes occur in patients already hospitalized for other reasons. There was a fine-tuned algorithm for managing stroke patients presenting to the ED, the same rapid assessment plan did not exist for patients suffering a stroke while already in the hospital. The concept of an In-House Stroke code was born to improve recognition, early intervention, and treatment of stroke in the in-patient population. As a result of our efforts the hospital received the Silver Plus 'Get With the Guidelines' for stroke awards in October of 2009. During the JC recertifications in 2008 and 2010 the hospital received no recommendations for improvement. **Methods:** Stroke unit nurses educated nursing staff throughout the hospital on the recognition of stroke and how to activate the in-house stroke code prior to implementation and yearly there after. The physicians and ancillary staff where educated as well. To activate the hospital emergency response system the nurse dials *** when a stroke is suspected on other units. The hospital operator pages the on call neurologist and stroke code nurse as well as CT, Lab, EKG, and X-Ray. The stroke code nurse immediately evaluates the patient then collaborates with the on call neurologist to decide the appropriate actions. The patient is then given priority in obtaining a CT scan and a stat lab panel is drawn to evaluate for early intervention and eligibility for t-PA. **Results:** Since implementation of an in-house stroke code procedure in 2005, 110 potential stroke patients have been identified and transferred to the stroke unit ensuring that these patients benefited from best practice in stroke care. There has also been an increase in the number of in-house patients treated with t-PA. In the four years since implementation, 16 patients have received t-PA compared to only four patients in the five years prior to the in-house stroke code program. In 2008, 83% of in-house stroke patients were evaluated in less than 15 minutes either by phone or at bedside by a neurologist. **Conclusion:** Success of the program is evidenced by the increase in early recognition, evaluation and treatment of in-house strokes. Bedside nurses are knowledgeable about the signs and symptoms of stroke and how to activate a stroke code rapid response team dedicated to this population of patients

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W P292

Baptist Hospital of Miami: Our Multidisciplinary Collaborative Journey to Primary Stroke Certification

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Baptist Hospital of Miami: Our Multidisciplinary Collaborative Journey to Primary Stroke Certification. **Background and Issue:** We hold the statement, 'Time is Brain' as our daily mantra in providing efficient and quality stroke patient care. Baptist Hospital of Miami, a Magnet Hospital, has developed a multidisciplinary collaborative approached to stroke care. In our pursuit of primary stroke certification, we have designed our processes to provide the most efficient quality care for stroke patients. Through the development of the Baptist Emergency Stroke Team (B.E.S.T.), we have developed an immediate response to care for stroke patients regardless of point of entry or location within the hospital. The stroke response is coordinated and led by a B.E.S.T. Responder Registered Nurse from the Neuroscience Unit who receives training on the National Institute of Health (NIH) Stroke Scale. A team of doctors and nurses initiate and complete laboratory, imaging, consultations, medication administration and provide interventional services in the appropriate timeframe as required by the Clinical Practice Guidelines of the American Heart Association and The Joint Commission. Through the inclusion and collaboration with departments such as, Laboratory Services, Rehabilitation Services, Care Management Services, and many others on Neuroscience Committees, we have been able to provide a continuum of care that has contributed greatly to our certification as a Primary Stroke Care Center. **Purpose:** To share our outcomes and multidisciplinary collaborative approach to stroke care at Baptist Hospital of Miami. **Method:** The performance metrics for the Baptist Hospital Stroke Program focus on the National Hospital Stroke Quality Measures and the turnaround performance times required by our clinical guidelines and The Joint Commission. The program uses quantitative data collection methods to analyze both performance metrics to evaluate our success and opportunities for improvements. **Results:** Through ongoing improvements of our stroke algorithms and analysis of our performance data, we have seen significant improvements in our national quality data and turnaround performance times. Our National Hospital Quality Stroke Measures goal is ninety percent compliance for all measures. We have been able to maintain this goal since March, 2010. Our turnaround performance times have also shown significant improvements achieving and in some areas exceeding the best practice, in all but two areas as of May 2010. **Conclusion:** Through exemplary multidisciplinary collaboration, we received our official notice of Primary Stroke Certification without recommendations for improvements on June 17th, 2010 by the Joint Commission. We were strongly encouraged to publish and present our program and it's outcomes at conferences to help other organizations become certified.

Author Disclosures: M. Guignard: None. M. Gauthreaux: None.

W P293

Partnership for Stroke How an Honor Roll Top 20 Hospital System, an East Texas Community Hospital, and a Foundation, created a Primary Stroke Center. The Journey

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Backround: The East Texas region has been identified as having a 'need' for quality stroke care in view of stroke incidence and mortality rates. This region is located in the 'Buckle' of the proverbial Stroke Belt. Additionally, this region along with the border communities of Texas, have high rates of uninsured and underserved populations. The East Texas Stroke Initiative is a project funded by the TLL Temple Foundation, and pairs Memorial Health System East Texas (a small non-profit community hospital system located in Lufkin, Texas), with The Methodist Hospital-Houston to create a Joint Commission certified Primary Stroke Center, to implement a widespread community education initiative for stroke prevention, and to reduce the devastating effects of stroke for the residents of the East Texas community and their families. The ultimate goal would create a 'ripple effect' from Lufkin, Texas across the entire region, dedicated to improving the health of the residents of the beautiful 'piney woods'. Need The stroke prevelence rate in Angelina County, which is where Lufkin is located is 5.2% compared to the state rate of 2.8%. The incidence of smoking and high cholesterol are a full 6 percentage points above the state rates. Other modifiable risk factors are just above, or just below the state rates. Age adjusted mortality rates in Angelina County are double for gender, both male and female and race, both caucasion and african american. This is not a voluntary project-but a medical emergency! Partnering The t-PA administration rate for the region was .003% at project initiation, and .007% for Memorial. The project married The Methodist Hospital, specifically the expertise of the Eddy Scurlock Stroke Center with Memorial Health System East Texas, to see what could be done to remedy the situation. Through project management, education both in-hospital and community-wide, quality initiatives, performance improvement, best practices modeling, evidence-based medicine, and good old fashioned dedication and hard work, the Stroke Program in Lufkin, was certified on August 16, 2010 with a 'clean' report, and praise from the surveyor. Almost 6,000 individuals have received stroke education in a variety of venues and a variety of ways. The surveyor stated that; 'It is the best community education initiative I have seen'. The t-PA administration rate closed the year 2009 at 5%, and through June, 2010 rests at 6.25%. The program has received an 2010 Outstanding Program Award, by the Texas Council on Cardiovascular and Stroke- one of only four outstanding awards given. Summation We would very much like to tell our story, and what our journey entailed. We are proud of the accomplishments thus far, and grateful for the opportunity that the TLL Temple Foundation provided. Maybe it will help reduce the human and financial toll, and give others the initiative and motivation to partner and succeed.

Author Disclosures: S. Monsour: None. K. Deaton: None. R. Jones: None. A. Loggins: None. J. Flewelling: None. J. Censullo: None.

W P294

Project To Improve Availability Of Stroke Patient Satisfaction Data And Capture Perceptions Of Care During Hospitalization

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Background and Purpose: In addition to the stroke committee's existing process for evaluating the hospital's stroke program through the American Heart Association's Get With the Guidelines Performance Measures, it was identified that an effective method for obtaining disease specific patient satisfaction data was needed. Because such data represents the patient's perception of the stroke program, it would offer significant insight regarding the delivery of stroke care through the eyes of the person who matters most - the patient. In an attempt to obtain patient satisfaction data, Press Ganey results were pulled and reviewed based on the DRG for stroke. This process revealed minimal data on which to base improvements to the program. The purpose of this project was to identify a process to obtain more patient satisfaction data and thus develop performance improvement projects for the stroke program.

Methods: A process existed for a Registered Nurse to contact patients after discharge for the purpose of assessing potential clinical needs, specifically medication compliance, ability to make follow up appointments, and support/services at home. This provided an opportunity to reinforce stroke education as well as assist the patient with needed community resources, such as transportation issues and prescription assistance. It was decided to also use this telephone call to ask patients about their satisfaction with, and perceptions of, care received during the hospital stay. Five questions were developed relating to stroke care, including education, participation in discharge planning, communication by nurses and physicians, services provided by the rehabilitation department, and recommendation of hospital for stroke care. These questions were asked during the follow-up telephone calls placed between 4-5 weeks after discharge. **Results:** Significant improvement in obtaining patient satisfaction data was identified. Comparing 1st and 2nd quarters of 2009 with 2010, the committee saw an increase from 3 satisfaction surveys using the Press Ganey surveys (7% of stroke patients) to 20 satisfaction surveys using follow-up telephone calls (43% of stroke patients). This represents an increase of 36%. From the responses in 2010, the stroke committee was able to identify performance improvement projects specific to stroke education and communication. **Conclusions:** The project to ask additional questions related to patient satisfaction during follow-up telephone calls provided the stroke committee with an increase in responses and feedback from stroke patients. This supplied the stroke committee with meaningful data on which to develop performance improvement projects relevant to the patient experience.

Author Disclosures: M. Richardson: None.

W P295

Best Practice Guidelines Improve Lipid Management Outcomes

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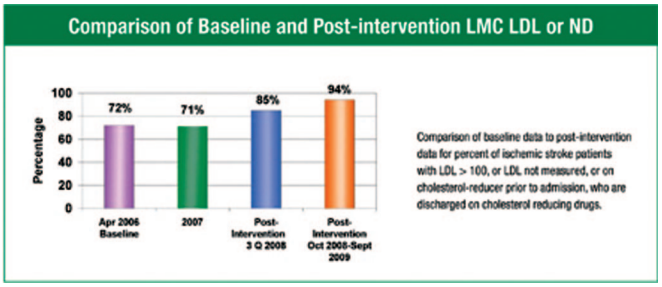
Background and Purpose: The "Get With the Guidelines(GWTG)-Stroke" ® program created by the American Heart Association (AHA)/American Stroke Association ® (ASA) is based on best practice guidelines. It offers a national electronic database to support and facilitate improvement of outcomes. The purpose of this study is to show how use of GWTG-Stroke facilitated improvement of lipid management outcomes for hospitalized patients. **Methods and Data Collection:** Lexington Medical Center (LMC) is a 385 bed county hospital in West Columbia, SC, surrounded by rural areas. LMC was the first SC hospital to participate in AHA/ASA GWTG-Stroke® program. A server report was redesigned to identify the stroke population based on diagnosis related groups. Thirty stroke patients were randomly selected and entered into the AHA/ASA GWTG-Stroke database as baseline data. Data was abstracted monthly by a registered nurse. **Interventions:** Participate in AHA/ASA GWTG-Stroke® ● Multi-disciplinary Performance Improvement Committee ● Stroke unit developed-increased from 16 beds to 26 ● Stroke pre-printed orders ● Stroke plan of care addendum ● Staff education with reporting of data at nursing, medical, and senior leadership committees ● Best practice guidelines provided to physicians. **Results:** Lexington Medical Center improved 22 % from April 2006 (baseline data) to post-intervention period of October 2008-September 2009. LMC received the AHA/ASA Bronze Performance Award ® and later the Silver Performance Award ®. These awards were based on all applicable stroke performance measures, including LDL 100 or ND.



Conclusions: These results show that outcomes can be improved by utilizing AHA/ASA GWTG®-Stroke. This national registry provides support to improve outcomes by providing tools to impact performance measures based on best practice guidelines. It was an efficient tool to facilitate improved lipid management outcomes at LMC.

Author Disclosures: V.S. Hicks, RN, BC: None.

W P296

Let The Data Do The Driving: Informing Clinical Decision-making In The Community Hospital

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Background: In 2007, when our 124-bed community hospital collaborated with a major medical center for Telestroke support, analysis of current practice was required. Using AHA's Get With the Guidelines (GWTG) performance metrics, we reviewed all stroke cases during six weeks in 2007 (n=30). Compliance for Lipid Management was 71%, Smoking Cessation, 50%, and no eligible patients (n= 4) received t-PA. Our Defect-Free score (all patients receive all appropriate interventions) was only 29%. With substantial opportunities for improvement, we faced one challenge shared by all other community hospitals: with relatively low numbers of cases, one outlier significantly impacts compliance scores. **Purpose:** To design and implement a highly reliable, evidenced-based program for stroke management using quality metrics to inform and improve clinical practice, achieving and sustaining at least 85% compliance with GWTG's measures. **Methodology:** We established a quality subcommittee–our quality improvement (QI) staff joined clinical experts from nursing, radiology, and laboratory–to optimize processes. We review all patients discharged with stroke/TIA. Our quality coordinator extracts data from the electronic medical record, inputs it into a national stroke registry, and e-mails a preliminary report to the clinical experts for confirmation of each "not met." The quality subcommittee analyzes the validated results, identifies trends and outliers, creates action plans, and then reports at the Stroke Steering Committee for the critical final step: information delivery to physicians and therapists, nurses and technologists, managers and administrators. Each department shares the same irrefutable evidence of process and performance opportunities for improvement. **Results:** Our new stroke program went live in Nov. 2008. With analysis complete for the first five quarters (n=218), we exceeded goals on all GWTG metrics. Lipid Management reached 97%, Smoking Cessation, 97%, t-PA compliance improved to 89% (n=9), and our Defect-Free score achieved 96%. We earned AHA's Bronze award in 2009 and became the first NH hospital to achieve Silver Plus status. **Conclusions:** Through partnership with our QI colleagues and the launch of a highly reliable reporting structure, data now informs clinical practice. Three activities were crucial to success: collecting and analyzing reliable data, using metrics to identify areas for improvement and triage our activities, and exchanging information with key stakeholders. Our new goals include concurrent case reviews, shortening data turnaround times, securing budgeted hours for data collection, and engaging more clinicians as we optimize patient outcomes through evidenced-based practice and clinical excellence.

Author Disclosures: C. Spencer: None. N. Connors: None.

W P297

Subcortical Lesion Load And Not Inflammation Are Associated With Poor Cognition After Ischemic Stroke

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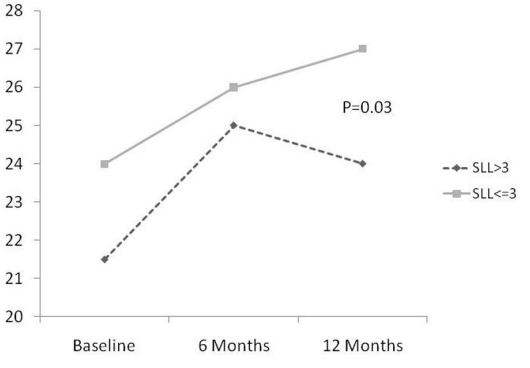
Introduction: Subcortical lesion load (SLL) refers to the quantity of hyperintenities present on FLAIR sequence in the white matter and basal ganglia on MRI. SLL is often present in stroke patients. Systemic inflammatory markers are also often elevated at stroke onset. Our study hypothesis was that patients with higher SLL are less likely to recover their cognitive function after a stroke or TIA and more likely to develop cognitive decline. In addition we sought to study the interaction between inflammation and SLL in terms of cognitive outcome. **Methods:** We hereby present preliminary results of mild ischemic stroke and transient ischemic attack (TIA) patients from the TABASCO (Tel Aviv Acute Ischemic Stroke Cohort) prospective consecutive cohort. All patients were cognitively intact before the stroke, had an MRI on admission along with cognitive assessment using the Montreal Cognitive Assessment (MoCA) test and the NEUROTRAX computerized assessment battery at baseline, 6 months and 1 year. Systemic inflammation was determined using WBC cound, CRP and fibrinogen levels drawn on admission. SLL was estimated semi-quantitavely using a simple 0 to 6 score for the white matter and basal ganglia. **Results:** 265 patients were available for assessment. Out of those 142 had complte Neurotrax data at 12 months and 74 had MoCA data at 12 months. On admission, the mean age was 65, median NIHSS was 2 and median MoCA was 25. Higher SLL (SLL>3) was associated with a decrease in executive and visual-spatial functions at one year (R=0.25, p=0.006) while memory was less impaired. Higher SLL was also associated with a much higher proportion of patients with lower MoCA at one year (45% in patiens with SLL>3 vs 11% in SLL≤3; p=0.007). Systemic inflammation by itself had little influence on cognition. When cognition over time was assessed, cognitive decline was noted following a brief improvement in patients with high SLL as opposed to patients without it who showed steady improvement. See figure. **Conclusions:** In this preliminary cohort, we found correlation between higher SLL on MRI and greater cognitive decline with dysexecutive syndrome, at one year post first ever stroke or TIA. Systemic inflammation at stroke onset does not seem to contribute to this decline. White matter pathway disruption, neuronal death and acceleration Alzheimer-like pathology may all play a role in this phenomenon.

Figure: MoCA changes over time



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W P298

Effect Of Hyperlipidemia On The Progression Of Cerebral White Matter Lesions: Retrospective Cohort Study

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Background and Prupose: Several studies supports hyperlipidemia is associated with a lower risk of intracerebral hemorrhage (ICH). ICH and cerebral white matter lesions (WML) are known as a kind of small vessel disease. We conducted a restrospective cohort study to determine hyperlipidemia and other factors are associated with the progression of WML. Methods- We reviewed records to identify subjects with WML on baseline brain magnetic resonance imaging(MRI) underwent in Seoul National University Hospital between January 2001 and December 2004. We enrolled 2 independent, hospital-based acute stroke cohort and non-stroke cohort. Serial brain MRI were performed from August 2007 to June 2010. WML were measured using semiautomated volumetric image analysis, Medical Image Processing Analysis and Visualization(MIPAV). Clinical data and baseline characteristics were collected prospectively. The associations between progression of WML and study variables were analyzed by univariate and mulivariable regression analyses. **Results:** Forty-two subjects in the acute stroke cohort and ninty three subjects in the non-stroke cohort were idendified consecutively. The average intervals between initial and follow-up MRI were 5.5 and 5.7 years, respectively. In univariate analyses, subjects without hyperlipidemia were associated with the progression of WML in both cohorts ($p<0.05$). In the multivariable analyses, after controlling for age, sex and risk factors in the univariate analyses ($p<0.1$), hyperlipidemia was only assoicated with less progression of WML in both cohorts ($p<0.05$). **Conclusions:** In this retrospective cohort study, patients with a history of hyperlipidemia have less progression of WML, regardless of stroke. These data represents hyperlipidemia may have protective effect on the progression of WML.

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W P299

The Short-term Functional Outcome in Patients with Lacunar Stroke. Observations from the SPS3 Study

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Background: It is generally believed that lacunar strokes carry a benign prognosis with low mortality and good functional outcome. However, conflicting data shows high rates of dependency, some greater than 20%. Consequently, there is inconclusive information about the short-term functional outcome in this stroke subtype. Identification of factors that predict functional outcome in this population is essential. **Methods:** Data are from the Secondary Prevention of Small Subcortical Strokes (SPS3) study. SPS3 is enrolling patients with MRI proven lacunes. The aims of this analysis were to describe the functional outcome of SPS3 participants and to develop a model to predict disability. Disability was defined as a modified Rankin score (mRS) $\geq$2, 3 months after entry into the trial. **Results:** Among 2317 patients, 588 (25%) had mRS $\geq$2 and the remainder a good functional outcome. Those with disability were more likely to be female (43% vs. 35%), African American (21% vs. 13%), have a history of hypertension (81% vs. 75%), diabetes (49% vs. 32%) and stroke (16% vs. 8%) ($p<0.0001$). Patients with pure motor or sensory motor syndrome, brainstem strokes, multiple infarcts on MRI and moderate to severe white matter abnormalities were also more likely to be disabled ($p<0.0001$). In the multivariate model, patients with ataxic hemiparesis were less likely to have a good functional outcome than those with pure motor hemiparesis (OR: 1.8; 95% CI: 1.0-3.2). In addition, both a history of diabetes (OR: 1.8; 95% CI: 1.2-2.7) and the presence of multiple infarcts on MRI (OR: 1.9; 95% CI: 1.2-3.2) were independent predictors of a poor functional outcome. **Conclusions:** The percentage of those with ongoing disability is unexpectedly higher than previously reported. Ataxic hemiparesis, diabetes and multiple infarcts predict disability in lacunar strokes. Data from the ongoing SPS3 trial will likely help to clarify this important issue.

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W P300

Prognostic Value of Silent Brain Infarcts and Leukoaraiosis Following First-Ever Ischemic Stroke in Young Adults

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Background: Prior findings are conflicting regarding the impact of silent brain infarcts (SBIs) and leukoaraiosis (LA) on outcome after ischemic stroke. Moreover, prognostic relevance of silent brain infarcts and leukoaraiosis in young ischemic stroke patients is largely unknown. **Methods:** We included consecutive MRI-scanned patients aged 15 to 49 with first-ever ischemic stroke treated in the Helsinki University Central Hospital, 1994-2007 (the Helsinki Young Stroke Registry). Follow-up was conducted between November 2009 and January 2010. Stroke severity was assessed with the NIH Stroke Scale and etiology classified according to TOAST criteria. Outcome measures were (1) nonfatal or fatal ischemic stroke, (2) composite endpoint of any nonfatal or fatal vascular event, and (3) death of any cause. **Results:** Of our 655 patients (mean age 40.0$\pm$8.0; 58.8% males; mean follow-up in surviving patients 8.7$\pm$3.8 years), 86 (13.1%) had SBIs and 50 (7.6%) LA. Cumulative risks of recurrent ischemic stroke (28.1% at 10 years; log rank $P<0.001$) and composite vascular endpoint (34.7%; $P=0.003$), but not of mortality (13.8%; $P=0.054$), were higher in patients with SBIs compared with those without SBIs (10-year risks 11.0%, 19.4%, and 9.0%, respectively). Cumulative risks of recurrent ischemic stroke (21.2% at 10 years; $P=0.031$) and mortality (31.9%; $P<0.001$), but not of composite vascular endpoint (30.0%; $P=0.088$), were higher in patients with LA than in those without LA (10-year risks 12.3%, 8.4%, and 20.5%, respectively). SBIs were independently associated with risk of recurrent ischemic stroke (odds ratio 1.92; 95% confidence interval 1.10-3.36) adjusted for age, gender, risk factors, stroke subtype, and presence of LA. LA was, in turn, associated with increased risk of death (3.87; 2.05-7.31) after adjustment for age, gender, risk factors, initial stroke severity, subtype, and presence of SBIs. Neither SBIs nor LA associated with the composite vascular endpoint. **Conclusions:** SBIs were predictor of recurrent ischemic stroke whereas LA was associated with increased long-term risk of death in young adults after first-ever ischemic stroke. These relationships persisted after adjustment for important prognostic factors such as age, stroke severity and subtype, and diabetes.

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W P301

Patterns of Antihypertensive Medication use and Persistence in Stroke patients

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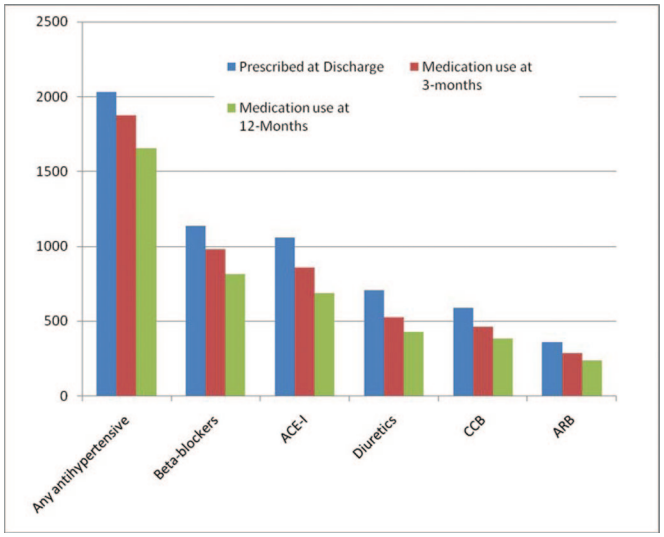
Background: Current guidelines recommend diuretics and angiotensin-converting enzyme inhibitors (ACE-I) as antihypertensive medications of choice for stroke secondary prevention. We evaluated stroke prevention blood pressure regimens after stroke in the Adherence eValuation in Acute Ischemic stroke_Longitudinal (AVAIL) registry to determine patterns of antihypertensive medication use at discharge, and up to 1-year post-discharge. **Methods:** The AVAIL registry is a prospective observational study of medication persistence following hospital discharge from an acute stroke or TIA. Medication persistence was determined via telephone by trained interviewers at 3 months and 12 months. Patient, provider, and system-level factors associated with persistence with antihypertensive classes of drugs at 12 months were modeled using logistic generalizing estimation equations (GEE). **Results:** The analysis included 2,007 AVAIL subjects enrolled at 101 sites participating in GWTG_Stroke who were discharged on any blood pressure medication. Of those prescribed antihypertensive medications, beta blockers were most commonly prescribed (56.1% or n=1140), whereas 52.2% (N=1062) were prescribed ACE-I and 34.9% (N=709) diuretics. Medication use at discharge, 3 months, and 12 months for each class are shown in the figure. Persistence at 3 and 12 months was 81.1% and 64.7%, respectively for ACE-I and 74.2% and 60.6% for diuretics. Factors independently associated with 12-month persistence with ACE-Is and diuretics include prior blood pressure medication use (ACE-I: OR 1.52; 95% CI 1.13-2.06; Diuretics: OR 2.00, 1.11-3.63) understanding how to refill medications (1.97, 1.09-3.40; 2.96, 1.36-6.02), and why medications are taken (OR1.53, 0.96-2.43; OR 2.24, 1.10-4.56). Working status was associated with persistence with ACE-Is (OR 1.56, 1.09-2.24) but associated with non-persistence with diuretics (OR 0.59, 0.36-0.98). **Conclusions:** Despite evidence-based guidelines, diuretics, in particular, are least prescribed at discharge and have the lowest long-term persistence of any antihypertensive class. Patient experience with antihypertensive medications prior to the stroke, and knowledge about why specific classes of medications are taken and how to refill them are important indicators of long-term use. Figure showing trends in medication use overall and for five classes of antihypertensives.



Author Disclosures: D. Olson: None. C. Bushnell: Other Research Support; Modest; BMS/Sanofi. M. Cox: None. E. Peterson: Other Research Support; Significant; Johnson and Johnson.

W P302

Pharmacist Telephone Interventions Improve Adherence to Stroke Preventive Medications and Reduce Stroke Risk Factors: A Randomized Controlled Trial

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Background: Adherence to stroke preventive medications and reduction of stroke risk factors have been shown to significantly reduce the recurrence of stroke. Our objectives were to determine if a telephone intervention conducted by a clinical pharmacist could improve medication adherence in stroke patients and optimize stroke prevention goals. **Methods:** Patients with a history of stroke were recruited from stroke clinic and randomized to a pharmacist intervention group or a usual care group. Patients in the pharmacist intervention group received telephone follow-up calls at 3 months and 6 months from time of randomization. The telephone follow-up call included evaluation of medication adherence based on pharmacy refill history as well as continuing stroke education and reassessment of stroke prevention goals with the patient. Recommendations for medication therapy and relevant clinical studies or laboratories were communicated to the primary care provider and/or stroke provider when appropriate. **Results:** Thirty patients were enrolled in the trial. At the end of 6 months, patients in the pharmacist intervention group were more likely to be fully adherent to all medications compared to the usual care group (56% vs. 36%). Adherence to anti-thrombotics specifically was also increased in the pharmacist intervention group at 6 months (100% vs. 88%). Patients in the pharmacist intervention group were also more likely to achieve stroke prevention goals than patients in the usual care group including blood pressure goals (73% vs. 57%), LDL-C goals (75% vs. 50%), and blood glucose control (75% vs. 50%). These improvements were maintained and actually continued to improve at one year. At one year, 88% of patients in the pharmacist intervention group were able to achieve blood pressure goals, 80% were able to achieve LDL-C goals, and 80% were able to achieve blood glucose goals. Only 54% percent of patients were able to achieve blood pressure, LDL-C, and blood glucose goals in the usual care group at one year. **Conclusions:** A telephone intervention conducted by a clinical pharmacist has significant impact on medication adherence and can optimize achievement of stroke prevention goals. Furthermore, the intervention has long-lasting effects as seen at one year. These findings suggest that clinical pharmacists should play a definitive role in secondary stroke prevention and can greatly improve quality of stroke care.

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W P303

Effect of Medications on Outcome after Ischemic Stroke

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Introduction: We previously derived a model using variables available to the clinician on day 1 post stroke to predict 3 month functional outcome (assessed by the modified Rankin Scale, mRS). The model included age, diabetes, severe white matter disease, pre- and post-stroke functional status, and stroke severity; mRS was further modified by occurrence of comorbid medical conditions. Whether the predicted mRS is affected by the comorbidities or the medications used to treat these conditions has not been elucidated. Goldstein et al showed that some classes of medications significantly impact post-stroke outcomes without considering the associated medical comorbidities. Following Goldstein's findings, we hypothesized that benzodiazepines and anticonvulsant would be associated with worse outcome, while antidepressants and stimulants would be associated with better outcomes after adjusting for known confounders. **Methods:** We used data from a cohort of 460 patients with an ischemic stroke that occurred in 2005 and for whom 90 day survival and mRS were available. Medications being taken at 3 months were divided into medication classes similar to those of Goldstein. We included whether or not a patient received a medication from within each class into our model of post-stroke outcome to ascertain its contribution to outcome variability. Given the large number of medication classes examined (30), a conservative critical p value would be $<$ 0.0017 for any individual medication class. **Results:** Patients were 48% female, 25% black and mean age was 67 years. Common drug use in this cohort included antiplatelet agents (82%), statins (54%), beta blockers (48%), ACE inhibitors (42%), proton pump inhibitors (36%), diuretics (35%), calcium channel blockers and anticoagulants (29% each), and antidepressants (25%); benzodiazepines (8%) and stimulants (2%) were less commonly used. No class had a significant effect on 3 month mortality. Anticonvulsants were associated with worse functional outcome ($p = 0.0026$), while antidepressants and stimulants were also associated with worse outcome ($p = 0.026$ and 0.0054 respectively). These medication classes explained between 5 and 10% of outcome variability (associated R2 of 0.06-0.10). No medication classes were significant at the Bonferroni corrected critical p value. **Conclusions:** Our results do not match those of Goldstein et al. We cannot rule out that medication use is important, but medications may be a surrogate for medical comorbidities, which are highly associated with outcomes. Further research in this area is needed to clearly define the independent effects of medications on post-stroke outcomes.

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W P304

Early And Late Recurrence After Ischemic Stroke; What Is the Difference?

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Background & objective: Recurrence is a major determinant of prognosis after stroke. It has been suggested that early and late recurrence have different risk factors. However there were few MRI-based studies comprising both early and late recurrence. The purpose of this study is to elucidate recurrence rates captured from immediately after stroke onset and to characterize the difference between early and late recurrence. **Methods:** From a prospective stroke registry, a consecutive series of patients, who were hospitalized due to ischemic stroke within 7 days from onset between November 2006 and February 2010, were collected. Each patient's clinical status was followed up to 1 year after onset. Recurrence was categorized into early ($\leq$ 21 days from onset) and late ($>$21 days from onset). Early recurrence was defined as any new neurologic deficits, which occurred after a period neurologic stability or improvement lasting at least 24 hours and were not attributable to edema, mass effect, hemorrhagic transformation, or other medical causes or which were confirmed by a new discrete lesion outside the index lesion on subsequent diffusion MRI. Late recurrence was defined same as for the index stroke. The cumulative risk of the recurrence was calculated using the Kaplan-Meier method and the clinical characteristics of patients with early recurrence were compared to those with late recurrence. **Results:** Among 1726 patients (age, 67.4$\pm$12.9 years; male, 58.5%), 164 (9.5%) had experienced a recurrent stroke. The cumulative risk of recurrence was 4.6% at 7 days, 5.5% at 21 days, 6.9% at 3 months, 7.9% at 6 months and 9.7% at 1 year. More than half of recurrence within one year after onset developed in the early period compared to the late (5.5% vs. 4.1%). Patients with early recurrence were more likely to have large artery atherosclerosis and to receive thrombolytic treatment than those with late recurrence (p'serosclerosis (3.37; 1.42 to 8.00), and thrombolytic treatment (2.55; 1.53 to 4.26) increased the risk of early recurrence, while age (1.02; 1.00 to 1.05) and history of stroke or transient ischemic attack (1.70; 1.02 to 2.84) raised the risk of late recurrence. **Conclusions:** This study shows that the risk of recurrent stroke is highest in the first week and rapidly declines after then. And it suggests that large artery atherosclerosis and thrombolytic treatment increase the risk of recurrence just after stroke onset, whereas previous history of stroke does in the later stage. This can be linked to the necessity of the different prevention strategy as time goes after stroke.

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W P305

Why do Ischemic Stroke Patients get Readmitted?

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Introduction: The Medicare Payment Advisory Commission reported that annual Medicare expenditures for potentially preventable readmissions may be as high as $12 billion. Analysis

of 2003-2004 Medicare claims data showed a 30-day readmission rate of 19.5% for all conditions. Centers for Medicare and Medicaid services may reduce reimbursements for hospitals with higher 30day readmission rates. Hypothesis: Stroke patients are disabled and may need readmissions for non-neurological conditions such as infections and falls. We sought to determine the frequency and causes of readmissions for ischemic stroke patients. **Methods:** Consecutive patients admitted to a JCAHO certified primary stroke center with a diagnosis of ischemic stroke or transient ischemic attack (TIA) over nine months were included. Electronic records were reviewed and data regarding demographics, TOAST mechanism, stroke risk factors, treatments administered and discharge outcome in terms of disability and discharge destination were collected. Charts were reviewed up to 30 days after discharge for readmissions to any hospital within the same healthcare system. In case of readmissions, the reason for admission and outcomes in terms of disability and discharge destination were determined. **Results:** In all, 265 patients (50.9% male; 79.6%African American; mean age 60.9 years) were included in the study. There were 205 (77.4%) radiologically confirmed strokes and 60 (22.6%) TIAs. Thirteen (5%) patients died during their first admission. Of the remaining 252 patients, 25 (9.9%) were readmitted within 30 days. The reason for readmission was determined to be neurological in 8/25 patients (32%; 4 ischemic strokes, 1 hemorrhagic stroke and 3 TIAs); and non-neurological in 17/25 patients (68%). The frequent non-neurological reasons for readmission were infections (6/25), metabolic/electrolyte disturbances (3/25) and trauma related to falls (2/25). The patient's age, race, TOAST mechanism, use of intravenous tPA or interventions, use of antiplatelets or statins, and traditional stroke risk factors did not predict readmission. Patients who were readmitted were more likely to have coronary artery disease (CAD) and congestive heart failure (CHF) than those who were not readmitted (45.5% vs 14.7%; p= 0.001 for CAD and 22.7% vs 8.8%; p value = 0.05 for CHF) An NIH stroke scale $\geq$10 predicted readmission (p value 0.02). Patients discharged home or to acute rehabilitation units were less likely to be readmitted than those discharged to subacute rehabilitation units or nursing homes (p value=0.01). **Conclusion:** Disabled ischemic stroke patients and those with cardiac disease are more likely to be readmitted, and the reason is often non-neurological. Demographic features, conventional risk factors, stroke mechanism and treatments administered do not help us predict readmission.

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W P306

Clinical-Radiological Severity Mismatch Phenomenon: Patients with Severe Neurological Deficits without Matching Infarction on Computed Tomographic Scan

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Objective: To determine the long-term outcome of patients with severe neurological deficits without a large infarction on computed tomographic (CT) scan. Background: Anecdotal observations suggest that some patients can manifest severe neurological deficits associated with small volume of cerebral infarction. **Methods:** We analyzed the prospectively collected data as part of the randomized, placebo controlled trial in patients with ischemic stroke presenting within 3 hours of symptom onset. Volume of infarction was measured from CT scan acquired at 3 months. Favorable outcome defined by no significant or slight disability on modified Rankin scale at 12 months. We determined the outcome of patients with National Institutes of Health Stroke Scale score (NIHSSS) $\geq$ 10 at 24 hours after symptom onset with infarct volume of less than 20 cc. **Results:** Of the 598 patients who had 12 month outcome data available, 91 (15%) met the criteria of clinical-radiological severity mismatch (mean age $\pm$ standard deviation of 65$\pm$12;51% were men). Compared with patients with NIHSSS $\geq$10 with infarct volume $\geq$20 cc, the patients with NIHSSS $\geq$10 and infarct volume $<$ 20 cc were older (mean age 65 versus 69 years, p=0.009) but there was no difference in the gender, race or vascular risk factors. Patients with clinical-radiological severity mismatch were more likely to have a favorable outcome at 12 months compared with those without mismatch (21 % versus 3.3%, P$<$0.001). **Conclusion:** We observed that approximately one-fifth of patients have clinical-radiological severity mismatch. Such patients appear to have a high rate of favorable outcomes at 1 year.

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W P307

Validation of a Model Predicting Post-stroke Outcomes

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Introduction: We previously derived models predicting short and long term mortality and functional outcome (assessed by the modified Rankin Scale, mRS) based on a cohort of 451 ischemic stroke patients identified in 1999. The models were designed to address questions frequently posed by stroke patients and their families about survival and outcome in the short and long term, and included data readily available to the clinician. For example, the model for 3 month mortality included age and pre-stroke disability, while the model for 3 month mRS included age, diabetes, severe white matter disease, pre- and post-stroke functional status, and stroke severity. We sought to validate these models in an independent cohort of 460 ischemic stroke patients identified in 2005. **Methods:** The Greater Cincinnati/Northern Kentucky Stroke Study is a population based stroke epidemiology study that ascertains all ischemic strokes in our region every 5 years. Cohorts of physician-confirmed ischemic stroke subjects were prospectively recruited during 1999 and 2005 to study factors related to outcomes. We validated 4 models that predicted: 3 month mortality and mRS, and long term mortality and mRS. Long term mortality and mRS were assessed at 4 years in the derivation cohort, and at 3 years in the validation cohort. Logistic regression and generalized linear models were used to predict mortality and functional outcome, respectively. Models were first tested by predicting outcomes in the 2005 validation cohort using the 1999 model parameter estimates. The predicted and observed outcomes were compared; the C-statistic or R^2 were used as measures of model fit. Subsequently, we refit the models allowing parameter estimates to vary but retained the same variables, and model fit was again assessed. **Results:** The validation cohort of 460 subjects with ischemic stroke was 48% female, 25% black. Mean age was 67 years. A total of 431 subjects survived to 3 months and 393 of these had a 3 month follow up mRS; 345 survived to 3 years and 172 of these had 3 year follow up mRS. Results are shown in the table. The model fit was similar in the validation cohort as the derivation cohort. Model performance was not significantly improved when parameters were allowed to vary. **Conclusions:** The simple models previously derived for predicting post-stroke outcomes performed well in an independent cohort. While a significant proportion of behavior remains unexplained, outcomes epidemiology allows us to build models that provide insight into important factors determining post-stroke survival and functional outcome.

	Derivation	Validation (derived parameter estimates)	Validation (revised parameter estimates)
	(c-statistic)	*(c-statistic)*	*(c-statistic)*
3 mo mortality	0.80	0.86	0.86
Long term mortality	0.74	0.76	0.80
	(R^2)	*(R^2)*	*(R^2)*
3 mo mRS	0.48	0.57	0.60
Long term mRS	0.51	0.53	0.66

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W P308

Home Time Is Extended In Ischemic Stroke Patients Who Receive Thrombolytic Therapy: A Validation Study Of Home Time As An Outcome Measure

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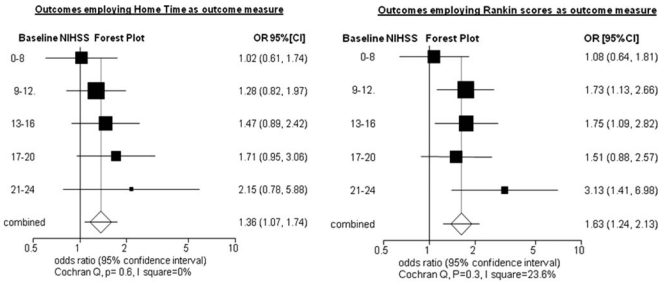
Background: 'Home Time' (HT) refers to the number of days over the first 90 after stroke onset that a patient spends residing in their own home or relative's home, versus any institutional care. It is an accessible and objective parameter, free from subjective bias, with potential as an outcome measure in acute stroke trials. We sought to validate HT and assess treatment responsiveness using independent data. **Methods:** We estimated HT in the SAINT I neuroprotection trial. We compared outcomes between thrombolysed (T) and non-thrombolysed comparators (C) employing HT and modified Rankin Scale (mRS). For our primary analysis we adjusted for baseline covariates that significantly influence HT, and in sensitivity analyses considered all variables that differed between groups at baseline. We report ordinal logistic regression and analysis of covariance with 95% confidence intervals (CI). We describe the relationship of HT with baseline NIHSS and its components and with day 90 mRS and Barthel Index. **Results:** SAINT I included 1699 patients from 23 countries, of whom 28.7% received alteplase. Home Time was explained by age, baseline severity, alteplase use, side of ischemic lesion, presence of diabetes, and country of patient enrolment (each P$<$0.05). We found an association between use of alteplase with better adjusted outcomes by either measure: odds ratio for extended HT=1.36, 95% CI=1.08-1.72, p=0.009; ANCOVA p=0.007 with 5.5 day advantage; odds ratio for more favorable mRS =1.6, 95%CI 1.28-2.00, P$<$0.0001, CMH p=0.046. HT was significantly associated with baseline NIHSS and each component of NIHSS except level of consciousness, dysarthria and ataxia. HT was significantly associated with day 90 mRS and Barthel index. **Conclusions:** Home Time is a responsive measure for use in multinational acute stroke trials. Its inclusion as a complementary outcome is reasonable. We propose treatment effects are adjusted for age, baseline NIHSS, side of stroke lesion, country of enrolment, and the presence of diabetes.



Odds ratio for more favourable Home Time (left) and modified Rankin scores (right) for each stratum of baseline severity. Combined odds were derived from random effects meta-analysis of odds across all strata. Cochrane Q and I square values refer to variability among strata of NIHSS levels. Alteplase was received by 13.8% patients in NIHSS category 0-8 (n=503); 28% in NIHSS 9-12 (n=440); 37.7% in NIHSS 13-16(n=321); 40.3% in NIHSS 17-20 (n=260); 46.2% in NIHSS 21-24 (n=126).

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W P309

Return Home: A Practical Measure of IV-tPA Efficacy

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Introduction/Hypothesis: Years after regulatory approval, debate lingers about the effectiveness of intravenous tissue plasminogen activator (tPA) for acute ischemic stroke, perhaps because standard outcome measures (clinical outcomes at 3 months) are logistically & economically challenging. Alternative outcomes may be useful in monitoring tPA's effectiveness. **Methods:** We queried the >8,700 ischemic strokes in the Colorado Stroke Registry (CSR), to see whether tPA affects the likelihood of home discharge (DC-Home). Selected patients arrived from the scene by EMS or private means, had onset in a community setting between 1/1/06 and 5/31/10, and had data on DC & tPA status. We excluded transfers between other hospitals and intra-arterial or research treatments. We used recursive partitioning to select cut points for variables in a logistic model of DC-Home. **Results:** 5,550 patients met inclusion/exclusion criteria. Our model included: age, National Institutes of Health Stroke Scale (NIHSS), arrival by private means rather than by EMS, and whether tPA was given. Data were missing in at least one field (almost exclusively NHISS) in 49% of records. These were excluded from multivariant analysis. No values were imputed or assigned. The analysis was based on complete data from 2,812 patients. Of them, 415 (14.7%) received IV-tPA & 1443 (51.3%) were DC-Home. The model's discrimination was good (AUC; 95% CI = 0.81; 0.795-0.825). In unadjusted analysis, tPA was negatively associated with DC-Home: OR; 95% CI = 0.71; 0.59-0.85. However, in the multivariate model it was positively associated: OR; 95% CI = 2.03; 1.54-2.67. This gives a risk ratio (95% CI) of 1.36 (1.2-1.48), increasing the probability of DC-Home from 52.4% to 71.4%. The number-needed-to-treat (NNT) is 5.3. **Conclusions:** Standard measures of tPA effectiveness are often unavailable. DC information is more readily available, and calling DC-Home a "good outcome" is reasonable, when the alternatives are rehabilitation, nursing facility, hospice or death. Thrombolysis is more likely to be administered to severe strokes. These are less likely to allow DC-Home, but when data are adjusted for age and stroke severity, the NNT for DC-Home is similar to the value for 3-month clinical outcomes, suggesting DC-Home may be a practical measure of tPA efficacy. Our conclusions are tempered by recognition of limitations that include the observational nature of our data and the incidence of missing data for NIHSS (particularly in non-treated patients). Additional analysis does not indicate that missing NIHSS values would alter our conclusions, but we cannot exclude the possibility. Finally, ours is a less-than-perfect model. There may be other determinants of DC-Home that would alter our results. We encourage others to attempt to replicate our findings with independent data.

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W P310

Concurrent Validity of the National Stroke Project Stroke Severity Score

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Background: The National Stroke Project (NSP) is a retrospective cohort of Medicare beneficiaries hospitalized with stroke or TIA. The NSP included an assessment of stroke severity (NSP-SS) that can be easily extracted from the medical record based on summing the number of up to four impairment domains (vision, speech, motor and sensation; range 0-4). The scale may be useful to adjust for stroke severity in outcome studies primarily using administrative data. **Purpose:** We aimed to determine the concurrent validity of the NSP-SS in comparison to the NIH-Stroke Scale (NIH-SS), a widely used and validated ischemic stroke impairment level scale. **Methods:** The NSP-SS and NIH-SS were retrospectively determined from the records of the same initial Emergency Department (ED) or in-hospital neurological examinations of 100 consecutive patients with a final diagnosis of ischemic stroke. The NIH-SS score was assigned using a previously validated algorithm. Values are means±SD. **Results:** The patients mean age was 66.9 ±15.9 years (49% women; 33% African American; 75% initially evaluated in the ED.; NIH-SS range 0-22, mean 7±5, median 6; NSP-SS range 0-4, median 2,IQR(1-3). Agreement between the scores was moderate (Spearman r=0.65, 95% CI (0.52 - 0.76) P<0.0001). When the scale results were dichotomized (NSP 0-1 mild, 2-4 severe; NIH-SS ≤6 mild, >6 severe), the two scales were concordant for 68% of cases; 27% of NSP-SS severe patients were mild based on the NIH-SS; 5% of NSP-SS mild patients were categorized as severe based on the NIH-SS. Logistic regression (dichotomized NSP-SS) found that 27% of the variance in the NSP-SS was explained by the NIH-SS (r^2=0.27; p<.0001). **Conclusion:** Although the correlation between scales was only moderate, the full NSP-SS may be useful as an adjustment for initial stroke severity for stroke outcome studies. The adjustment, however, may be compromised by differences in patient populations related to impairment domains not fully captured by the NSP-SS (e,g.level of consciousness, aphasia vs. dysarthria, hemispatial neglect).

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W P311

Reliability and Validity of Proxy Derived Modified Rankin Scale Assessment

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Background and Purpose: The modified Rankin scale (mRS) is the most prevalent functional outcome measure in acute stroke trials. Cognitive or communication issues may preclude standard mRS interview; in these circumstances information is derived from interview with a proxy. The properties of proxy assessment have not been described. **Methods:** Over a five week period, a team of undergraduate students trained and certified in mRS assessed a convenience sample of consenting stroke survivors at a University Hospital. Using a standard mRS approach, paired researchers (blinded to each other's scores) performed independent interviews of patients and appropriate proxies. Reliability was described using kappa statistics (with 95 % confidence interval [CI]) and percentage agreement with chi-square testing. **Results:** Seventy-nine stroke survivors were assessed (median age 79 years [IQR:72-85]). Proxies were family members, nurses or physiotherapists. Median mRS from patient derived interview was 3 (IQR:2-4); median mRS from proxy derived interview was 3 (IQR:2-4). Inter-observer variability for assessment of stroke survivors was moderate and similar to previous studies of mRS reliability (k=0.54, CI:0.65-0.75), [67% matched]. Inter-observer variability for paired assessment of proxies was moderate (k=0.40 CI:0.36-0.46), [52% matched], with greatest variability in therapist interviews(Table) but no difference in overall agreement rates (p=0.53). Comparing scores from patient and proxy interview, suggested no difference between groups in patient agreement (p=0.76); kappa statistics described overall agreement as fair (k=0.28, CI:0.24-0.32) [45% matched], with poorest agreement for therapist derived proxy scores (Table). **Conclusions:** Proxy derived mRS scores may differ from direct assessment of stroke survivors and trialists should be cautious in interpretation of these scores. Of the various parties that may be used for proxy assessment, no group was significantly more reliable or valid in their assessment, although there was a trend towards less variability with nurse derived scores. Table: Reliability of paired assessments of mRS p>

	Patient (n=79)	Any proxy (n=88)	Family (n=18)	Nurse (n=45)	Therapist (n=25)
Patient	k 0.54 67%	k 0.28 45%	k 0.25 41%	k 0.32 48%	k 0.16 44%
Any proxy		k 0.40 52%			
Family			k 0.55 64%		
Nurse				k 0.33 48%	
Therapist					k 0.21 49%

Table: Reliability of paired assessments of mRS

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W P312

Reliability and Validity of a translated Modified Rankin Scale Assessment - a pilot study in Mandarin and English

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Background and Purpose: The modified Rankin Scale (mRS) is a favoured functional outcome measure in international randomised controlled trials (RCTs). Recognition of inter-observer variability in mRS assessment despite training and certification of raters justifies greater rigour. Central adjudication of digitally recorded mRS assessments has been proposed, facilitating full blinding and enhanced reliability through involvement of an adjudication committee. International, multilingual RCTs must however consider the linguistic, social and cultural factors which could influence mRS scoring. We conducted a study to assess feasibility and validity of digitally recorded and translated mRS assessments. **Methods:** Ten trained and certified mRS assessors between two university hospitals (5:Glasgow, UK and 5:Beijing, China) scored digitally recorded mRS assessments of consenting patients from each site. Both native language and translated versions were scored by the respective teams. In the initial sample (n=20), two versions of the translated transcript were prepared, one by a mRS-certified clinician and the other by a linguist with no medical background. These non-native language mRS interviews were scored twice, using each transcript in turn at least 2 months apart. A larger sample of mandarin clips was subsequently scored to further assess inter-observer variability. Reliability was described for each group using standard (k) and quadratically weighted (k_w) kappa statistics. **Results:** Sixty nine mRS clips were scored (9 English, 60 Mandarin). Median mRS score was 3 (IQR 2-4). Inter observer reliability for native language assessment was good (n=69), k 0.61 (95%CI 0.59-0.64), k_w 0.91 (95%CI 0.86-0.96). Translated mRS assessments maintained good reliability (n=89), k=0.60 (95% CI 0.58-0.62), k_w 0.90 (95%CI 0.85-0.95). Putting an mRS trained clinician in the translation role had no demonstrable impact on the reliability of translated mRS assessments; k=0.67 (95% CI 0.62-0.72), k_w 0.91 (95%CI 0.81-1.01) with medical input (n=20) and k=0.64 (95% CI 0.59-0.69), k_w 0.91 (95%CI 0.82-1.01) with linguist only transcription (n=20). **Conclusions:** Inter-observer variability of translated interviews appears comparable to previous studies of reliability with standard mRS assessment. Translation by an mRS trained clinician does not confer significant advantage, suggesting that prior experience of communication and cognitive difficulties in stroke survivors may not be crucial for transcription. Use of translated mRS assessments is feasible and should not be a barrier in the use of digitally recorded and centrally adjudicated mRS assessments in multilingual RCTs

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W P313

Comparison of Healthy Life Years Lost due to Stroke between two patient-centered metrics derived from Patients' Preference vs. Experts' Consensus

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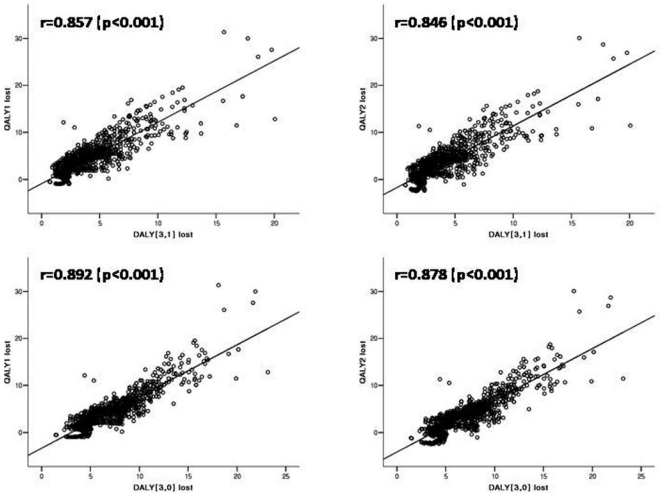
Background: For measuring a disease burden or an interventional efficacy with a patient-centered common metric, two approaches have been widely employed. One is based on patients' or general population's preference, which elicits quality weight (QW) and quality-adjusted life years (QALY). The other is based on disease experts' consensus, which generates disability weight (DW) and disability-adjusted life years (DALY). The correlation between the patients'-deriving and the experts'-deriving outcomes has not been explored in a stroke population. **Methods:** We prospectively compiled the data for baseline characteristics, 3-month modified Rankin disability Scale (mRS), and 3-month EuroQol in patients with acute ischemic stroke who admitted within 7 days from onset to a tertiary hospital between June 2006 and Jul 2007. For each patient, QALY lost and DALY lost were derived from the data of age, gender, 3-month mRS outcome, mRS-specific DW derived from a prior study, and QW derived from EuroQol which patients directly indicated. Two sets of QALY lost were generated: one was calculated by assuming QW of healthy individual as 1 ($QALY_1$ lost), and the other by employing age-specific QW obtained from Korean general population ($QALY_2$ lost). Similarly, two sets of DALY lost were generated by incorporating age-weighting (DALY[3,1] lost) or not (DALY[3,0] lost). Then, we analyzed the correlations between two sets of QALY and DALY lost values, and investigated whether the correlations remain robust across different age, gender, and initial stroke severity. **Results:** 1524 patients were included in this study: age, 66.7±12.5(SD); median NIHSS (interquartile range), 4 (2-7); male 60.6%; DALY[3,1] lost, 3.64±0.06; $QALY_1$ lost, 3.85±0.09; $QALY_2$ lost, 3.04±0.09. The Pearson's correlation coefficients were 0.857 ($p<0.001$) between $QALY_1$ and DALY[3,1], 0.892 ($p<0.001$) between $QALY_1$ and DALY[3,0], 0.846 ($p<0.001$) between $QALY_2$ and DALY[3,1], and 0.878 ($p<0.001$) between $QALY_2$ and DALY[3,0] (Figure). Interaction analyses revealed that the correlations between QALY and DALY vary by age, gender, and initial stroke severity ($p<0.1$ for all). However, those interactions were quantitative rather than qualitative. **Conclusion:** This study demonstrated that an expert-deriving DALY lost was closely correlated with a patient-deriving QALY lost. As being a more comparable and externally validated measure, the DALY lost would be a good alternative to QALY lost for a health policy-decision making in stroke field.



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W P314

Quality Of Life After Stroke And Its Correlation With Severity Of Impairment And Functional Status

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There is an increasing national emphasis on measuring health-related quality of life and other patient-reported outcomes of care. It is unclear ow these measures correlate with other traditional stroke outcome measures assessing functional status and severity of impairment, which are typically reported by the provider. The aim of this study was to determine the correlation between the generic health-related quality of life measure - European Quality of Life (EQ5D) and the following stroke outcome measures: Stroke Impact Scale 16 (SIS-16), modified Rankin (mRS), National Institutes Health Scale Score (NIHSS), Barthel Index (BI) as well as the depression scale Patient Health Questionnaire 9 (PHQ9). **Methods:** Several patient-reported measures have been systematically collected from all stroke patients seen in the Cleveland Clinic's cerebrovascular clinic using electronic tablets since August 2008. Spearman correlations were computed between EQ5D and each stroke outcome measure overall and after stratification by TOAST stroke mechanism. Tests were conducted to identify if correlations were different than zero, indicating no linear relationship. Correlations were computed using the first available visit per patient. **Results:** There were 741 patients identified with stroke representing 1,115 visits to the outpatient stroke clinic. Of those, 47.7% were female, 75.5% were Caucasian, and 47.2% were $\geq$ 60 yrs old. Mean EQ5D score was 0.73 [95%CI .71-.75]. Median Rankin score was 2. Patients with TOAST stroke mechanism of "Other determined etiology" had lowest EQ5D score (0 .68 [.62-.74]), while those with 'small vessel disease' had the highest EQ5D (0.78 [.74-.82]). Overall, there were moderately strong correlations between the EQ5D and each of the functional status measures (see Table). Negative correlations were seen with PHQ9 (r_s = -0.657), Rankin (r_s = -0.604), and NIHSS (r_s = -0.463), indicating that quality of life improved as each of these measures decreased (less depression and less severe disabilities).). Highest correlation occurred with SIS16 (r =.704) and lowest occurred with NIHSS (r=-.463). **Conclusion:** Patients with stroke being seen in a tertiary care center's outpatient stroke clinic had reasonable quality of life. Correlations with EQ5D and other stroke functional and impairment scales were moderate - and was the highest for the Stroke Impact Scale and lowest for the NIHSS. The QoL measure was not redundant with these stroke outcomes scales. Addition of an overall Quality of Life metric should be considered when evaluating overall outcomes after stroke.

Table: Correlation* between EQ5D and functional status measures, overall and by mechanism					
	PHQ9	SIS16	Rankin	NIHSS	Barthel
Overall	-0.657 (p<.0001)	0.704 (p<.0001)	-0.604 (p<.0001)	-0.463 (p<.0001)	0.531 (p<.0001)
LAA	-0.632 (p<.0001)	0.688 (p<.0001)	-0.643 (p<.0001)	-0.517 (p<.0001)	0.489 (p<.0001)
Cardioembolism	-0.708 (p<.0001)	0.836 (p<.0001)	-0.749 (p<.0001)	-0.609 (p<.0001)	0.752 (p<.0001)
Small vessel occlusion	-0.662 (p<.0001)	0.749 (p<.0001)	-0.527 (p=.0002)	-0.253 (p=.0929)	0.440 (p=.0105)
Other etiology	-0.641 (p<.0001)	0.801 (p<.0001)	-0.588 (p<.0001)	-0.418 (p=.0017)	0.634 (p<.0001)
Undetermined etiology	-0.621 (p<.0001)	0.695 (p<.0001)	-0.471 (p<.0001)	-0.337 (p=.0010)	0.297 (p=.0132)
* Spearman correlation along with test to identify if different than zero.					

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W P315

Depression After Stroke - Association With Patient Characteristics And Functional Status

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Depression is common occurrence after stroke and negatively impacts stroke outcomes. The aims of this study were to (1) determine the frequency of depression in patients seen in stroke clinic, (2) identify specific demographic and clinical factors associated with depression following stroke (3) evaluate the correlation between depression and functional status after stroke, and (4) explore the association of specific neurological impairments as defined by NIHSS with depression. **Methods:** Patient-reported PHQ9 scale was systematically collected using electronic tablets on all patients seen in the Cleveland Clinic's Cerebrovascular Clinic beginning August 2008. To evaluate the association of specific factors with depression, regression models were built using generalized estimating with the PHQ9 score as the dependent variable. Spearman correlations were calculated to evaluate correlation of PHQ9 score with the following stroke outcome measures: modified Rankin Scale (mRS), Stroke Impact Scale 16 (SIS-16), Barthel Index (BI), and the NIHSS. To explore the relationship of somatic symptoms, which may occur after stroke, with the PHQ9 score, analysis of individual PHQ9 elements and outcome scale scores was also performed. **Results:** PHQ9 scores were available from 804 clinical visits, representing 599 patients with mean age = 58.4, mean NIHSS = 1.7, median mRS of 1. Mean PHQ9 score was 5.9% (95CI% 5.4 6.4); 23.4% had PHQ9 $\geq$10 suggesting moderate depression and 11.4% had PHQ9 $\geq$15 suggesting severe depression . Females were more depressed than males (p=.0005) as were new patients over established patients (p=0.004). There was no association with PHQ9 and time since stroke (p=0.17). There were moderately strong correlations between the PHQ9 and other functional status measures, indicating higher depression with higher degrees of disability. Correlation was smallest with NIHSS. [See table]. Among individual PHQ9 questions, highest correlation occurred with Q1 ("interest in activities") and Q4 ("fatigue"), both of which may be due to direct stroke effects, although total PHQ9 score had highest correlation with other outcome scales. There was a significant association with PHQ9 and each individual NIHSS item except "vision" and "best language". **Conclusion:** Depression as identified by PHQ9 occurred in 23.4% of stroke patients seen in an outpatient setting, despite the relatively low disability in this cohort. There is a correlation with disability and less so with severity of impairment. Systematic collection of depression may provide a significant opportunity to improve overall outcomes after stroke.

Table: Correlation* between PHQ9 and functional status measures, days since stroke					
	SIS16	Rankin	NIHSS	Barthel	Days since stroke
PHQ9	-0.517 (p<.0001)	0.475 (p<.0001)	0.292 (p<.0001)	-0.332 (p<.0001)	-0.068 (p=.1674)
Q1: Little interest	-0.414 (p<.0001)	0.371 (p<.0001)	0.260 (p<.0001)	-0.322 (p<.0001)	-0.052 (p=.2774)
Q2: Feeling down	-0.321 (p<.0001)	0.312 (p<.0001)	0.185 (p<.0001)	-0.168 (p=.0004)	-0.017 (p=.7330)
Q3: Sleep problems	-0.318 (p<.0001)	0.284 (p<.0001)	0.133 (p=.0022)	-0.190 (p<.0001)	-0.007 (p=.8801)
Q4: Fatigue problems	-0.463 (p<.0001)	0.353 (p<.0001)	0.181 (p<.0001)	-0.213 (p<.0001)	-0.086 (p=.0749)
Q5: Appetite problems	-0.206 (p<.0001)	0.126 (p=.0033)	0.015 (p=.7340)	-0.101 (p=.0335)	-0.050 (p=.2986)
Q6: Self deprecation	-0.318 (p<.0001)	0.321 (p<.0001)	0.239 (p<.0001)	-0.271 (p<.0001)	-0.015 (p=.7623)
Q7: Concentration problems	-0.298 (p<.0001)	0.341 (p<.0001)	0.227 (p<.0001)	-0.168 (p=.0004)	-0.086 (p=.0768)
Q8: Slow motion	-0.391 (p<.0001)	0.362 (p<.0001)	0.305 (p<.0001)	-0.317 (p<.0001)	-0.050 (p=.3083)
Q9: Suicide	-0.207 (p<.0001)	0.248 (p<.0001)	0.209 (p<.0001)	-0.203 (p<.0001)	0.016 (p=.7466)
* Spearman correlation along with test to identify if different than zero					

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W P316

The Psychosocial Impact of Stroke on Patients and their Primary Family Caregivers: The Caring for Adults Recovering from the Effects of Stroke (CARES) Project

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Background and Purpose: The negative effects of stroke on depression and other measures of psychosocial functioning have been well described in previous research, but less is known about the effects of stroke on primary family caregivers. In this project, race and gender differences in psychosocial outcomes were examined using an epidemiologically-derived sample of first-time stroke survivors and their primary family caregivers recruited from the national REasons for Geographic and Racial Differences in Stroke (REGARDS) study. **Methods:** REGARDS participants who experienced verified incident stroke events and their primary family caregivers (N = 139) were enrolled in the CARES project and interviewed by telephone approximately 9 months after the stroke event. Individually-matched stroke-free controls from the REGARDS sample and noncaregiving family member controls were also enrolled. Stroke and control dyads were matched on race, gender, age of stroke survivor ($\pm$ 5 years), relationship, and co-residence status. The interviews collected data on general physical health, psychosocial functioning, health care utilization, and the severity of any stroke-related impairments. The Center for Epidemiological Studies Depression scale (CESD) and the Mental Composite Summary (MCS) of the 12-item Short Form provided measures of mental health functioning for all participants. Analyses of covariance were used to examine stroke vs. control, race, and gender effects for both stroke survivors and caregivers. **Results:** Consistent with previous research, stroke survivors reported significantly more depressive symptoms and poorer mental health functioning than matched controls (ps $<$ .0001), with no evidence of a differential impact by race or gender (ps $>$ 0.05). Caregivers also reported significantly more depressive symptoms and poorer mental health functioning than noncaregiving controls (ps $<$ .05). Standardized effect sizes indicated a similar impact of stroke on the mental health functioning of caregivers and stroke survivors. Female caregivers reported more mental health problems than men, but no differential caregiving effects were found by race. Caregiver depressive symptoms and mental health functioning were significant predictors of stroke survivor depressive symptoms and mental health functioning, respectively (*B*s = 0.40 and 0.35, respectively, ps $<$ .0001). **Conclusions:** A stroke event has similar impacts on mental health functioning for both patients and their primary family caregivers. Deleterious mental health effects appear to be linked between caregivers and stroke survivors, and female caregivers are at heightened risk for poor psychosocial outcomes.

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W P317

Acute Stroke Mortality as a Measure of Program Quality: Does Unadjusted Mortality Rate Paint a Clear Quality Picture for Public Reporting?

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Background: Mortality, as an outcome indicator for public reporting, is in demand by consumer agencies. The Agency for Healthcare Research and Quality (AHRQ) has proposed methods for calculation of unadjusted raw stroke mortality that were accepted by the National Quality Forum for CMS implementation. We explored the implications of using AHRQ methodology at a Comprehensive Stroke Center. **Methods:** Administrative data from 2009 was used to identify cases with a principal diagnosis of stroke and ICD-9 codes meeting AHRQ criteria. Cases lacking disposition and those not associated with infarction or hemorrhage were excluded. No attempt to correct ICD-9 codes was made from their original assignment. Recorded disability and prognostic measures were verified against documented clinical exams and imaging. **Results:** The sample consisted of 386 cases (Table). Age was 59$\pm$16 yrs; 191 (49.5%) cases were transfers. Neurosurgery admitted 168 (43.5%), stroke neurology admitted 163 (42%) of which 61% were ICH, and the remaining 55 (14%) were admitted by others. Unadjusted stroke mortality was 22% (n=86). Hemorrhage accounted for 92% (n=79) of stroke mortality (n: 46 IPH; 14 SDH; 19 SAH); transfers accounted for 17% of deaths. Neurosurgery had 31 (18.5%) deaths, stroke neurologists had 38 (23%), and other service physicians had 17 (31%); p=ns. Age (r =.166; p=.001), GCS (r = -.756; P<.001), NIHSS (r =.652; P<.001), ICH score (r =.689; P<.001), Hunt & Hess (r =.722; P<.001), and Fisher score (r =.493; P<.001) were significantly correlated with stroke mortality. Exclusion of patient transfers with GCS $<$ 8 reduced mortality to 16.6%, while exclusion of cases with ICH scores $\geq$ 4 decreased mortality to 14.7%. Due to our large volume of hemorrhages, a logistic regression model was constructed to predict the effect of GCS and transfers on mortality; for each 1 point GCS increase, the survival OR doubled. **Conclusions:** Raw unadjusted stroke mortality is likely to favor both non-stroke center designated hospitals and primary stroke centers that do not admit, or transfer hemorrhage and severe ischemic stroke patients, potentially misleading public perception of stroke center quality. Methods that incorporate ICH score or GCS for non-ICH hemorrhage, NIHSS score and Hunt & Hess score for severity adjustment should be explored.

ICD-9	N	ICD-9	N
430 – Subarachnoid hemorrhage	124 (32.1%)	431 – Intracerebral hemorrhage	145 (37.6%)
432.10 – Subdural hemorrhage	53 (13.7%)	433.01 – Basilar artery occlusion with infarct	2 (0.5%)
433.11 – Carotid artery occlusion with infarct	16 (4.1%)	433.21 – Vertebral artery occlusion with infarct	1 (0.3%)
434.01 – Cerebral thrombosis with infarct	12 (3.1%)	434.11 – Cerebral embolism with infarct	33 (8.5%)

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W P318

Challenges in Assessing Hospital level Stroke Mortality As a Quality Measure: Association of Ischemic, Hemorrhagic or Total Hospital Stroke Mortality Rates

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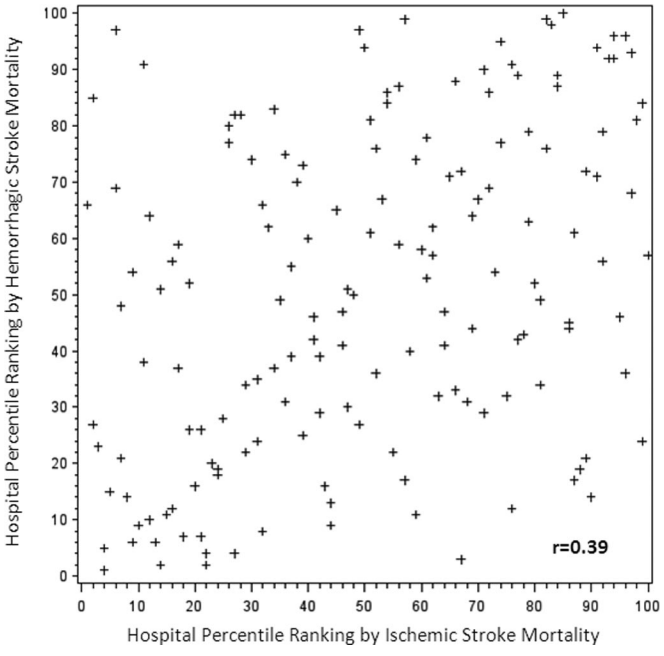
Background: Public reporting efforts often profile hospitals based on overall stroke mortality rates. Yet the 'mix' of stroke cases may impact on this rate. Specifically, hemorrhagic strokes are less common but face much higher mortality than ischemic strokes. Our goal was to assess the degree to which hospital stroke mortality rankings varied whether one assessed hemorrhagic vs. ischemic vs. total stroke outcomes. **Methods:** Using the 2006 New York Statewide Planning and Research Cooperative System data, we examined hospital risk-adjusted ischemic, hemorrhagic and total (combined) stroke in-hospital mortality rates. Observed and expected mortality rates were calculated using AHRQ Inpatient Quality Indicator Software and hospital ranks were based on their observed/expected ratio. Levels of agreement among top, middle, and bottom hospital performance groups (top 10th, middle, bottom 90th) were assessed using kappa statistic. **Results:** Overall in-hospital mortality for ischemic, hemorrhagic and total stroke mortality rates were 7.4%, 27.4%, and 12.2%, respectively. Comparing ischemic vs. hemorrhagic stroke mortality, there was weak correlation in percentile rates (r=0.39, Figure 1) and poor agreement in hospital performance groups (kappa=0.24). Total hospital percentile rankings were slightly more correlated with hemorrhagic stroke (kappa=0.55) and ischemic stroke mortality ratings (kappa=0.69) but many hospitals still switched classification depending on mortality metrics. **Conclusions:** Hospital stroke mortality ratings varied considerably depending on whether ischemic, hemorrhagic or total stroke mortality rates were used. Future efforts should consider providing data on separate stroke types and outcomes.



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W P319

Weekend versus Weekday Admission and Mortality for Acute Ischemic Stroke

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Introduction: Hospital staffing may be reduced in spectrum on weekends. Prior studies of weekend disparities in stroke care have focused on in-hospital mortality. We hypothesized that 90-day mortality was higher in stroke patients hospitalized on weekends versus weekdays, and that this difference would be minimized in certified stroke centers. **Methods:** We used the Myocardial Infarction Data Acquisition System (MIDAS) database, which includes demographic and clinical data on patients discharged with a primary diagnosis of cerebral infarction from all non-federal acute care hospitals in New Jersey between 1996 and 2007. Out-of-hospital deaths were assessed by matching MIDAS records with New Jersey death registration files. The primary outcome variable was all-cause mortality within 90 days of hospital admission. The primary independent variable was weekend versus weekday admission. Covariates included patient demographics, comorbid conditions, year of admission, intravenous tPA, and New Jersey stroke center designation. Measures of initial stroke severity were not available. Multivariable logistic-regression models were used to adjust for available confounding variables. Statistical significance was defined as a p-value $\leq$ 0.01. **Results:** 134,441 patients were admitted with a primary diagnosis of cerebral infarction during the study period. 23.4% were admitted to a comprehensive stroke center, 51.5% to a primary stroke center, and 25.1% to a non-stroke center hospital. Baseline patient characteristics were similar for all groups. Intravenous tPA was given more often on weekends than weekdays (1.62% vs. 1.34%, P<0.0001). 90-day mortality was greater in stroke patients admitted on weekends compared to weekdays (17.24% vs. 16.52%, p=0.001). The overall adjusted odds of death at 90 days were significantly greater for weekend admission (OR 1.05, 95% CI 1.02-1.09). Admission to a New Jersey certified stroke center was independently associated with a reduction in mortality (Table 1). No difference in mortality was observed for patients admitted to comprehensive stroke centers on weekends versus weekdays (16.43% vs. 16.60%, p=0.7). **Conclusions:** Stroke patients admitted on weekends to New Jersey hospitals had a significantly higher risk of death by 90 days. However, no such difference in mortality was observed at comprehensive stroke centers. Mortality after stroke was lower in certified stroke centers.

Table 1. Adjusted Risk of Death by 90 Days

Terms in Cox model	Odds Radio (95% Confidence Interval)
Weekend admission	1.05 (1.02-1.09)
Year of admission	
1998-1999 vs. 1996-1997	1.01 (0.96-1.06)
2000-2001 vs. 1996-1997	1.02 (0.97-1.07)
2002-2003 vs. 1996-1997	1.05 (0.99-1.10)
2004-2005 vs. 1996-1997	0.98 (0.93-1.03)
2006-2007 vs. 1996-1997	0.82 (0.77-0.86)
Age	1.05 (1.05-1.05)
Sex	1.03 (0.99-1.06)
Race	
Black vs. White	0.96 (0.92-1.01)
Other vs. White	0.87 (0.82-0.92)
Comorbid Conditions	
Hypertension	0.58 (0.56-0.60)
Diabetes	1.01 (0.97-1.04)
Atrial Fibrillation	2.02 (1.95-2.09)
Renal Disease	2.95 (2.79-3.13)
Intravenous tPA	1.50 (1.33-1.70)
Stroke Center	
Comprehensive vs. Other	0.94 (0.90-0.99)
Primary vs. Other	0.95 (0.92-0.99)

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W P320

Mortality Due to Stroke in Da Nang, Vietnam

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Background: As developing countries such as Vietnam experience the health transition to chronic disease, the morbidity and mortality from stroke contribute a huge burden on the health of the people. Objectives: We sought to investigate patient characteristics associated with

stroke mortality in hospitalized patients in Da Nang, Vietnam. **Methods:** In a collaboration between the Da Nang Ministry of Health and the University of Washington, Seattle, a stroke registry was recently developed and implemented at Da Nang Hospital utilizing the WHO Stoke STEPS instrument. Physicians and nurses from the ICU, Cardiology, or General Internal Medicine units collected the information which was entered into a computer system on-site. **Results:** Data from April, May and June, 2010, resulted in a total of 210 strokes defined as definite based on CT imaging. Of these, 97 were classified as ischemic (46.2%), 90 as hemorrhagic (42.9%), and 23 were unspecified (11.0%). Mean age of stroke patients was 48.2 (SD 16.8) years and 84 (40%) occurred in females. Of these, 143 (65.1%) were discharged from the hospital after a mean length of stay of 22.5 (SD 14.6) days. Eleven patients (5.2%) died in hospital and an additional 56 (26.7%) were in grave condition/dying and family or patient requested that he/she be released to die at home. Of those who either died in hospital or were released to die at home, 77.6% had hemorrhagic strokes while only 22.4% were ischemic ($p<.001$). Mortality did not differ by age although a higher percent of men (37.3%) than women (21.5%) either died or went home to die ($p=.01$). Higher rates of atrial fibrillation and diabetes but not hypertension were reported in patients with mortal strokes. In multivariate logistic regressions models adjusted for age, gender and previous stroke, persons with hemorrhagic strokes were almost 8 times as likely to subsequently die compared to those with ischemic strokes (OR: 7.69, 95% CI: 3.76-15.73). Men were twice as likely to die from stroke as women (odds ratio 2.00, 95% CI: 1.05, 3.80) adjusted for age and previous stroke. In adjusted models, the following factors were found to significantly predict mortality: modified Rankin scale prior to stroke, presence of atrial fibrillation, diabetes mellitus, hypercholesteremia, and current tobacco use. While presence of hypertension at admission was not associated with mortality, the maximum blood pressure reached during the hospital stay was significant ($p <.001$). **Conclusions:** These data document the high case fatality from stroke in Vietnam (over 30%). Efforts to document out-of-hospital deaths and to address the risk factors related to mortality after a stroke event are urgently needed.

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W P321

Neurological Morbidity And Mortality Following Attendance At A Transient Ischaemic Attack Clinic

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Introduction: Half of patients who attend transient ischaemic attack (TIA) clinics do not have cerebrovascular disease and have an alternative explanation for their symptoms. This may be an underlying neurological disorder that will later become manifest. We examined the risk of future non-stroke neurological death or hospital admission in a large cohort referred with suspected TIA. **Methods:** Data from the West Glasgow Stroke Registry were used. The Registry contains data on patients attending our TIA clinic from August 1992 onwards. We dichotomised clinical diagnoses at baseline as being TIA (including minor stroke) or non-TIA. Subjects were followed up by record linkage to death and hospital discharge records until 27 December 2006. Our endpoint was the next occurrence of any non-stroke neurological event, defined using ICD-10 and ICD-9 classifications. We compared outcomes between the groups using a Cox proportional hazard model adjusted for age, sex and further potential confounding variables. **Results:** We studied 3533 patients who attended the TIA clinic between August 1992 and January 2005: 1631 (46.2%) were male and mean (SD) age was 64.7 (13.6) years. 1890 (53.5%) had a baseline diagnosis of TIA and 1643 had non-TIA. There was a minimum of 24 months follow-up for each patient and median (IQR) follow-up was 165 (84.2 to 246.3) months. 514 patients (14.5%) suffered a non-stroke neurological event during follow-up. Of those with non-TIA at baseline, 252 (15.4 %) later suffered a non-stroke neurological event, compared to 262 (13.9%) with TIA (HR 1.37, 95% CI 1.10 to 1.69, $p=0.003$ after adjustment). Compared to patients with TIA at baseline, a greater proportion of those non-TIA later suffered admission or death with epilepsy (46 (2.8%) vs. 23 (1.2%), $p=0.001$), nerve, nerve root and plexus disorders (29 (1.8%) vs. 16 (0.8%), $p=0.015$) and demyelinating diseases (8 (0.5%) vs. 1 (0.1%), $p=0.01$). Inflammatory neurological disorders, atrophies, movement disorders and the dementias were similarly common between groups. Other disorders of the nervous system not covered in the above categories were also more common in those with non-TIA at baseline (22 (1.3%) vs. 10 (0.5%), $p=0.01$). **Conclusion:** Patients who attend TIA clinics with transient neurological symptoms but not TIA are at slightly greater risk of future non-stroke neurological events than those with TIA. Further work should aim to help better identify such individuals at first TIA clinic attendance as this may allow earlier diagnosis and treatment of underlying neurological disorders.

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W P322

TIA Clinic Triage Strategy Reduces the Cost of TIA Evaluation

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Objectives: Several studies have shown that an expedited outpatient evaluation of patients presenting with TIA symptoms is effective and safe. We investigated whether the community costs of TIA evaluation using an outpatient TIA clinic triage strategy are lower compared to the costs of an inpatient evaluation. **Methods:** The TIA Workup as Outpatient: Assessment of Clinical Evaluation and Safety (TWOACES) study prospectively enrolled three groups of patients: direct referral to TIA clinic from a primary care physician, emergency department (ED) evaluation followed by referral to outpatient TIA clinic, and ED evaluation followed by hospitalization. We retrospectively identified a representative sample (15%) of Medicare reimbursed patients in each group to compare costs for patients who had an inpatient TIA evaluation vs. an outpatient evaluation. The assessment included reimbursements for all services and procedures related to TIA diagnosis ordered by the attending physician. Any tests ordered to evaluate concomitant diagnoses other than TIA were excluded. We estimated potential cost savings by comparing costs of the TWOACES triage strategy with hypothetical costs of hospital admission for all TIA patients. Costs were compared using Mann-Whitney U test. Differences between medians in costs were computed using Hodges-Lehman estimates. **Results:** During the 2.5-year period of the TWOACES study, there were 43 patients with direct referral to TIA clinic from primary care, 157 with ED to TIA clinic referral, and 67 with ED evaluation followed by hospitalization. The median per patient Medicare cost for direct referrals to TIA clinic was $1,884 (IQR $1,866-$1,897), for ED to TIA clinic $4,049 ($3,594-$4,756), and ED to hospitalization $5,804 ($4,027-$7,173). The median Medicare cost for hospitalized patients was $3,587 (95% CI $1,450 - 5,396, $p=0.006$) greater than the cost of direct referrals to TIA clinic and $1,427 (-$326 - $3,088, $p=0.108$) greater than the cost of ED to TIA clinic referrals. Therefore, the annual healthcare cost reductions obtained in the TWOACES study are estimated to be $151,312 ($4,467-$286,738) compared with the hypothetical cost of hospitalization of all patients. Distributing these cost reductions across all 267 TIA patients enrolled in TWOACES, the healthcare cost reduction per TIA patient encountered was $1,417 ($42-$2,685). **Conclusions:** Our analysis demonstrates that the TWOACES TIA triage strategy is cost saving from the community perspective. We estimate that Medicare saved more than $1,000 per patient using this triage approach. A TIA clinic does not require a significant investment and may be particularly desirable for a hospital that runs near full capacity because of the opportunity to admit other patients into beds freed up by the outpatient evaluation of TIA patients.

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W P323

Brain Magnetic Resonance Imaging is Utilized in Less than One-third of Admitted Transient Ischemic Attacks Patients in the United States

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Objective: To investigate the utilization of brain magnetic resonance imaging (MRI) among admitted transient ischemic attack (TIA) patients in United States (US) hospitals between 2003 and 2007 Background: MRI is superior to CT imaging in the detection of acute infarcts and its application has lead to a new definition of TIA and ischemic stroke. However, due to costs, availability, and contraindications, MRI may be more difficult to obtain. **Methods:** We used the Nationwide Inpatient Sample (NIS), representative of 20% of inpatient admissions in the US, to identify adult ($\geq$18 years old) patients admitted with a discharge primary diagnosis of transient ischemic attack (DRG code 524) between 2003 and 2007. We then selected only those in whom procedures were coded and calculated the proportion of brain MRI use (ICD-9-CM procedure code 88.91) for each year. Trend statistics were performed using the Cochran-Armitage test. For 2007, we also assessed individual patient and hospital characteristics in univariable analyses. Significant candidate variables were then analyzed in a multivariable stepwise logistical regression model to determine odds ratios (OR) and 95% confidence intervals factors associated with brain MRI use following TIA. A p-value < 0.05 was considered significant. **Results:** Between 2003 and 2007, there were 185,172 patients diagnosed with TIA in the NIS. Among these, 45,173 (24.2%) were adults who had procedure codes recorded. The use of brain MRI in these admitted TIA patients increased each year ($p < 0.001$ for trend): 2003: 21.6%; 2004: 22.6%; 2005: 24.7%; 2006: 26.5%; and 2007: 29.3%. In a multivariable model, the following were independently associated with utilization of brain MRI after TIA in 2007: younger age (adj. OR 0.996, 0.992-1.000), non-elective admission (adj. OR 2.25, 1.53-3.30), lower illness severity subclass (highest class: adj. OR 0.19, 0.08-0.48), lower mortality subclass (highest class: adj. OR 0.43, 0.19-0.97), teaching hospital status (adj. OR 1.69, 1.50-1.89), eastern US (adj. OR 1.44, 1.29-1.62), urban location (adj. OR 1.29, 1.05-1.60), and large hospital size (adj. OR 1.61, 1.33-1.95). Insurance status, race, and sex were not significantly associated with MRI utilization following TIA. Total hospital charges were not different between those who underwent MRI and those who did not ($p = 0.131$). **Conclusions:** Despite recommendations by major organizations and evidence to support the role of MRI in acute TIA evaluation, less than one-third of patients admitted with TIA are evaluated with brain MRI in this large inpatient sample. Several patient-related and hospital-related factors may influence MRI utilization following TIA. More physician education and study of limiting factors including availability and cost are needed.

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W P324

One Year Outcomes of Acute Ischemic Stroke and TIA Patients undergoing CT- versus MRI- based Evaluations: A Retrospective Comparison

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Background: Many clinicians advocate for MRI-based work-ups for patients with ischemic cerebrovascular symptoms asserting that patient management is improved. Previous studies have shown that MRI is more sensitive and specific than CT in the diagnosis of acute stroke.

The American Stroke Asssociation guidelines for TIA evaluation state that an MRI, including DWI, is the preferred brain diagnostic imaging modality. The basis for this recommendation is that MRI-based evaluations offers improved prognostic information. There are no studies evaluating the outcomes of patients who undergo CT- versus MRI-based evaluations. We sought to compare one-year outcomes of stroke and TIA patients who underwent different imaging modalities. **Methods:** Patients were identified from a prospectively collected database of stroke and TIA patients. All patients discharged from a single institution between January 1, 2008 and Dec 31, 2008 were included. Electronic medical records were used to collect demographic, clinical, and diagnostic testing data. Death, stroke, and myocardial infarction within one year of admission were compared between patients who had CT alone, MRI alone, or CT and MRI during hospitalization. Multivariable analysis was performed to identify independent predictors of death, recurrent stroke, and myocardial infarction within one year. **Results:** 727 patients were identified: 1 did not have CT or MRI and was excluded, 161 had CT alone, 29 had MRI alone, and 536 had CT and MRI. On univariate analysis, patients who had both CT and MRI were significantly less likely to die while those who had MRI alone were more likely to have a recurrent stroke at 1 year follow-up. After adjusting for age, gender, admission NIHSS, treatment with tissue plasminogen activator, atrial fibrillation, coronary artery disease, diabetes mellitus, hyperlipidemia, and hypertension, use of an MRI during hospitalization was not associated with any outcome measure at one year. Variables that were significantly associated with death at 1 year included NIHSS and age. **Conclusions:** In this retrospective analysis, use of an MRI during hospitalization was not associated with a reduced risk of death, recurrent stroke, or myocardial infarction with one year. The results suggest that treatment strategies may not necessarily have been influenced by imaging modality or that changes in treatment strategy based on MRI did not improve outcome. A randomized trial of different imaging modalities may be warranted.

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W P325

Stroke Etiology Significantly Influences Inpatient Cost

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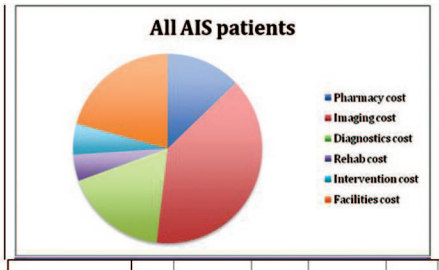
Background: Evaluation of patients with acute ischemic stroke (AIS) is tailored to patient demographic characteristics and the likelihood of the etiology. The etiology could impact stroke severity and management, affecting length of stay and cost. We hypothesized that the cost of inpatient care and the distribution of costs for an acute ischemic stroke (AIS) would be dependent on stroke etiology. **Methods:** We identified patients admitted with AIS to the stroke service by retrospective chart review. Gross total patient charges were analyzed, as were costs subdivided into pharmacy, imaging, diagnostic, interventional, rehabilitation, and facility fees and compared in patients based on TOAST classification. We adjusted for factors that affect outcome (age, baseline NIHSS score, and admission glucose level) and length of stay (LOS). **Results:** 209 patients were included in the analyses; 59.3% were male. The figure shows the distribution of total cost and the total and subgroup costs in the each TOAST classification category relative to each corresponding median value for the whole population. About 1/3 of the total cost was due to imaging. There was significant variation in LOS among stroke etiologies ($p=0.012$). The total cost per day, however, was highest in the large vessel and cryptogenic "more than one cause" and "no cause" groups. Independent predictors of total cost included age (0.029, negative relationship), NIHSS (<0.001), LOS (<0.001), and stroke etiology (0.020), gender was not ($p=0.538$). Stroke etiology was an independent predictor of diagnostic ($p=0.008$), facilities ($p=0.013$), and rehab costs ($p=0.016$). **Conclusions:** Stroke etiology is an independent predictor of total cost of hospitalization for AIS. Large vessel strokes may absorb more health care dollars, and cryptogenic strokes may be associated with additional diagnostic testing. Since length of stay is a significant independent predictor of all domains of inpatient cost, inefficiencies in diagnostic evaluation of patients without a clear etiology at onset should be avoided.



	Total cost	Pharmacy cost	Imaging cost	Diagnostics cost	Rehab cost	Intervention cost	Facilities cost	Length of stay (median) range
AIS patients	1.00	1.00	1.00	1.00	1.00	1.00	1.00	5 (1-52)
Cardioaortic embolic	1.01	0.74	1.02	1.36	1.34	0.77	1.08	5 (1-45)
Large Vessel	1.58	1.58	1.38	1.54	1.29	4.63	1.45	6 (1-52)
Small Vessel	0.56	0.39	0.78	0.73	0.82	0.24	0.65	4 (1-34)
More than one cause	1.31	0.59	0.69	1.40	0.94	0.60	1.78	4 (4-5)
No cause identified	0.91	1.59	0.81	0.76	0.72	0.77	0.62	4 (1-40)
Other Causes	1.44	1.62	1.55	1.60	1.97	5.63	1.02	5.5 (4-24)

Demonstrates the total cost and subtotal costs as a factor of the median cost of all patients with AIS.

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W P326

Influence Of Chads2 Score In The Severity And Prognosis Of Ischemic Strokes Due To Atrial Fibrillation

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Objectives. To determine the prognostic value of CHADS2 score in first-ever ischemic stroke (IS) due to atrial fibrillation (AF). **Methods:** We analyzed 372 consecutive patients with IS without previous disability (mRS>2) and known AF admitted between 1995-2009. Variables studied were: CHAD2 score (0 to 4), prevalence of vascular risk factors, congestive heart failure (CHF), ischemic heart disease (IHD), peripheral arterial disease, concomitant intra or extracranial stenosis ≥50%, antithrombotic treatment, stroke severity according NIH stroke scale and 90-day poor outcome (mRS 3-6). Association between CHAD2 score and poor outcome was assessed using logistic regression models adjusted for variables tested in univariate analysis and P<0.1. **Results:** 75.3% of patients had CHAD2≥2 and 28.3% were using oral anticoagulants (only 33 % had INR>2). Increasing CHAD2 score was associated with higher stroke severity and worse 90-day outcome. Age, female gender, stroke severity, CHF, current smoking and IHD were associated with poor outcome in univariate analysis. Stroke severity [OR=1.26 (95%CI: 1.20-1.33), P<0.001] and CHADS2 score [OR=1.56 (95%CI: 1.16-2.09), p=0.003] were independently associated with poor outcome. After removing stroke severity from the model, CHADS2 score [OR=1.46 (95%CI: 1.15-1.85), p=0.002], male sex [OR=0.52 (95%CI: 0.32-0.85), p=0.009], previous anticoagulation with INR >2 [OR=0.33 (95%CI: 0.16-0.69), p=0.003] and IHD [OR=2.35 (95%CI: 1.24-4.44), p=0.009], were the variables associated with poor outcome. **Conclusions:** CHADS2 score is a strong predictor of poor outcome independent of stroke severity. Anticoagulation with INR>2 is associated with less severe strokes and better outcome.

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W P327

Guideline Discordant Periprocedural Interruptions in Warfarin Therapy are Frequent among Patients with Atrial Fibrillation

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Background and Purpose: Periprocedural interruptions in warfarin therapy increase stroke risk in atrial fibrillation patients, and are not indicated for all procedures. Current guidelines recommend continued warfarin therapy in patients undergoing colonoscopy, cataract removal, dental and dermatologic procedures. We sought to determine the indications for and frequency with which patients on warfarin for atrial fibrillation are requested to interrupt their therapy temporarily for a medical or dental procedure. **Methods:** An anonymous postal survey was sent in October and November of 2009 to all patients followed for over one year by the University of Michigan Anticoagulation service (n=2,133). The survey queried demographics, vascular risk factors, and indications for taking warfarin. Patients were also asked how many times in the prior 12 months they were requested to interrupt warfarin therapy for a medical or dental procedure or test, and the specific indication for the requested interruption in warfarin therapy. Descriptive statistics were used to assess patient demographics and presence of vascular risk factors (yes vs. no and missing). The frequency of at least one request for interruption in warfarin therapy was calculated overall and for each procedure. **Results:** Of the 1,686 respondents (79% response rate), 966 (57%) who used warfarin for atrial fibrillation were available for analysis. Their mean age was 74 years (sd=11 years). The majority were male (62%) and Caucasian (96%). Seventy percent reported a history of hypertension and 54% reported heart disease. There were a total of 798 periprocedural requests to interrupt warfarin therapy among 947 respondents (median 1, IQR 0-1). At least one request to interrupt warfarin therapy in the prior year was experienced by 481 of the 947 (51%). Fifty percent of requests to interrupt warfarin were for indications not supported by guideline statements. Among all requests for interruption of warfarin therapy, those for dental procedures (a combination of dental cleaning and other dental procedures) were the most common 25% (n=210), followed by surgery 19% (n=158), and colonoscopy 18% (n=153). **Conclusion:** Despite the high risk of stroke in patients with atrial fibrillation and well known benefit of anticoagulation, interruptions in warfarin therapy are frequent and often discordant with current guidelines. As a result, patients are left vulnerable to needless risk of stroke and other thrombotic events. Educational interventions targeting the patient, proceduralist, and anticoagulation manager focusing on guideline discordant periprocedural warfarin interruptions could have significant public health impact.

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W P328

How Well do Recent Studies of AF Patients Reflect the Real World AF Patient?

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As data from randomized clinical trials (RCTs) are applied in clinical practice settings, understanding how the patients with AF enrolled in recent large RCTs compare to patients with AF in the real world is important. A number of risk scores are available for risk stratification in AF. Gage's published $CHADS_2$ score is well established and used in treatment guidelines. Our objective was to compare the patients in recent AF trials to patients with AF in the real world, based on the $CHADS_2$ risk score along with other baseline characteristics. **Methods:** Patients with chronic non-valvular AF were identified in 4 data sources from diverse settings: electronic medical record (EMR) data from Christiana Care (CCHS) and Regenstrief Institute (RMRS), claims from United Health Care (UHC) in the US; and clinical data from GPRD from the UK. These cohorts with AF were then compared to those in recent studies of novel oral anti-coagulants (RE-LY and ROCKET AF) based upon overall $CHADS_2$ score, $CHADS_2$components and other baseline characteristics. **Results:** See Table. All cohorts had similar distribution with respect to age and gender. UHC and RMRS have a slightly younger population, and CCHS has almost 50% females. The RCTs had fewer patients with CHADS2 $\leqslant$ 1 than did the observational cohorts. ROCKET AF was almost entirely composed of patients with CHADS2 $\geq$ 3. The differences observed between CHADS2 in real world and clinical trial populations may relate to requirements for additional risk factors in inclusion criteria for the trials. Observational studies may include incident or prevalent AFpatients, while RCTs tend to enroll prevalent patients. **Conclusions:** Demographic characteristics are similar across these data sources; females may be under-represented in the RCTs. The distribution of $CHADS_2$ scores is different between the real world populations and the RCTs. The RCTs enrolled fewer CHADS 0-1 patients and more CHADS 3-6 patients. The proportion of patients with $CHADS_2$ score $\geq$ 3 was very high in ROCKET-AF and in RE-LY was higher than in 3 of the 4 observational cohorts. Observational studies tend to include a more heterogeneous population reflective of those ultimately prescribed a medication. The data suggest that the differences in the study populations should be taken into consideration when applying RCT results to clinical practice.

	Randomized Trials		Real World Observational Cohorts			
Therapy	RE-LY	ROCKET-AF	UHC	CCHS	RRMS	GPRD
Patients (N)	18,113	14,269	111,278	1000	3329	74,095
Age	71.5	73.1	66.9	70.1	63.7	73.8
Female %	36	40	38.8	50.3	44.1	48.5
$CHADS_2$ Score 0-1	31.9	0.4	54.2	60	43	57
$CHADS_2$ Score 2	35.6	13.3	23.9	23	24	27
$CHADS_2$ Score $\geq$ 3	32.4	86.3	21.9	17	33	16

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W P329

High Rate of Enrollment of Black Subjects in Genetic Substudy of Intracerebral Hemorrhage Natural History Study

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Background: Historically, researchers have found that black patients have been significantly less likely than whites to participate in clinical research, particularly research involving genetic studies. Sociological factors such as distrust of the medical community, suspicion of genetic testing, and dislike of the general research process have all contributed to low recruitment rates of minorities including blacks. The purpose of this study is to examine recruitment rates by race in the overall DECIPHER intracerebral hemorrhage natural history project and in the genetic substudy. **Methods:** For all patients eligible for the DECIPHER study, we systematically record reasons for refusal for both the overall study and, if applicable, for the genetic substudy. Variables include whether patient or family was being approached and reasons for refusal. All recruiting coordinators for the DECIPHER project receive training in cultural competence and all materials have been culturally tailored. **Results:** Of 234 eligible patients, 135 (58%) agreed to participate in the DECIPHER project (62% of blacks vs. 49% of non-blacks, p=0.049). Of the 135 who consented, 44% were female, 72% were black, and 119 (88%) agreed to participate in the genetic substudy (87% of the black population vs. 91% of whites enrolled, p=0.76). The three most common reasons for refusal for the overall study were 1) distrust of research, 2) family refusal due to patient's poor prognosis, and 3) claustrophobia / dislike of MRI. The two most common reasons for refusal for the genetic substudy were 1) family refusal due to patient's poor prognosis (25%) and 2) family refusal due to discomfort with proxy consent process (25%). **Conclusions:** Despite previous studies showing lower rates of recruitment of blacks in clinical research, in our DECIPHER project, there was a statistically significant greater enrollment of blacks vs. non-blacks. For the genetic substudy, rates of recruitment were high for both populations and not significantly different. Coordinator training in cultural competence along with trial materials specifically designed to increase trust likely contributed in the overall success of recruitment of the black subjects in the DECIPHER project. Subjects willing to participate in clinical research in general appear to be more willing to participate in genetic research compared to the overall population. Supported by NIH NINDS grant U54 NS057405 (PI: Kidwell, CS).

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W P330

UCLA ICH Grading System is a Better Prognostic Tool for Spontaneous Intracerebral Hemorrhage When Assessed at 24 hours After the Event

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Background and Purpose: Spontaneous intracerebral hemorrhage (ICH) comprises approximately a fifth of all strokes. UCLA validated a "simple, reliable grading scale" for prognostication of ICH patients. The grading system consists of five components including Glascow Coma Scale (GCS), patient's age, whether or not there is infratentorial involvement, and the presence or absence of intraventricular hemorrhage (IVH) at admission. About one-third of the patients experience growth of their hematoma in the first 24 hours. Our goal was to investigate if the ICH score (ICHs) at 24-hours is more accurate and reliable as a predictor of clinical outcome. **Methods:** - We conducted a retrospective analysis of prospectively collected data of consecutive patients who suffered a spontaneous ICH between 2006 and 2009. We excluded those who did not have a CT scan within the 16-32 hour window. Along with their medical records, all variables of ICHs at admission and 16-32 hours (mean 24 hours) were measured. We used the manual outlining method to measure hematoma on each slice of their head CT to calculate the total hematoma volume. Clinical outcomes were assessed using discharge modified Rankin Scale (dmRS). The data was compiled and was analyzed for strength of associations using SPSS software version 14.0. **Results:** - Of the 260 patients, 78 met the criteria (Mean age= 69.21,SD+/- 14.08; Male= 44, 56%). Mean length of stay was 9.48 (SD+/- 11.84) and mean dmRS was 4.21 (SD+/- 1.55). Refer to table for association values. **Conclusion:** Based on our data ICHs at 24-hours after admission had the strongest positive correlation with dmRS amongst other variables such as admission ICHs, 24-hours hematoma volumes or GCS. This study suggest that assessing the ICHs at 24-hours may be a better prognostic indicator than the initial ICHs. A larger prospective study is warranted to further examine the relationship.

	Association with mRS		
	r	p	N
Hematoma Volume at Admission	.399	<.001	73
Hematoma Volume at 24 hours	.383	.001	73
GCS at admission	-.394	.001	73
GCS at 24 hours	-.425	<.001	71
ICH score at admission	.428	<.001	73
ICH score at 24 hours	.458	<.001	73

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W P332

Is the Risk of Fatal Brain Edema Increased with Thrombolysis Among Patients with Acute Ischemic Stroke?

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Background: Anecdotal reports suggest that thrombolysis may increase the risk of fatal brain edema. The brain edema following thrombolysis may occur secondary to reperfusion or neurotoxic effect of thrombolytic agents. The aim of this study is to assess the association

between brain edema and intra-arterial (IA) or intravenous (IV) thrombolysis. **Methods:** A review of consecutive patients admitted with acute ischemic stroke to two academic institutions from 2006 to 2010 was performed. The study sample was dichotomized based on occurrence of in-hospital mortality and occurrence of fatal brain edema. Univariate analysis was conducted to compare these subgroups defined by occurrence of fatal edema or in-hospital mortality. A multivariate analysis was performed to adjust for age, sex and initial stroke severity as measured by National Institute of Health Stroke Scale (NIHSS) score. **Results:** There were 548 patients who suffered from ischemic stroke (mean age 66±16 years; 46% were women). Mean admission NIHSS score was 7±6 and > 10 in 112 patients (22%). 128 patients (23%) were treated with thrombolysis (IV, n=65 [51%]; IA, n=30 [23%]; IV+IA, n=33 [26%]). In-hospital mortality was documented in 39 patients (7%). Of those, 27 patients (5%) died from brain edema. Other causes of death included cardiac arrest, respiratory failure, status epilepticus, and withdrawal of care. In univariate analysis, initial NIHSS score had the strongest association with both in-hospital mortality (median NIHSS 14 vs 4; P<0.0001) and fatal brain edema (median NIHSS 16 vs 4; P<0.0001). Age was only associated with in-hospital mortality (median age 71 vs 66; p=0.05) but not with fatal brain edema (p=0.5). Thrombolysis (any type) was not associated with in-hospital mortality (p=0.7) or fatal brain edema (p=0.5). There was no association between the type of IA thrombolysis (pharmacologic and/or mechanical) and the outcome variables. In multivariate analysis, only severe NIHSS (score >10) was associated with fatal brain edema (odds ratio [OR] 11.9, 95% confidence interval [CI] 4.8-32.9; P<0.0001) while age, IV, IA, and any thrombolysis were not associated with fatal brain edema. **Conclusion:** Stroke severity but not thrombolysis (IV and/or IA) is associated with fatal brain edema after ischemic stroke.

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W P333

Older Patients are at Higher Risk for Blood-Brain Barrier Disruption Following Treatment with IV-tPA, Independent of Impaired Kidney Function

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Background: Disruption of the blood-brain barrier (BBB) can be characterized by the imaging marker Hyperintense Acute Reperfusion Marker (HARM). This marker has been defined as delayed gadolinium enhancement of the cerebrospinal fluid (CSF) space on fluid-attenuated inversion recovery (FLAIR) MRI. HARM has been associated with risk of hemorrhagic transformation, thrombolytic therapy, and worse clinical outcome. HARM has also been associated with increased age, but it is unknown whether this association is confounded by impaired gadolinium clearance due to age-related decreases in renal function. **Methods:** Patients (n=187) were selected from the LESION project of the NINDS Stroke Branch Registry, if they had the following features: treatment with IV-tPA, gadolinium enhanced MRI at baseline, and FLAIR MRI at 2 hr or 24 hr post tPA. HARM was defined as enhancement of sulcal spaces in 10 or more FLAIR slices. The estimated glomerular filtration rate (eGFR) was calculated by the Chronic Kidney Disease Epidemiology Collaboration equation (CKD-EPI) using admission plasma creatinine values. The association between baseline renal function and HARM was examined through stepwise conditional logistical regression. Age, race, sex, NIHSS at presentation, hypertension history, diabetes history, plasma creatinine, eGFR, number of gadolinium doses and MRI field strength were entered into the model as potential covariates of HARM. **Results:** HARM was independently associated with age (p = 0.003; odds ratio, 1.047; confidence interval, 1.016-1.079), after adjustment for eGRF, number of gadolinium doses, and MRI field strength. The other factors were not significant predictors of HARM. **Conclusion:** Age is an independent predictor of BBB disruption seen as HARM even after adjusting for the effects of the eGFR. These findings suggest that older patients are at higher risk for BBB disruption following treatment with IV-tPA, independent of their kidney function.

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W P334

Gender Moderation in the Association between Mitochondrial Uncoupling Protein Genetic Variants and Carotid Plaque

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Background and Objective: Sirtuins (SIRTs) and mitochondrial uncoupling proteins (UCPs) have been implicated in cardiovascular diseases through controlling the production of reactive oxygen species. This study sought to investigate the association of SIRT and UCP genetic variants with the presence of carotid plaque and the potential gender moderation in their association. **Methods:** A total of 1,018 stroke-free subjects (61% female, mean age=70±9 yrs) who underwent ultrasound measurement and genotyping were sampled from a multi-ethnic cohort of northern Manhattan. Multiple logistic regression were performed to investigate the association of genetic variants (SNPs and haplotypes) in SIRT and UCP genes (*SIRT1-7, UCP1-5*) with the presence of carotid plaque, after controlling for the significant socio-demographic and vascular covariates (age, gender, smoking, waist-hip ratio, diabetes and hypertension) as well as population stratification identified via principal component approach. SNP-by-sex interaction was examined and stratified analysis was followed if the interaction term in the model yielded an effect of p < 0.1. Multiple testing was adjusted with permutation. **Results:** After adjustment for covariates, *UCP5* SNP rs5977238 showed the strongest association with carotid plaque with an additive effect of OR=0.5 (95%CI=0.3-0.7, p=0.0008, permutation adjusted p=0.03) and 4 other *UCP5* SNPs were associated with plaque presence with a nominal P<0.05. A *UCP5* haplotype (TTTCACATT) of 9 SNPs were also significantly associated with decreased risk for plaque (OR=0.5, p=0.0002, permutation adjusted p=0.01). Another significant association was found for *SIRT6* SNP rs107251 (OR=1.7, 95%CI=1.2-2.4, p=0.001). Interaction analyses revealed a gender-specific effect for *UCP3* SNPs (rs1685356, p=0.007; rs1726745, p=0.01) and *UCP1* SNPs (rs7693034, p=0.06; rs6818140, p=0.06). Specifically, a significant increased risk was found for A-carrier women at rs1685356 or rs1726745 (OR=1.4, 95%CI=1.1-1.8, p=0.01) but not for men (p ≥ 0.13). In contrast, a significant decreased risk was detected for C-carrier women at rs7693034 or rs6818140 (OR=0.7, 95%CI=0.5-0.9, p ≤ 0.01) but not for men (p≥ 0.61). **Conclusion:** Our findings suggest that genetic variations in *UCP1,3,5* and *SIRT6* may be associated with subclinical atherosclerosis. Gender difference in the effect of *UCP1,3* variants may indicate a gene-environmental interaction. Further fine mapping studies in larger populations are needed to validate the observed association and evaluate the gene-environmental interaction.

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W P336

Lobar Tissue Loss in Cerebral Amyloid Angiopathy

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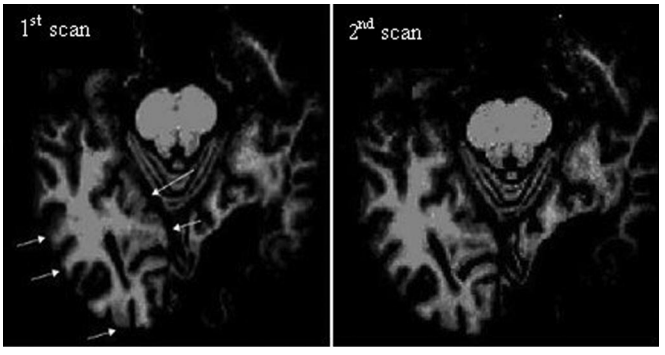
Background: Brain atrophy occurs with aging, particularly in association with neurodegenerative processes. Recent studies suggest that cerebrovascular disease may also contribute to brain tissue loss. We investigated the possibility that advanced cerebrovascular β-amyloid deposition (cerebral amyloid angiopathy, CAA) is associated with cortical tissue loss, particularly in the occipital brain regions most heavily affected by CAA. **Methods:** 24 nondemented CAA subjects (mean age ± SD 73.4 ± 9.9, 16 men/8 women) and 20 nondemented controls (68.7± 12.4, 12 men/8 women) were scanned on a 1.5 T (Seimens) scanner, using structural Multiecho MPRAGE (MEMPRAGE, 1 mm isotropic) scan, acquired twice and averaged. Images were processed and analyzed for volume in specified cortical (grey plus white matter, averaged across the two hemispheres) regions of interest (ROI) using FreeSurfer (www.nmr.mhg.harvard.edu). Damage related to prior hemorrhagic strokes was patched; regions patched more than 12% were excluded. Follow-up structural scans were collected for 13 of the CAA subjects after a mean stroke-free interval of 14.6±4.0 months. Serial scan processing was performed via a parcellation template based on both timepoints to minimize within-subject variation in parcellation. **Results:** In cross-sectional comparison, the CAA subjects showed nonsignificant reductions relative to the controls. In longitudinal analysis, we observed significant tissue loss in occipital lobe over the inter-scan interval (mean change between scans -1.8%, [95% confidence interval -3.4 to -0.2%], p=0.03), with greatest tissue loss in the lingual ROI (-3.4% [-5.3 to -1.4%], p=0.003). An example is shown in the Figure, with arrows pointing to ROIs (lateral occipital, lingual, cuneus) with evident atrophy on the follow-up scan. Parietal (-0.4%), frontal (+0.4%), and temporal (-0.2%) lobes showed no detectable tissue loss (all p>0.5), suggesting that atrophy occurred preferentially in the occipital regions favored by CAA. **Conclusions:** These results indicate that advanced CAA is associated with tissue loss in the occipital lobe over a relatively short period of longitudinal follow-up. Cortical atrophy may thus be another manifestation of this small vessel disease of the brain.



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W P337

Serum SDF1-A Levels Significantly Increase Following Stroke And Are Associated With Increased Hematopoetic Stem Cell Mobilization

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Background: Hematopoietic Stem Cells (HSC)/ Hematopoietic Progenitor Cells (HPC) have recently been demonstrated to correlate with improved neurological function following stroke, suggesting a potentially critical role for HSC/HPC's in limiting stroke injury and/or facilitating stroke recovery. HSC/HPC's are known to mobilize to the peripheral circulation from bone

marrow in response to stroke. Stromal Derived Growth Factor 1-Alpha (SDF1-A) along with its receptor CXCR4 is a potent chemo attractant released by areas of injury. SDF1-A has been shown to mobilize HSC/HPC from the bone marrow to the blood and lead to 'homing' of the cells to an area of injury. **Methods:** Animals underwent a murine intraluminal filament model of focal cerebral ischemia. Animals were divided into 4 groups (n=5 each): 4hrs sham surgery, 4hrs post reperfusion, 24hrs sham surgery, and 24hrs post reperfusion. Neurological deficit score was recorded prior to euthanasia and serum SDF1-A was assessed in all groups. HSC/HPC were enriched using nanoparticles tagged with LIN negative and SCA1 positive markers and counted on a hemacytometer. **Results:** Serum SDF1-A levels were elevated at 4hrs and 24 hours compared to sham controls (107±3.8% and 137±11% versus 100±0.04% and 100±0.06%, respectively; 4hrs vs sham: P=NS, 24hrs vs sham: P<0.05). Bone marrow showed an increased production of HSC/HPC at 4 hrs (106±26%) and significantly higher at 24 hrs (272±35%). Mobilization of the HSC/HPC was slightly higher at 4 hrs (167±26%) and significantly higher at 24 hrs (606±91%; P<0.05). Neurological deficit score at 4hrs and 24hrs post reperfusion were 1.846±0.21 and 2.04±0.178, respectively. **Conclusions:** Serum SDF1-A levels significantly increased following cerebral ischemia, leading to increased mobilization of HSC/HPC from the bone marrow to the blood. These data suggests that SDF1-A mobilization of HSC/HPC in response to cerebral ischemia may be a relevant pathway for cerebral injury repair following stroke.

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W P338

Therapeutic Modulation of Cerebral Microbleeds in Cerebral Amyloid Angiopathy

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Cerebral amyloid angiopathy (CAA) is a common cause of intracerebral hemorrhage (ICH) in the elderly and is associated with MRI evidence of cerebral microbleeds. CAA may also coexist with ischemic stroke. Presence of CAA produces increased microbleeds and vasogenic edema after active (AN1792) and passive (bapineuzumab AAB-001) anti-amyloid-beta (Aβ) immunotherapy. We investigated this phenomenon using old amyloid-precursor-protein-transgenic (APP-Tg) mice, a model which is characterized in part by CAA and cerebral microbleeds. In this model, anti-Aβ immunotherapy dramatically exacerbates CAA and microbleeds. We therefore used 20 month old APP-Tg2576 mice to investigate the effect of ischemic stroke prevention agent dipyridamole (effective in European Stroke Prevention Study 2 as monotherapy in its extended release formulation) on the anti-Aβ immunotherapy-induced cerebrovascular lesions. Old APP-Tg2576 mice with extensive CAA were passively immunized by a weekly dose of 10mg/kg (i.p.) per mouse using anti-Aβ40 C-terminal specific monoclonal antibody for 9 weeks. Mice were fed a dipyridamole diet that included high-fat chow given *ad libitum*. Passive immunization of APP-Tg2576 mice reduced amyloid plaque load and microglial activation, but also produced 3-fold increase in cerebral microbleeds. Dipyridamole use had no effect on the number of microbleeds, had minimal effect on cerebral amyloid deposition, and was associated with no observable adverse events in immunotherapy-treated mice. Thus, immunotherapy produced marked increase in cerebral microbleeds in this mouse model of CAA, and treatment with dipyridamole did not worsen this phenomenon. These data suggest that dipyridamole, used clinically to prevent ischemic stroke, may have a therapeutic role in patients requiring ischemic stroke prevention in the presence of CAA and cerebral microbleeds.

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W P339

The Novel TrkB Agonist, 7,8-Dihydroxyflavone Enhances Stem Cell Mobilization After Stroke

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Background: Increasing levels of circulating Hematopoietic Stem Cells (HSC)/Hematopoietic Progenitor Cells (HPC), bone marrow derived mononuclear cells that promote repair in areas of injury, have been demonstrated to correlate with improved neurological function following stroke, suggesting a potentially critical role for HSC/HPC's in limiting stroke injury and/or facilitating stroke recovery. Flavonoids, found in plants and fruit, exert anti-oxidative effects. Recent studies have demonstrated that 7,8 Dihydroxyflavone (DHF) is a potent TrkB agonist mimicking Brain Derived Neurotropic Factor, thus making it a powerful potential tool for treating neurological disorders. Stromal Derived Growth Factor 1-Alpha (SDF1-A) along with its receptor CXCR4 is a potent chemo attractant released by areas of injury. SDF1-A has been shown to mobilize HSC/HPC from the bone marrow to the blood and lead to 'homing' of the cells to an area of injury. We investigated the effect of DHF on HSC/HPC function following cerebral ischemia. **Methods:** Ischemic damage was induced in adult male Long Evans hooded rats (350-400g) with a peri-MCA injection of the vasoconstriction peptide ET-1. The rats were sacrificed at 24 hours post surgery and their bone marrow and blood HSC/HPC enriched using nanoparticles tagged with LIN negative and CD90 markers. **Results:** Stroked animals showed an increase in bone marrow production of HSC/HPC versus control animals (31.9±7 versus 2±0.5, P<0.05). The mobilization of the HSC/HPC from the bone marrow to the blood was also significantly higher in the stroked animals versus control animals (43±19 versus 3.6±0.3, P<0.05). Following stroke, DHF pre-treated HSC/HPC's demonstrated significantly improved migration along an SDF-1 gradient compared to controls (129±1.0 versus 108±1.15, P<0.05), despite the fact that DHF alone provided no independent migratory stimulus. **Conclusions:** The results suggest that DHF may be a viable compound to facilitate HSC/HPC migration post-stroke.

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W P340

The Differential Genetic Expression in Unstable and Stable Carotid Plaques may be a Predictor of Stroke Risk

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International Stroke Conference 2011 Objective: Stroke is the third leading cause of death in the United States. As the majority of strokes result from plaque rupture, elucidating the pathways that contribute to plaque vulnerability is critical for therapeutic intervention. This study tested the hypothesis that immune complex stimulation of macrophages induces a pattern of gene expression present in vulnerable human carotid plaques and that the overall gene expression of vulnerable and stable carotid plaques, even within the same plaque, are different and will reveal novel differences in cellular composition. **Study Design:** *a. Tissue analysis:* Specimens were analyzed using trichrome staining to classify samples as histologically vulnerable or stable. *b. Assessment of gene expression:* Quantitative RT-PCR (Q-PCR) was used to compare human femoral plaques (stable) with proximal and distal regions of carotid plaques for 22 genes implicated in plaque rupture. Additionally, four samples each of stable and vulnerable carotid plaques were compared using gene array analysis and results were validated using Q-PCR. *c. Recapitulation of unstable gene expression pattern in vitro:* The effect of oxidized LDL, C-reactive protein, TNF-á, or immune complexes on gene expression in human macrophages was compared to that present in unstable carotid plaques. **Results:** Genes expression of stable carotid and femoral plaques were similar; paired comparison between vulnerable and stable regions of carotid plaques showed significant differences in 16 genes that impact plaque stability: 1) matrix metalloproteinases (higher in vulnerable), 2) matrix metalloproteinase inhibitors (lower in vulnerable) and activators (higher in vulnerable), 3) activating Fcã receptors (higher in vulnerable) and 4) Fcã receptor signaling molecules (higher in vulnerable). We investigated the effect of Fc receptor cross-linking on the expression of plaque instability genes *in vitro*. Ligation of FcãR with immune complexes, but not oxidized LDL, C-reactive protein, or TNF-á, induced a gene expression profile similar to vulnerable plaques. Additionally, human genome array analysis and qPCR revealed novel genes differentially expressed between vulnerable and stable plaques, some of which are linked through pathways and proteins products that my impact stability. An example is coagulation cascade. Finding other biochemical links between these genes may help find proteins that can be measured in the bloodstream and be used as a predictor of stroke.

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W P341

In Critical Care Setting Brain Natriuretic Peptide is an Unreliable Marker for Assessing Congestive Heart Failure in Acute Stroke Patients

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Background and Purpose: Brain Natriuretic Peptide (BNP) is known to be released from cardiac tissue and to a lesser degree from the hypothalamus. BNP is known to correlate with the presence and severity of congestive heart failure (CHF). In the general population screening test for CHF using BNP level of 50 pg/mL as a cut-off has a sensitivity (SN) and specificity (SP) of 97% and 67%, respectively. While the SN and SP for a cut-off of 100 pg/mL are 90% and 76%, respectively. An elevation of BNP has been reported to occur during acute stroke. Our study aimed at determining the sensitivity and specificity of BNP as a test for CHF in patients with acute stroke. **Methods:** A retrospective analysis of prospectively collected data on patients who suffered an acute stroke between 2005-2009 was performed. Patients who presented with transient ischemic attack or no value for BNP were excluded. The patients were then subdivided into two groups, with CHF and without CHF based on echocardiogram. Statistical analysis was completed to determine the mean BNP values, and an independent samples t-test was used to establish equality of means. The data was then analyzed to determine SN, SP, positive predictive value (PPV), and negative predictive value (NPV) for CHF with BNP >50 pg/mL (Test A), >100 pg/mL (Test B), >300 pg/mL (Test C) and > 500 pg/mL (Test D). **Results:** Of 2958 patients 221 matched the study criteria. The mean BNP for stroke patients with CHF (N=109, 21 ICH patients and 88 ischemic) was 1975.8 pg/mL, while the mean BNP for stroke patients without CHF (N=112, 22 ICH patients and 90 ischemic) was 1075.9 pg/mL (p= .009 for the mean difference). For Test A the SN=94%, SP=15%, PPV=53%, NPV=74%. For Test B the SN=83%, SP=31%, PPV=54%, NPV=65%. For Test C the SN=61%, SP=45%, PPV=52%, NPV=60%. For Test D the SN=49%, SP=68%, PPV=60%, NPV=58%. A 10-fold increase of BNP is required to achieve a 68% specificity for CHF in stroke patients as compared to the general population (>500 pg/mL vs. > 50 pg/mL). **Conclusion:** Although BNP has been shown to be a valuable marker for diagnosing CHF and predicting patient outcomes, it is not a very sensitive or specific marker for assessing CHF in patients who have suffered ischemic or hemorrhagic strokes.

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W P342

Effect of PFO Physiology on Circulatory Proteomic Profile in Ischemic Stroke Patients

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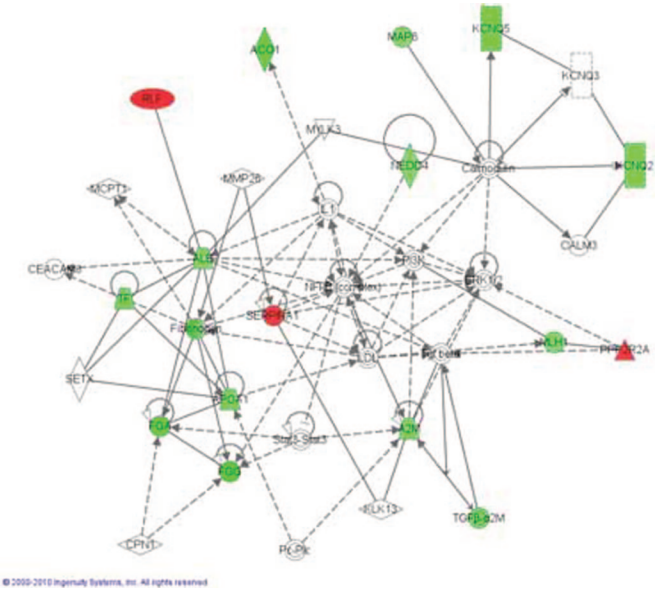
Patent foramen ovale (PFO) is an independent stroke risk factor associated with more than 150,000 strokes per year. Clinical trials to investigate treatment options are ongoing, but controversies regarding PFO remain unresolved. Traditionally it is thought that PFOs are implicated in paradoxical embolism by allowing venous clots to travel directly to the brain. However, this simple explanation is likely incomplete, as only a small portion (10-17%) of PFO stroke patients have known hypercoagulable states. A better understanding is needed of the molecular landscape of this complex multi-organ disease involving the brain, heart and circulation. We conduct discovery proteome profiling of plasma markers in PFO patients undergoing clinical endovascular PFO closure, which is a good bedside model to study the direct effects of an open vs closed PFO on circulatory protein signaling. **Methods:** 53 PFO non-migraineur stroke patients were recruited per IRB-approved protocol, and plasma was collected at baseline, pre and post PFO closure in the left and right atrium. Samples were processed and data generated on Orbitrap XL MS. Intra-patient pre- vs post-closure proteomic profiles were compared, with each patient serving as their own control to reduce potential confounders. Data were analyzed by SIEVE and Ingenuity Pathways. **Results:** After successful PFO closure, the plasma protein profile changes dramatically. Ingenuity pathway analysis revealed a decrease of coagulation markers such as tissue factor (TF) and fibrinogen, synthesis of fibrinogen's various alpha (FGA) and gamma (FGG) chains, and differential expression of protease inhibitors such as alpha 2 macroglobulin (A2M) and SERPINA 1, important in vascular disease. Cell differentiation factors such as RLF (relaxin like factor or insulin-IGF relaxin factor), and factors that exert negative control of cell growth, such as PPP2R2A, are upregulated - perhaps suggesting a pattern of repair focused on cell differentiation rather than division. **Conclusion:** These findings demonstrate the feasibility and strength of direct quantitative proteomic exploration in human plasma, using a systems approach incorporating anatomical and temporal dimensions, in a bedside model with each patient as their own control to limit confounding medications and co-morbidities. As an initial step in understanding the molecular landscape of PFO-related circulatory physiology, our results highlight relevant changes in coagulation, cell-signaling and differentiation induced by PFO repair. However, these data are hypothesis generating and further studies are needed.



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W P343

Elevated High-sensitivity C-reactive Protein in Acute Stage Cerebral Infarction Predicts Progression of Carotid Intima-media Thickness

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Objectives: Carotid artery intima-media thickness (IMT) is known as an index of arteriosclerosis and a risk of cardiovascular diseases. Some inflammatory markers are reportedly associated with atherogenesis. However, the association between the increased inflammatory markers in the acute stage stroke and future risk of atherosclerosis is not yet clarified. We tried to elucidate the relationship between the inflammation in acute stage ischemic stroke and progression of arteriosclerosis. **Methods:** We examined consecutive 107 acute ischemic stroke patients who were admitted within 72 hours from the onset. Their mean age was 71.6 years old, and 70 patients were male. Carotid IMT was measured by B-mode carotid ultrasound on both sides. The maximum IMT of the common carotid artery was defined as CIMT. We concurrently monitored atherogenic parameters including high-sensitivity C-reactive protein (hsCRP), IL-6, and oxidant LDL (oxLDL), and atherosclerotic markers including the ratio of LDL-cholesterol/HDL-cholesterol (LDL/HDL ratio), tryglyceride (TG), blood sugar, estimated GFR, and uric acids. Those parameters were compared according to the first, second and third tertiles of CIMT. Neurological severity was evaluated by NIHSS upon admission (a-NIHSS) and at discharge (d-NIHSS). According to the stroke etiology, the subjects were classified into 3 groups; atherothrombotic brain infarctions (ATBI), Lacunar infarctions (LI) and Cardiogenic embolisms (CE). To evaluate the progression of atherosclerosis, the CIMT measurements were repeated 6 months after the onset, and the difference in CIMT between the baseline and follow-up studies was defined as Delta-CIMT. We investigated the relationship between CIMT and those risk factors. **Results:** Forty-four patients were diagnosed as ATBI, 29 as LI and 34 as CE. The mean CIMT was significantly greater in ATBI group than in other 2 groups, and the mean Delta-CIMT was also significantly greater in ATBI group than in LI group ($p=0.001$). The oxLDL ($p=0.005$), LDL/HDL ratio ($p=0.034$) and hsCRP ($p=0.033$) were significantly greatest, and the estimated GFR ($p=0.015$) was significantly smallest in the third tertile of CIMT. IL-6 was significantly associated with a-NIHSS ($p=0.006$) and tended to correlate with CIMT. The hsCRP was positively correlated with CIMT in ATBI and LI groups ($p=0.033$) as well as with Delta-CIMT ($p=0.014$). The baseline IMT and TG were also significantly associated with Delta-CIMT. **Conclusions:** These results suggest that, in acute stage ATBI patients, some serum lipid and inflammatory markers are associated not only with carotid atherosclerosis as but also with its future progression. The measurements of serum lipid parameters and hsCRP will be useful in the assessment of the future risk of stroke patients.

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W P344

Tissue Plasminogen Activator Impairs Hematopoietic Stem Cell Function, Thus Potentially Limiting Stroke Recovery

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Background: Intravenous Tissue Plasminogen Activator (tPA) is the only FDA approved pharmacological recanalization therapy for stroke, however tPA has been associated with deleterious effects on the blood brain barrier in experimental models. A potential contributor to vascular integrity and/or repair following stroke are Hematopoietic Stem Cells (HSCs)/ Hematopoietic Progenitor Cells (HPCs), circulating bone marrow derived mononuclear cells that promote repair in areas of injury. HSC/HPC's have recently been shown to mobilize to the peripheral circulation from bone marrow in response to stroke. Furthermore, increasing levels of circulating HSC/HPCs have been demonstrated to correlate with improved neurological function following stroke, suggesting a potentially critical role for HSC/HPC's in limiting stroke injury and/or facilitating stroke recovery. Stromal Derived Growth Factor 1-Alpha (SDF1-A) along with its receptor CXCR4 is a potent chemo attractant released by areas of injury. SDF1-A has been shown to mobilize HSC/HPC from the bone marrow to the blood and lead to 'homing' of the cells to an area of injury. We hypothesized that tPA inhibits HSC/HPC's function, potentially limiting tPA's beneficial effects in acute stroke therapy. **Methods:** Animals ($n=10$) were euthanized 24 hours post ischemia/reperfusion following a murine intraluminal filament model. Infarction was confirmed using TTC staining of 2 mm sections of the brain. HSC/HPC were harvested from bone marrow and blood using LIN negative and SCA1 Positive labeled nanoparticles. The harvested cells were counted using a hemacytometer; the HSC/HPC were then either left untreated or treated with 10nM TPA and migrated towards SDF1-A in a Boyden Chamber. The level of the SDF1-A receptor (CXCR4) was also assessed by real time PCR of the untreated and tPA treated HSC/HPC. Experiments, and their analysis, were performed in a blinded manner. **Results:** Mean infarct volume was $43\pm10\%$. Pre-treatment with 10nM tPA reduced HSC/HPC migratory capability towards SDF1-A ($100\pm1.3\%$ versus $173\pm1.0\%$, $P<0.05$). Pre-treatment with 10nM tPA also reduced expression of CXCR4 from $100\pm7.9\%$ to $35.8\pm7.1\%$, $P<0.05$). **Conclusion:** These data indicate that exposure of HSC/HPC's to tPA abrogates their migratory response to SDF1-A. mRNA analysis of HSC/HPC cells following treatment with tPA demonstrates a down regulation of the CXCR4 receptor. These results suggest that tPA may reduce the ability of the HSC/HPC to home to ischemic brain following stroke and possibly interferes with repair mechanisms associated with HSC/HPC.

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W P345

Higher Coated-platelet Levels are Associated with Stroke Recurrence Following Non-lacunar Brain Infarction

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Background: Coated-platelets are a subset of platelets with high procoagulant potential observed upon dual agonist stimulation with collagen and thrombin. Coated-platelet levels are elevated in patients with non-lacunar ischemic stroke and decreased in patients with spontaneous intracerebral hemorrhage compared to controls. Because prior findings suggested that extremes in coated-platelet potential may be associated with either thrombotic or hemorrhagic events, a study was initiated to investigate a possible relationship between coated-platelet levels and stroke recurrence in patients with non-lacunar ischemic stroke. **Methods:** Coated-platelet levels were determined in 140 consecutive patients with a diagnosis of non-lacunar stroke based on TOAST criteria. The clinical diagnosis was established by a neurologist who was unaware of the patient's coated-platelet levels. All patients underwent initial brain CT scan followed by brain MRI studies, or repeat brain CT (if MRI was contraindicated) within 24 hours to confirm the presence of cerebral ischemia. The individuals performing the coated-platelet assay were not aware of the clinical diagnosis. Stroke recurrence data were obtained through stroke clinic visits, chart reviews or telephone interviews performed at 3, 6, 9 and 12 months following the initial infarct. **Results:** Among the 140 patients with initial non-lacunar stroke, follow-up data were available for 132 patients (94%). Cumulative incidence of recurrent stroke at 12 months was 14% (95% CI: 9-23%, 16 recurrences). Coated-platelet levels (mean$\pm$SD) in all stroke patients with follow-up were 40.6$\pm$13.7% (range 10.6-69.7%). Patients were separated into tertiles of coated-platelet levels (lowest 10.6-33.5%, middle 33.6-45.2% and highest 45.3-69.7%). The time to recurrent stroke differed significantly among the coated-platelet level tertiles (overall log-rank test, $p=0.0092$). Pair-wise comparisons (based on a Bonferroni-adjusted alpha level of 0.0167) suggested that the risk of recurrent stroke was higher in the highest and middle coated-platelet tertiles compared to the lowest tertile ($p=0.0037$ and $p=0.0018$, respectively), while the risk did not differ significantly between the middle and highest tertiles ($p=0.76$). Differences in risk were not explained by multiple potential confounding variables. **Conclusions:** Higher levels of coated-platelets are associated with stroke recurrence in patients with non-lacunar ischemic stroke. This work is supported by OCAST (Dr. Prodan) and AHA (Dr. Dale).

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W P346

Coated-platelet Levels are Elevated in Patients with Transient Ischemic Attack Compared to Controls

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Background: Coated-platelets are a subset of platelets with high procoagulant potential observed upon dual agonist stimulation with collagen and thrombin. While coated-platelet levels are elevated in cortical ischemic stroke, lower levels are present in patients with spontaneous intracerebral hemorrhage or with hemorrhagic transformation of ischemic stroke. Because the risk of subsequent ischemic stroke is increased in patients with transient ischemic attack (TIA), we undertook a study to investigate coated-platelet production in patients with TIA. **Methods:** Coated-platelet levels were determined in 60 patients with a diagnosis of TIA and 60 controls frequency-matched for gender and race and within the same age range as the patient population. The diagnosis of TIA was established by a board certified neurologist and was consistent with the most recent tissue-based definition of TIA: a transient episode of neurological dysfunction without acute infarction. The absence of infarction was demonstrated by normal diffusion-weighted MRI studies. The ABCD2 score, designed to stratify the short-term risk for recurrent stroke following TIA, was recorded in all patients. The individuals performing the coated-platelet assay were not aware of the clinical diagnosis, and the neurologists establishing the diagnosis of TIA were not aware of the patient's coated-platelet levels. **Results:** Coated-platelet levels were significantly higher in TIA patients compared to controls (mean $\pm$ SD, 38.4 $\pm$ 15.1% versus 31.0 $\pm$ 13.2%, $P = 0.005$). A significant positive linear correlation was detected between ABCD2 scores and coated-platelet levels in TIA patients ($P = 0.003$, $r = 0.45$). **Conclusions:** Coated-platelet synthesis is increased in TIA patients compared to controls. In addition, coated-platelet levels in TIA patients positively correlate with ABCD2 scores. These findings lend support to the hypothesis that TIA and ischemic stroke represent a spectrum of conditions dependent on similar prothrombotic processes. This work is supported by OCAST (Dr. Prodan) and AHA (Dr. Dale).

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W P347

Peroxynitrite Disrupts Cerebrovascular Actin Cytoskeleton and Reduces Myogenic Reactivity in Diabetes after Oxygen-glucose Deprivation

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Diabetes is a risk factor for cerebrovascular disease and is a reliable predictor of poor stroke outcome. Elevated oxidative stress in diabetes contributes to endothelial dysfunction and heightened small-vessel resistance. It is unclear, however, how diabetes influences cerebrovascular reactivity, especially under ischemia/reperfusion (I/R) conditions. **Purpose:** We tested the hypothesis that in the presence of diabetes, I/R makes the affected brain more susceptible to edema and bleeding by augmenting peroxynitrite ($ONOO^-$) levels in the vasculature, resulting in nitration of the vascular smooth muscle (VSM) actin cytoskeleton and reduction in cerebrovascular reactivity. **Methods:** Middle cerebral arteries from age-matched Wistar (n=6-8) and type 2 diabetic Goto-Kakizaki rats (n=6-8) were exposed to normoxia, oxygen-glucose deprivation (OGD), or OGD followed by acute treatment with the $ONOO^-$ decomposition catalyst, FeTPPs, then their vascular reactivity, nitrotyrosine levels and VSM actin content were determined. **Results:** Basal levels of $ONOO^-$ were increased in diabetes (41.0 $\pm$ 7.8 vs. 19.8 $\pm$ 3.1 pixels). $ONOO^-$ was increased in controls and remained high in diabetes after OGD (39.4 $\pm$ 6.1 vs. 33.8 $\pm$ 11.4) but were reduced in both groups after FeTPPs treatment (19.0 $\pm$ 2.1 vs. 24.1 $\pm$ 5.1). % myogenic tone was higher across the autoregulatory range (40-120 mmHg) in diabetes, compared to controls (21.5 $\pm$ 2.2 vs. 15.3 $\pm$ 1.7%). OGD reduced % myogenic tone in both groups (9.7 $\pm$ 1.4 vs. 6.9 $\pm$ 0.93%); however, basal levels were restored in diabetes but not controls following FeTPPs treatment (18.8 $\pm$ 1.8 vs. 9.1 $\pm$ 0.79%). Confocal imaging of VSM actin showed similar levels of filamentous (f-) actin in control and diabetes at baseline (46.2 $\pm$ 2.2 vs. 44.9 $\pm$ 1.4 arbitrary units). OGD reduced f-actin levels (23.9 $\pm$ 5.1 vs. 35.4 $\pm$ 4.9) but they were restored with FeTPPs treatment (39.0 $\pm$ 0.90 vs. 42.8 $\pm$ 4.9). At baseline, globular (g-) actin localization was uniform within the cytosol and periphery of VSM cells, whereas OGD concentrated g-actin within periphery in both groups. After FeTPPs treatment, g-actin relocated to the cytosol in diabetes but remained in the periphery in controls. **Conclusions:** These results suggest that $ONOO^-$ generated by OGD contributes VSM actin cytoskeleton disruption, resulting in reduced cerebrovascular myogenic reactivity, particularly in diabetes. Whether this effect contributes to increased edema and bleeding in diabetic animals after acute ischemic stroke needs to be confirmed by *in vivo* studies.

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W P348

Cigarette Smoke Induces Oxidative Stress and Phenotypic Modulation in Cerebral Vascular Smooth Muscle Cells

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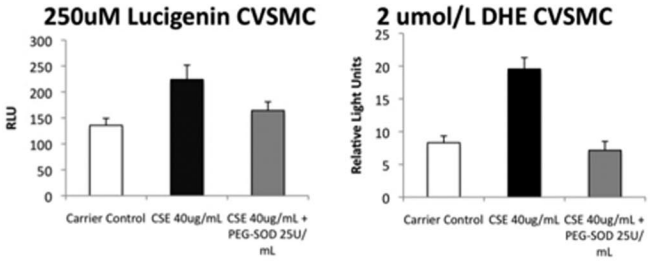
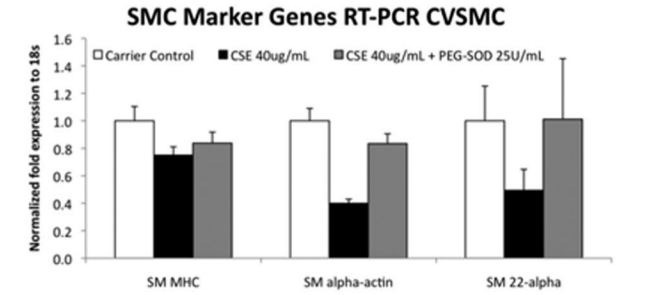
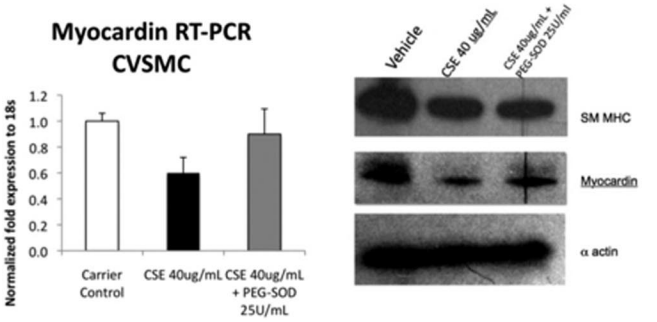
Molecular mechanisms by which cigarette smoke contributes to cerebral aneurysm pathology are unknown. We investigated the role of cigarette smoke-induced oxidative stress in the phenotypic modulation of cerebrovascular smooth muscle cells (CVSMC), which is a hallmark of aneurysm pathology. **Methods:** Human CVSMC's were treated with 4, 40 and 400ug/mL cigarette smoke extract (CSE) with or without 25U/mL polyethylene glycol-superoxide dismutase (PEG-SOD), a potent oxygen free radical scavenger. Oxidative stress was analyzed with 250uM lucigenin chemiluminescence using a luminometer and 2umol/L dihydroethidium using confocal microscopy. Fluorescence excitation was set at 480 nm with emission detection at 570 nm long pass filter. Smooth muscle cell (SMC) marker gene and protein expression was analyzed with RT-qPCR and western blotting, respectively. These were done in untreated cells, CSE treated CVSMC's and cells treated with concurrent CSE and PEG-SOD. **Results:** A dose-dependent increase in oxidative stress (not shown) was seen in CSE-treated CVSMC's that was reversible with PEG-SOD. CSE treatment produced profound dose-dependent phenotypic modulation in CVSMC with decreased expression of SMC marker genes (SM MHC, SM alpha-actin and SM 22-alpha) and myocardin and upregulation of matrix remodeling genes including MMP-3 (not shown) with RT-PCR. Western blot analysis demonstrated similar results with loading control alpha-actin. Strikingly, phenotypic modulation was prevented with concurrent treatment with PEG-SOD. **Conclusion:** CSE induces dose-dependent oxidative stress in cultured CVSMC that is prevented with PEG-SOD. Moreover, CSE induces profound phenotypic modulation in CVSMC including downregulation of SMC marker genes and myocardin as well as upregulation of matrix remodeling genes. This phenotypic modulation is abrogated with PEG-SOD treatment implicating a critical role for superoxide in this process. The present results have implications for the pathophysiology of cerebral aneurysms and this may represent a novel target for future therapy.







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W P349

Mechanisms of Natural Vitamin E, Alpha-Tocotrienol, in Pial Collateral Recruitment and Remodeling During Acute Ischemic Stroke

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Background: Vitamin E is a generic term for tocopherols and tocotrienols. The lesser characterized isoform á-tocotrienol (T3) exhibits neuroprotective properties not shared by tocopherols (TP). Previous work in a large animal model of stroke demonstrated that prophylactic supplementation of T3, but not TP, attenuates stroke mediated brain injury and improves pial collateral circulation. In the clinical setting, pial collaterals have been documented to perfuse, via retrograde flow, the proximally occluded parent vessel and improve stroke outcomes. While improving pial circulation is a therapeutic target of recognized value, mechanisms of pial recruitment and remodeling during stroke are unknown. The paucity of experimental systems to test the significance of pial circulation in stroke has limited research efforts. **Objective:** To employ T3 as an experimental tool to identify mechanisms of pial collateral recruitment and remodeling during ischemic stroke. Method: Mice (C57/BL6, n=10) were randomized and supplemented with 200mg/kg of T3 or vehicle placebo (PBO) for 15wks prior to middle cerebral artery occlusion (MCAO). Following 30min of MCAO, and while ischemia persisted, mice were injected with 5μl of fluorescent conjugated lectin (*Lycopersicon esculentum*) to visualize the perfused pial circulation in the stroke affected hemisphere. Immunohistochemistry directed laser microdissection pressure catapult (LMPC) of pials from the MCAO territory for downstream gene and protein analysis. **Results:** T3 supplemented mice had significantly smaller stroke lesion volume as compared to PBO controls and improved pial perfusion in the MCAO territory. This corresponded with improved functional recovery following stroke. Quantitative RT- PCR and Western blot protein expression analysis identified T3-induced pial targets including chloride intracellular channel 1 (CLIC-1), TIMP-1, and matrix metalloproteinase 2 (MMP-2). T3 supplementation increased expression of CLIC-1 and TIMP-1 and attenuated MMP-2 activity. **Conclusion:** This work identifies for the first time an experimental system for invoking pial collateral circulation during stroke. T3 supplementation improves stroke affected pial circulation and attenuates post-stroke outcomes.

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W P350

The Protective Effect Of Spironolactone On Cerebral Ischemia/reperfusion Injury In Nicotine Exposed Mice

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Purpose: A substantial body of evidence suggests that cigarette smoking and nicotine enhance the process of "vascular aging" and has aggravating effect on cerebrovasuclar ischemic events. This study examined the effect of mineralocorticoid receptor inhibitor spironolactone (SPIRO) in reducing the nicotine induced- prestroke and poststroke changes in cerebrovascular endothelium. **Methods:** C57BL/6 mice were chronically exposed to nicotine (2 mg/kg/body weight) via s.c. implanted miniosmotic pumps for 14 days which resulted in plasma nicotine levels of ~100 ng/ml, reflecting plasma concentrations in average smokers. For analysing the prestroke effect of SPIRO in nicotine-exposed animals, the mice were treated with SPIRO (i.p., 0.02mg/kg body weight) from day 7 of nicotine exposure. For analyzing the postroke changes, the mice started to receive SPIRO (i.p., 0.02mg/kg body weight) either before (7 days) or after (2 hrs) transient middle cerebral artery occlusion (tMCAO, 30 min of occlusion followed by reperfusion 1-7 days). In both experimental conditions mice were sacrificed and were used for analysis of brain edema, blood brain barrier permeability, inflammatory response and infarct volume. **Results:** Nicotine exposure mice had significant proinflammatory changes of cerebrovasuclar endothelium associated with increased permeability of BBB for small molecules (inulin permeability) - prestroke changes, and also worse cerebrovascular injury that was reflected in increased infarct size, greater brain edema, higher mortality rate and worse neurological deficits than in non-nicotine exposed mice-poststroke changes. Application of SPIRO (0.02 mg/kg body weight per day, i.p.) during the chronic nicotine exposure markedly reduced infarct size and the neurological damage induced by tMCAO. Application of SPIRO after MCAO (2hrs) also affected the outcome of brain I/R injury (reduced infarct size, decreased mortality, improved neurological score). Screening of 62 different proinflammatory cytokines, chemokines and adhesion molecules by real time RT-PCR and antibody-based protein array, indicated that SPIRO added during nicotine exposure and after tMCAO significantly reduced the expression of some cytokines chemokines, adhesion molecules, that were upregulated by nicotine. There is also significantly reduced infiltration of leukocytes in brain parenchyma. **Conclusions:** SPIRO attenuated the detrimental effects of nicotine at BBB in prestroke condition as well as in brain I/R injury suggesting that SPIRO could be potential treatment for stroke in cigarette smokers.

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W P351

Plasma Aldosterone Increases Rapidly After Cerebral Ischemia with Reperfusion Injury

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We, and others, have shown that inhibition of the mineralocorticoid receptor (MR) reduces the damage caused by cerebral ischemia in rats. Very little is known about how ischemia affects plasma aldosterone, the endogenous agonist for the MR. We tested the hypothesis that aldosterone would increase dramatically after cerebral ischemia / reperfusion injury. 12-week-old male Sprague Dawley rats underwent a middle cerebral artery (MCA) occlusion for 1 hour followed by 5 (n=6) or 23 (n=8) hours of reperfusion. Sham operated rats served as controls (n=6). Plasma was collected from these rats and aldosterone levels were measured by ELISA. We found a fifteen-fold increase in plasma aldosterone in the 5-hour reperfusion rats (31.66±9.23 vs 493.51±116.91pg/ml, sham vs control, $P<0.05$). Plasma aldosterone remained elevated 23 hours after reperfusion (299.57±64.38pg/ml, $P<0.05$ compared to sham). Aldosterone or MR activation has previously been linked to matrix metalloproteinase (MMP) activation, inflammation and cell proliferation in other parts of the cardiovascular system. We measured the mRNA expression of several markers of these pathways in the MCAs from the rats that underwent ischemia / reperfusion injury. The MCA that experienced ischemia was compared to the contralateral (control) MCA in a paired fashion, and the results were expressed is fold change from control and normalized to B2-microglobulin expression. After 5 hours of reperfusion there was a trend toward and increase in matrix metalloproteinase (MMP)-9 expression (1.01±0.00 vs 20.51±8.86, control vs ischemic, p=0.08), this became significant after 23 hours of reperfusion (1.01±0.01 vs 7.45±2.2, control vs ischemic $P<0.05$). MMP-12 expression was also elevated after 23 hours of reperfusion (1.07±0.03 vs 3.50±0.04, control vs ischemic, $p< 0.5$), and surprisingly, the expression of its substrate, elastin was reduced (1.01±0.00 vs 0.74±0.07, control vs ischemic, $P<0.05$). At this time, markers of cell proliferation and macrophage infiltration were also increased in the MCA that

had been ischemic as evidenced by an increase in mKi67 (1.04±0.03 vs 3.27±0.46, control vs ischemic, P<0.05) and CD68 (1.00±0.00 vs 1.43±0.17, control vs ischemic P<0.05) respectively. We have previously reported that the structure of the MCA changes after reperfusion resulting in a vessel with a lumen diameter that is 20ìm larger than a control vessel. MMP activation, inflammation and cell proliferation have all previously been implicated in the vessel remodeling process. Therefore, it is possible that aldosterone may stimulate vessel remodeling, macrophage infiltration, cell proliferation and intracellular matrix breakdown in the injured vessels post-stroke.

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Th P1

Neurologic Safety Event Rates in the SENTIS Control Population

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Introduction: To evaluate the safety of treatment in a single arm ischemic stroke trial or in ongoing randomized trials, it is necessary to know the expected rate of neurologic adverse events (AEs) in control subjects. **Hypothesis:** The study determined whether prospectively evaluating all neurologic AEs and applying time from randomization criteria in the control arm could provide rates of expected neurologic safety events to compare against treatment arm events. **Methods:** As specified in the Data and Safety Monitoring Board (DSMB) charter, the DSMB adjudicated all neurologic AEs for the multi-center Safety and Efficacy of NeuroFlo Technology in Ischemic Stroke (SENTIS) trial, randomizing patients aged 18 years and older with National Institutes of Health Stroke Scale (NIHSS) scores of 5-18 within 14 hours of symptom onset with follow-up of 90 days. The current study determined control group rates for those events critical for trial safety determinations, including intracranial hemorrhage (ICH), cerebral edema, neurologic worsening/stroke progression and new ischemic stroke. An AE was classified as serious (SAE) if it resulted in neurologic deterioration considered clinically relevant by the DSMB, was associated with a 4-point NIHSS increase, was fatal, life threatening, required or prolonged hospitalization, or required intervention to prevent permanent impairment. The number of AEs occurring within the following defined time periods after randomization provided a basis for determining treatment relatedness: 24-hr (range 5-48 hrs) imaging for ICH (by AE forms and core lab), 7 days for cerebral edema and neurologic worsening/stroke progression, and 30 days for new stroke. **Results:** The SENTIS control group included 257 patients, 49.4% female with a mean age of 68.3 and median baseline NIHSS of 10.0. Any ICH during follow-up occurred in 27% (70/257), 63% (44/70) on the 24-hr scan of which 1.9% (5/257) were categorized as SAEs. Cerebral edema was seen in 6.6% (17/257), 94% (16/17) of events occurring within 7 days of randomization of which 3.5% (9/257) were categorized as SAEs. Neurologic worsening/stroke progression occurred in 22% (57/257), 74% (42/57) of events occurring within 7 days of which 13% (33/257) were SAEs. New ischemic stroke occurred in 4.7% (12/257), 83% (10/12) of events occurring within 30 days of which 1.9% (5/257) were SAEs. **Conclusions:** Prospective capture of neurologic safety events in the control group of the SENTIS acute stroke trial showed that ICH SAEs occurred in 1.9% on the 24-hour scan while cerebral edema SAEs occurred in 3.5% and neurologic worsening/stroke progression SAEs in 13% within 7 days and new stroke SAEs in 1.9% within 30 days of randomization. Knowing the expected neurologic AE rate will allow better assessment of safety in single arm and future stroke trials.

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Th P2

CLOTBUST-Hands Free Operator Independent Ultrasound Device: Initial Safety Testing in Healthy Volunteers

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Background & Purpose: Low intensity transcranial ultrasound augments tPA-induced arterial recanalization. We aimed to evaluate normal volunteers in the first phase of a study of the safety and estimated peak negative pressure of an operator-independent ultrasound device developed to deliver ultrasound energy exposure levels administered in the CLOTBUST trial. **Subjects & Methods:** An 18-transducer 1-2.5 MHz emitting frequency head frame exposed both temporal windows and suboccipital window in volunteers free of cerebrovascular disease. The transmission characteristics were set to emulate the acoustic characteristics of commercially available transcranial Doppler systems and to never exceed the FDA-mandated ultrasound exposure limits. Volunteers underwent 2 hours of insonation with transducer activation one at a time. Estimated peak negative pressures were calculated based on our previously developed acoustic attenuation model. Measurements were taken in volunteers who received the insonation via the "best pair" temporal transducers placed on both sides of the skull. Safety was captured using serial neurological examinations (NIH Stroke Scale) and pre- and post-insonation multimodal with/without gadolinium MRI for detection of any lesions and the blood brain barrier (BBB) permeability interpreted by an independent expert using a specific algorithm. **Results:** A total of 15 healthy volunteers (40% men; 49±16 yrs; 27% African-Americans; NIHSS score 0) were continuously insonated for 2 hours with the device. Five volunteers received pulsed wave ultrasound via the "best pair" temporal transducers (group 1), 5 via sequential activation of the suboccipital transducers (group 2), and 5 via sequential activation of all bilateral temporal and suboccipital transducers (group 3). Group 1 volunteers had an average temporal bone thickness of 2.3 mm (range 1.5-3.0 mm). The mean estimated in vivo peak negative pressure at 3.2 cm intracranial depth was 59±17 kPa, and the maximum derated intensity (Ispta.3) levels did not exceed the 720 mW limit. All subjects were safely insonated with no adverse effects as indicated by the neurological examinations during, immediately after the exposure and at 24 hrs (all NIHSS scores 0), and no breach of the BBB was found on all MRI's. **Conclusion:** Our novel device was well tolerated by the healthy volunteers and did not cause any neurological dysfunction and did not affect the integrity of the BBB. The device delivered estimated peak negative pressures across the proximal vessels of the circle of Willis at > 19 kPa levels, the lower threshold needed for optimized microstreaming as the key factor in achieving sonothrombolysis. The safety of the device is currently being tested in stroke patients receiving IV tPA as part of a NIH-sponsored clinical trial.

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Th P3

Reduced Low Density Lipoprotein Cholesterol Fraction Is Not A Risk Factor For Hemorrhagic Transformation After Intravenous Thrombolysis Therapy For Acute Ischemic Stroke

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Background and Purpose: Current available data on the relationship between hemorrhagic transformation (HT) of acute cerebral ischemic stroke following intravenous tissue plasminogen activator therapy (IV-tPA) and reduced low density lipoprotein cholesterol (LDL-C) fraction is limited and available data show conflicting results. The primary purpose of this study was to assess this relationship and other potential factors that may influence hemorrhagic transformation of acute cerebral ischemic stroke after IV-tPA in a homogenous patient population. **Method:** We reviewed the medical records of 388 patients from a database of IV-tPA recipients (according to AHA/ASA guidelines) at four Joint Commission Certified Primary Stroke Centers and one community hospital with an active stroke unit. We included 189 patients that received IV-tPA alone and in whom pertinent clinical and laboratory information was available. **Results:** The mean age (±standard deviation [SD]) was 71.3 (±13.9) years and 54.3% were men. Treatment violation with IV-tPA occurred in 8 patients (4.2%). Twenty-two patients (11.6%) had any HT after IV-tPA treatment and in 9 patients (4.8%) it was symptomatic. There was no difference in the LDL-C level among patients with HT and those without HT (100.8 vs 95.3 mg/dl; OR1.004; 95% CI, 0.992 - 1.016; p=0.5). However, a prior history of diabetes mellitus (31.8% vs 12.6%; OR 3.245; 95% CI, 1.185-8.883; p=0.02) or prolonged mean time from symptom onset to presentation at the emergency room (74.4 minutes vs 56.0 minutes; OR 1.015; 95% CI, 1.002-1.027; p=0.02) was associated with an increased risk of HT. Factors that were more prevalent in patients with HT compared to those without HT, but did not reach statistical significance on the univariate logistic regression analysis included: prolonged time (±SD) in minutes from symptom onset to IV-tPA administration (137.8 ±29.6 vs 125.5 ±37.2; p=0.14); total cholesterol (178.4 vs 168.1 mg/dl, p=0.26); triglycerides level (143.4 vs 121.0 mg/dl; p=0.18); history of hypertension (94.7% vs 78.7%; p=0.13); and aspirin intake (63.6% vs 47.9%; p=0.17). **Conclusion:** Prior history of diabetes mellitus and prolonged time of symptom onset to hospital arrival, but not reduced LDL-C, is associated with increased frequency of HT following IV-tPA after ischemic stroke.

Table 1: Comparison of patients with and without hemorrhagic transformation after IV-tPA for acute ischemic stroke

	Total (n=189)	Hemorrhagic transformation (n=22)	No hemorrhagic transformation (n=167)	p value
History of diabetes mellitus	28 (14.8%)	7 (31.8%)	21 (12.6%)	**0.02**
History of hypertension*	147 of 183 (80.3%)	18 of 19 (94.7%)	129 of 164 (78.7%)	0.13
Aspirin intake	94 (49.7%)	14 (63.6%)	80 (47.9%)	0.17
Total cholesterol in mg/dL (±SD)	169.3 (±40.3)	178.4 (±50)	168.1 (±38.8)	0.26
Mean LDL-C level in mg/dL (±SD)	95.9 (±36)	100.8 (±44.7)	95.3 (±34.8)	0.5
Triglyceride level in mg/dL (±SD)	123.6 (±73)	143.4 (±86.9)	121 (±70.8)	0.18
Mean time (±SD) in minutes from symptom onset to arrival in emergency room	58.1 (±33.9)	74.4 (±26.9)	56.0 (±34.2)	**0.02**
Mean time (±SD) in minutes from symptom onset to IV-tPA	126.9 (±36.5)	137.8 (±29.6)	125.5 (±37.2)	0.14

*The presence or absence of hypertension was documented in 183 of 189 patients

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Th P4

Microalbuminuria: An Independent Risk Factor For Intracerebral Hemorrhage After I.v. Thrombolysis For Acute Stroke

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Background: Intracerebral hemorrhage (ICH) represents one of the most feared complications of thrombolysis. Age, clinical stroke severity at admission, high blood pressure, hyperglycemia, and early CT changes are well known predictors of ICH. In recent years, the role of microalbuminuria (MA) as a risk factor for cerebrovascular disease has become apparent. The aim of our study was to determine the predictive value of MA for intracerebral hemorrhage after thrombolysis. **Methods:** Thrombolysed acute stroke patients were consecutively studied. Clinical data, early CT changes, vascular risk factors and other known predictors for ICH after thrombolysis were prospectively collected. Severity of stroke was assessed by NIHSS. ICH was categorized according to the SITS criteria. The urinary albumin excretion was measured in 24-h collection of urine. **Results:** Overall 55 patients were included. With 96%, the majority of patients had a previous history of hypertension, 45% had diabetes, 24% had atrial fibrillation, and 11% had a previous stroke. The median NIHSS at admission was 8 (range 3-34, IQR 8). Ten patients (18.2%) suffered from ICH after thrombolysis, 3 with HI1, 2 with HI2 and 5 with PH2. In the univariate analysis ICH was associated with MA (r=0.4, p=0.003), stroke severity (r=0.23, p=0.04), cholesterol level (r=-0.3, p=0.02) and ASA pretreatment (r=0.23, p=0.04). In the logistic regression analysis MA (OR 12.5, CI 1.2-133.4, p=0.036) and cholesterol level (OR 0.97, CI 0.95-0.99, p=0.04) remained as independent predictors for ICH after thrombolysis. We didn't find any difference in MA between the HI and PH. **Conclusion:** In our study MA was independently associated with ICH after thrombolysis. We hypothesize that premorbid endothelial damage as suggested by increased microalbuminuria may contribute to the pathophysiology of hemorrhagic complications after i.v. thrombolysis.

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Th P5

Telestroke Guided IV tPa Treatment Achieves Similar Clinical Outcome As Thrombolysis At Comprehensive Stroke Center

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Background: Many acute ischemic stroke patients eligible for treatment with intravenous tissue plasminogen activator (IV tPA), never receive treatment due to lack of stroke expertise and experience. To fill this void, a telestroke network was established between the UPMC Stroke Institute and regional community hospitals to provide acute stroke expertise. Vascular neurologists provided 24/7 coverage using real time 2 way audio video telemedicine and neuroimaging access at these facilities. To assess the adequacy of this approach, we compared clinical outcomes following systemic thrombolysis at telestroke facilities versus treatment at comprehensive stroke center. **Methods:** All patients treated with IV tPA at 12 community hospitals by telestroke during an 19 month period were compared to patients similarly treated following face to face evaluation by the same group of vascular neurologists at a university tertiary care stroke center over the same time interval. Time to treatment and time from door to treatment and functional outcome at 90 days were obtained prospectively. Favorable outcome was defined as modified rankin score of $\leq$ 2. **Results:** Between June 2008 and December 2009, eighty three patients were treated with IV tPA after a telestroke consultation and 59 patients received IV tPA at the stroke center. Favorable outcome rates were comparable between the groups at 42.1% in the telestroke group and 37.5% in patients treated at the stroke center (p=0.7). There was no significant difference between the groups in the rate of symptomatic (1% v. 5%, p=0.1) or asymptomatic hemorrhage (19% v. 16%, p=0.7). Time from stroke onset to treatment was similar in the 2 groups but time from door to treatment was significantly longer in the telestroke group. **Conclusion:** Telestroke guided IV tPA at community hospitals under supervision of stroke experts achieved similar clinical outcomes compared to treatment administered in person by the same physicians at a tertiary care stroke center. A delay in door to treatment time was introduced when using telestroke but this did not result in worse outcomes. Telestroke is a viable alternative to in person acute stroke evaluation when stroke expertise is not readily available.

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Th P6

Antiplatelet and Anticoagulation Therapy Before an Ischemic Stroke Neither Precludes nor Complicates Intravenous Thrombolysis

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Objectives: To ascertain the effect of baseline antiplatelet (AP), anticoagulation (AC), or dual antithrombotic (AP+AC) therapy on the likelihood of receiving intravenous thrombolysis with recombinant tissue plasminogen activator (tPA) after acute ischemic stroke and on subsequent hemorrhage rates. **Methods:** We queried the Colorado Stroke Registry, a shared database of 38 Colorado hospitals. Patients with complete records of outpatient ischemic stroke seen within 180 minutes of onset were included in the analysis. The CSA database tracks standard contraindications to tPA, including INR $>$ 1.7. **Results:** Of the 15,625 records, 1,322 (8.5%) met inclusion criteria. The table shows INR and NIH Stroke Scale values for all patients in the groups of interest and for those without contraindications to tPA. Of the 777 patients (59%) without contraindications, 55% received tPA. AP patients were *no more likely* than controls (patients not previously on antithrombotics) to have tPA contraindications (39% vs. 40%, p = 0.67), and eligible patients were *as likely* to receive tPA (58% vs. 54%, p = 0.33). AC patients were *more likely* than controls to have tPA contraindications (66% vs. 40%, $p < 0.0001$), but eligible patients were *as likely* to receive tPA (70% vs. 54%, p = 0.14). AP+AC patients were *no more likely* than controls to have tPA contraindications (50% vs. 40%, p = 0.19), and eligible patients were *as likely* to receive tPA (43% vs. 54%, p = 0.33). AP, AC, or AP+AC therapy *did not* increase the risk of symptomatic intracerebral hemorrhage (SICH), serious systemic hemorrhage (SSH), or other serious complications (OSC), as seen in the table. **Conclusions:** Pre-stroke AP, AC, or AP+AC therapy does not decrease the likelihood of IV tPA treatment in the absence of published contraindications. In contrast to some reports, eligible patients on AP, AC, or AP+AC therapy who receive IV tPA do not appear to have an increased risk of serious complications. We recognize, however, that numbers are small in some subgroups, and a type-II statistical error cannot be excluded.

	All Patients				
	Control	AP	AC	AP+AC	P
N (%)	903 (68)	309 (23)	68 (5)	42 (3)	
INR mean (SD)	1.1 (0.5)	1.1 (0.5)	1.7 (0.9)	1.6 (0.7)	<0.0001
NIHSS mean (SD)	8.9 (7.6)	8.8 (7.6)	10.4 (8.4)	8.8 (7.4)	0.648
	Patients with no contraindications to tPA				
N (%)	543 (70)	190 (24)	23 (3)	21 (3)	
INR mean (SD)	1.1 (0.6)	1.1 (0.6)	1.3 (0.3)	1.2 (0.4)	<0.0001
NIHSS mean (SD)	9.7 (7.9)	9.3 (7.7)	9.8 (7.3)	9.6 (7.7)	0.905
	Outcomes after tPA treatment				
SICH: Y/N (%Y)	15/284 (5)	7/104 (6.3)	0/16 (0)	0/9 (0)	0.638
SSH: Y/N (%Y)	2/297 (0.7)	1/110 (0.9)	0/16 (0)	0/9 (0)	0.970
OSC: Y/N (%Y)	4/295 (1.3)	4/107 (3.6)	1/15 (6.3)	0/9 (0)	0.302

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Th P7

Thromboelastography (TEG) in Acute Ischemic Stroke

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Background: TEG demonstrates the dynamics of coagulation (see figure 1). R=time to clot initiation; K=speed of clot buildup; Delta=time to maximum rate of thrombus generation (intensity of thrombin burst); G=clot strength (increased in platelet-rich clots). There are limited data available about TEG and its utility in acute ischemic stroke (AIS). We studied TEG in patients with AIS to: 1. compare baseline TEG values in AIS vs controls; 2. distinguish clot subtype; 3. determine extent of fibrinolysis after tPA bolus. **Methods:** Consecutive patients with AIS who presented within 3 hours of onset were included. Venous blood was drawn upon arrival to the ED and 10 minutes after initiation of tPA. **Results:** A total of 32 AIS patients and 46 controls were evaluated; 15/32 AIS patients had both pre- and post-tPA TEG. Mean age was 67±18 years, 50% were female; of 32, 14 were of cardioembolic etiology, 3 were large artery atherosclerotic, 4 due to small artery occlusion, and 11 other/unknown. Baseline R was 5.8

minutes shorter ($p<.0001$) and K was 1 minute shorter ($p<.0001$) in AIS patients compared to controls after correcting for age. Delta averaged 0.6 ± 0.6 minutes (vs 0.7-1.1 minutes in controls). All these findings indicate hypercoagulability in AIS. Nineteen AIS patients had elevated G values indicating platelet-rich clots (G = 11.3 ± 2.3 Kd/cm2) while the remaining patients had lower G values (G = 7.9 ±0.6 Kd/cm2) ($p<.001$) which, along with lower delta, indicates "red" clot with more thrombin contribution and less platelets (see figure 2). G significantly decreased post-tPA compared to baseline ($p<.0001$) confirming the fibrinolytic effect of tPA. **Conclusion:** AIS patients are hypercoagulable due to robust thrombin generation, and form clots with varying strength and composition, which undergo fibrinolysis by tPA. TEG may provide a way to monitor and adjust thrombolytic therapy so that it is safer and more effective, as well as individualized to the patient.

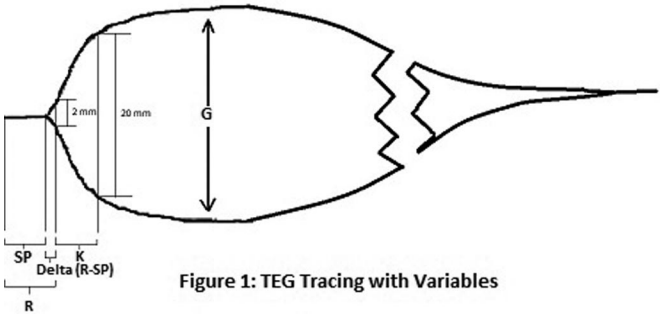
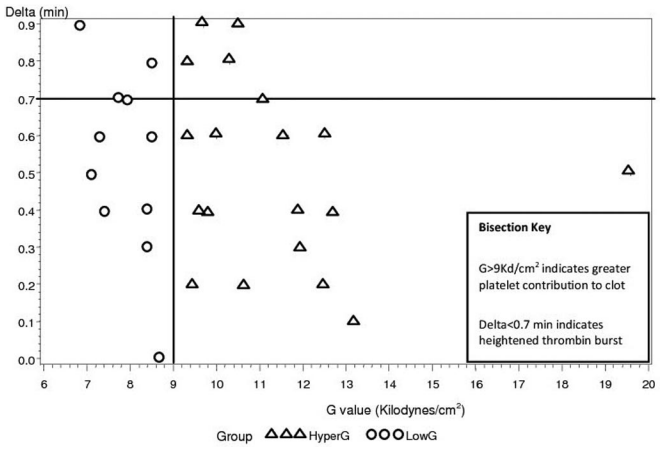


Figure 1: TEG Tracing with Variables

Figure 2: Trends in Coagulability in AIS Patients as measured by TEG



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Th P8

Baseline Total Cholesterol Levels and Risk of Symptomatic Hemorrhagic Transformation after Intravenous Thrombolysis in Acute Ischemic Stroke Patients

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Objectives: There are evidences that low cholesterol levels (CLs) are associated with intracranial hemorrhage. Aim of this study was to evaluate if baseline CLs might have influence on the risk of symptomatic hemorrhagic transformation (HT) after i.v. thrombolysis in acute ischemic stroke (AIS). **Methods:** We analyzed all the data of AIS patients treated with i.v. rt-PA in Italy from 2003 to 2009 included in the international internet-based SITS-ISTR (Safe Implementation of Treatment in Stroke - International Stroke Thrombolysis Register). Symptomatic intracerebral hemorrhage (SICH) was defined as any type of hemorrhage associated with any clinical worsening at NIHSS (NINDS definition). We also considered ECASS and SITS-MOST definitions of SICH. CLs were generally obtained within 24 hours from thrombolytic treatment. Univariate and multivariate analyses were performed. **Results:** Overall, 4194 patients were included, for 2577 (61.5%) we have data on baseline total CLs. Median value was 191 mg/dl (80-499). We identified three different CLs based on percentiles 25, 50 and 75: ≤164 mg/dl (648/2577 patients, 25.1%), ≤191 mg/dl (1292/2577, 50.1%) and ≤221 mg/dl (1940/2577, 75.3%). Compared to those with higher levels, patients with CLs ≤164, ≤191 and ≤221 mg/dl were more likely to be male ($p=0.001$), older ($p<0.01$), with more diabetes, AF, congestive heart failure, on prior antiplatelet ($p<0.0001$), anticoagulant ($p<0.01$) and/or, only the subgroup ≤191 mg/dl, antihypertensive therapy ($p=0.027$). Moreover, they had lower baseline SBP (respectively, $p=0.031$, <0.0001, <0.0001), lower baseline DBP (only for the subgroups ≤191 and ≤221 mg/dl, respectively $p=0.043$ and 0.049), higher rate of cardioembolic stroke ($p<0.0001$), and early clinical improvement at 24 hours (only in the third subgroup, $p=0.039$), less use of aspirin and higher use of other antiplatelets and oral anticoagulants ($p<0.01$) during the hospital stay. There are not significant differences for the functional outcome at 3 months. Patients with CLs ≤164 mg/dl tend to have a higher mortality ($p=0.006$), but this data is not confirmed at the multivariate analysis. At the univariate analysis CLs ≤164 mg/dl were associated with SICH according to SITS-MOST definition (very severe SICH) ($p=0.046$). At the multivariate analysis CLs did not result as independent predictors of SICH according the different definitions. **Conclusions:** Our study did not show an association between lower baseline total CLs and the risk of HT after i.v. thrombolysis in AIS. More studies are necessary to address this issue, particularly considering also the LDL-CLs and the use of statins at stroke onset.

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Th P9

Level Of Consciousness And Gaze Paralysis In The Baseline NIH Stroke Scale (NIHSS) Exam Are Independent Predictors Of Death After Ischemic Stroke

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Background: The risk of death after an ischemic stroke depends on the patient's age, size and location of the infarction. The baseline NIHSS score, a marker of infarct size, is associated with the risk of death. We aimed to investigate whether abnormalities in individual items of the baseline NIHSS exam, might be independently associated with death at three months after a cerebral infarction. **Methods:** We retrospectively analyzed all subjects enrolled in the AbESTT-I and AbESTT- II trials (abciximab vs. placebo). All patients had a baseline NIHSS exam on admission. The occurrence of death in the 3 months following the stroke was recorded. We performed univariate comparisons between baseline NIHSS items and death. We also performed a multivariate logistic analysis using death as the dependent variable with each of the baseline NIHSS items as covariates. The analysis was adjusted for age, sex, race systolic blood pressure, abciximab use and total NIHSS score. **Results:** A total of 1204 patients were analyzed. The mean NIHSS was 9.7 (SD 5). 129 (10.7%) subjects died within 3 months of their stroke. Total NIHSS score and all the individual NIHSS items except limb ataxia were associated with increased mortality risk at 3 months. However, in multivariate logistic analysis only level of consciousness ($p=0.007$) and gaze paralysis on NIHSS ($p=0.002$), and to lesser degree language ($p=0.03$), were independently associated with mortality at 3 months. The risk of death in a patient with normal level of consciousness and gaze score was 5%. The risk increased to 59% if these 3 items were abnormal. **Conclusion:** The presence of an abnormal level of consciousness, horizontal gaze palsy and to a lesser degree language in the baseline NIHSS are associated with 3 months mortality after ischemic stroke. These are independent of the other elements of the NIHSS and confounders. We hypothesize that these three items are a marker of a multilobar MCA infarction with associated risk of hemorrhagic transformation, cerebral edema or increased intracranial pressure. Table1: Probability of death at 90 days with combinations of LOC, gaze & language.

		90 day mortality	90 day mortality when language is factored
Abnormal LOC	Abnormal gaze	30%	Normal (18%) Abnormal (59%)
Abnormal LOC	Normal gaze	19%	Normal (14%) Abnormal (23%)
Normal LOC	Abnormal gaze	21%	Normal (20%) Abnormal (23%)
Normal LOC	Normal gaze	5%	Normal (4%) Abnormal (7%)

Table1: Probability of death at 90 days with combinations of LOC, gaze & language.

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Th P10

Normal CTA should raise suspicion of Stroke Mimics In Candidates for i.v. Fibrinolysis

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Background and Purpose: An increasing number of patients with stroke mimics (SM) receive treatment with intravenous fibrinolysis. Factors explaining this trend include greater familiarity

with rt-PA among clinicians, time constraints of therapy, and limited capacity for confirmatory diagnostic tests. Although an emerging body of literature indicates that SM rarely develop complications, these patients are exposed to the inherent dangers of fibrinolytic therapy without any expected benefits, and require observation in intensive care units. We report herein our experience with emergency CT angiography (CTA) in patients treated with i.v. rt-PA, and analyze its capacity to distinguish SM from acute ischemic strokes (AIS). **Materials and Methods:** Retrospective analysis of 193 patients treated with i.v. rt-PA between 2007-2008. CTA of the head and neck was done in 163 of these patients during their initial Emergency Room assessment. The remainder of patients had MRA (n=18) or no vascular imaging (n=12). Patients were classified into 3 groups: AIS with confirmed brain ischemia on follow-up imaging (n=142), TIA or "aborted" stroke (AbS)_defined as cases of compelling AIS symptoms without diffusion-weighted imaging abnormalities (n=21), and SM (n=30). Arterial occlusion (AO) was defined as presence of ≥1 distal arterial cutoffs, and atherosclerosis as any region of arterial wall irregularity leading to focal stenosis on CTA. Chi-squared statistics and step-wise logistic regression analysis were used. **Results:** AO was noted in 78 AIS patients (57.8%) but in none of the AbS and SM cases ($p< 0.001$). Atherosclerosis was noted on 116 (86.6%) AIS patients, 10 (58.8%) AbS, and 6 (21.4%) SM. CTA did not distinguish SM from AbS, but advanced age and cardiovascular risk factors were significantly overrepresented in the latter ($p<0.001$). Overall, the finding of any arterial wall abnormality on CTA increased the odds of AIS over SM (OR=23.6, 95%CI: 8.43-66.2, $P<0.001$) and AIS over AbS (OR 4.51, 95%CI: 1.52-13.36, $P<0.01$). None of the patients with SM had hemorrhagic complications. **Conclusions:** Emergency CTA may help discern whether i.v. rt-PA candidates truly need treatment. The finding of normal CTA should encourage clinicians to re-evaluate patients and may justify an emergency MRI to confirm diagnosis, if feasible. This study should be interpreted with caution, as further research is needed to validate our observations.

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Th P11

The Role Of Sonolysis, Sonothrombolysis With And Without Microbubble In Acute Ischemic Stroke: A Systematic Review And Meta-analysis Of Randomized Control Trials And Case Control Studies

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Background: Continuous monitoring with 2-MHz, single-element pulsed-wave ultrasonography had a biologic effect of diagnostic ultrasonography that aids systemic thrombolytic therapy in patients with acute ischemic stroke. Objectives: To describe and assess the evidence from case control studies (CCS) and randomized control trials (RCT) on the efficacy, tolerability and safety of sonolysis (TCD alone) sonothrombolysis (continous TCD monitoring with IV thrombolysis) with and without microbubble (MBs) in acute ischemic stroke patient. **Search Methods:** Several electronic databases and grey literature were searched under different Mesh terms from 1970 until now without any language limitation by one reviewer. Then, full article were retrieved for the relative subject. Selection criteria: RCT and CCS on sonolysis ,sonothrombolysis alone or with MBs in acute ischemic stroke patients, adult patient > 18 years old, with or without IV thrombolysis treatment. Outcome measures are: complete recanalization (CR) rate in 2 hours and 24 hours, modified rankin scale (mRS) and Barthel index (BI) at 3 months and symptomatic intracerebral hemorrhage (sICH). Data collection and analysis: Data will be extracted from the CCS and RCTs into the Rev Manger software. Meta-analysis was performed on the selected RCTs and CCS. Pooled and subgroup analysis were planned. Heterogeneity was assessed using Mantel Haenzel analysis method with random effect. **Results:** A total of 1287 titles were reviewed from electronic literatures. Thirty eight studies were retrieved and analyze carefully. Then, 28 articles were excluded and 10 studies (6 RCTs and 4 CCS) were included in our Meta-analysis. Sonolysis and Sonothrombolysis alone or with MBs are safe and carry the same risk of sICH as IV rtPA alone (OR of sICH: 1.17 (95 % CI: 0.56- 2.41). (P = 0.68). They are effective (OR of CR in 2 hours: 4.0, CI 95% :2.44-6.58, P < 0.00001) and have 2.80 times likelihood of good long term outcome (3 months mRS 0-1or 0-2) (OR= 2.31 (CI: 1.6- 3.34) (P < 0.001). Further subgroup analysis based on the presence of MBs revealed that sonothrombolysis with MBs is safe (OR of sICH: 1, CI: 0.35 - 2.87, P=1)) and effective (OR of CR at 2 hours: 2.95, CI: 1.43- 6.06) (P=0.003) and OR of good long term outcome: 1.99, CI: 1.2- 3.29, P=0.007). Finally, subgroup analysis based on sonolysis alone versus none or ASA alone in acute ischemic stroke revealed that sonolysis alone is safe (OR of sICH: 0.57, CI: 0.07- 4.92, P= 0.61) and effective (OR of CR in 2 hours: 23.5, CI: 1- 555, P=0.05) and OR of good long term outcome: 2.78, CI: 1.10-7, P=0.03). **Conclusions:** This type of novel treatment in acute ischemic stroke is safe and effective in enhancing recanalization rate and improving long term outcome. The evidence of safety and efficacy of MBs as an enhancing model of sonothrombolysis in acute ischemic stroke is evolving.

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Th P12

Early And Ultraearly Thrombolysis In Acute Stroke: Sex Differences In Stroke Outcome

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Background: The earlier thrombolysis is given after ischemic stroke, the better outcome. The number needed to treat for favourable outcome is 3 for patients treated within first 90 minutes. A recent study has shown that ultraearly thrombolysis treatment (≤ 70 min) is associated with better outcome in patients with moderate to severe strokes. Our objective is to study this effect according to sex. **Methods:** multicenter prospective study of acute ischemic stroke patients treated with intravenous (IV) tPA in five stroke centres. Variables analysed: onset to treatment time (OTT), demographic data, vascular risk factors, baseline blood pressure and glycaemia, stroke etiology according with the International Classification of stroke, basal NIHSS and 3-months modified Rankin scale (mRS) score (worse outcome was defined as mRS >2). Using multivariate logistic regression, the association between OTT and 3-months favourable outcome (mRS 0-2) according sex was studied. **Results:** a total of 1147 patients were included, 53% men. Mean age (SD) was higher in women than in men (69.2 [14.2] vs. 66 [13.4], P thrombolysis (≤ 70 min) was associated with a better outcome only in severe strokes (NISHH > 16), both in women and men: OR 3.21 (1.11 to 9.23) and 9 (1.02 to 78.69) respectively. Early treatment (<90 min) was associated with better outcome in severe strokes, but it reached the statistic significance only in women: OR 2.76 (1.26 to 5.86) and 2.64 (0.95 to 7.29) respectively. **Conclusion:** Ultraearly thrombolysis (≤ 70 min) is associated with better outcome in severe strokes in both sexes. However, women could get great benefits than men from early treatment (< 90 min).

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Th P13

Intra-venous Tissue Plasminogen Activator For Acute Central Retinal Artery Occlusion: A First Randomized Controlled Trial

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Introduction: Central retinal artery occlusion (CRAO) or an eye stroke causes monocular vision loss with a poor chance of spontaneous recovery. A metanalysis of all reported cases suggests that vision improvement occurs in 48.5% of patients. We therefore hypothesize that the use of intravenous tissue plasminogen activator (tPA) would result in reperfusion of acute CRAO with improved VA. **Methods:** A multi centered, subject blinded, placebo controlled, randomized controlled trial (RCT) of 0.9 mg/kg of tPA was conducted in subjects with CRAO diagnosed by an ophthalmologist within 24 hours of symptom onset. The primary outcome was a change in VA of 3 lines or more equivalent to an increase of ≥0.3 log MAR score. **Results:** 16 patients were randomized. 2/8 (25%) of the tPA group achieved an improvement of VA of 3 lines or more as opposed to none in the placebo group; both receiving tPA within 6 hours of symptom onset. There was a significant improvement of the mean logMar VA of 0.4 at 3 months favouring tPA ($p=0.02$). One intracranial hemorrhage occurred post tPA and two had ocular neovascularization. **Conclusion:** This is the first randomized controlled trial that demonstrates the efficacy of IV tPA in CRAO if administered within 6 hours of symptom onset. The study provides sufficient signal to pursue a larger phase 3 RCT with a narrower therapeutic time window.

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Th P14

Oxidative Damage In Ischemic Stroke. A Biomarker Study

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Introduction: The role of oxidative stress has been questioned following repeated failures of neuroprotective compounds with purported free-radical scavenging activities to improve stroke outcomes. We performed a detailed prospective study to evaluate the changes of multiple markers of oxidative damage in a cohort of ischemic stroke subjects and matched controls. **Study Design:** Consecutive patients diagnosed with acute ischemic stroke who presented within 6-hours following the onset of symptoms to the National University Hospital, Singapore, were included in this study. Peripheral blood and urine samples, obtained immediately on presentation and serially 6-hrs, 12-hrs, 18-hrs, days 1-4, 7 and 14 following the onset of stroke, were assayed for F_2-isoprostanes, hydroxyeicosatetraenoic acids (HETEs), F_4-neuroprostanes, 24-hydroxycholesterol, allantoin and uric acid. **Results:** Sixty-six subjects with ischemic stroke and 132 controls were included in this study. The mean (SD) age of stroke subjects was 65.2 (13.1) years, comprising 34 (52%) males and 32 (48%) females, who presented with NIHSS of 16.7 (7.2). A majority of these subjects had cardioembolic (n=34, 52%) and large artery atherothrombotic strokes (n=30, 46%), 31 (47%) of whom with left hemispheric, 28 (42%) right hemispheric and 7 (11%) brainstem strokes. Ninety days following stroke onset, 9 (6%) subjects developed symptomatic intracerebral hemorrhage and

10 (16%) had excellent outcomes (modified Rankin scale, one or less). The initial blood and urine samples were collected at a median of 171 minutes (range, 122-245 minutes) following symptom onset. Plasma F_2-isoprostanes, HETEs, F_4-neuroprostanes, 24-hydroxycholesterol and allantoin were altered to different extents immediately following stroke onset. A bimodal pattern of change was observed in the esterified and free forms of plasma F_2-isoprostanes, as well as urinary F_2-isoprostanes, highest immediately and on days 1-3 following the onset of stroke. The extent of rise in the esterified form of plasma HETEs was highest 6-12 hours following the onset of stroke, a finding that was similarly observed with plasma F_4-neuroprostanes, 24-hydroxycholesterol and allantoin. By contrast, plasma uric acid was significantly lower on days 1-3 following the onset of stroke compared to controls. In multivariate analyses, elevated levels of urinary HETEs predicted the development of symptomatic intracranial hemorrhage, while elevated plasma esterified HETEs, uric acid and allantoin, and lower plasma free F_2-isoprostanes, were associated with excellent functional recovery. **Conclusions:** Our data support the participation of oxidative damage in the pathogenesis of ischemic stroke and in predicting stroke outcomes. Depending on the time of sampling, different patterns of change can be observed in markers of oxidative damage following ischemic stroke.

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Th P15

Tissue Plasminogen Activator for Acute Cerebellar Strokes

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Background: Cerebellar infarction is an important subcategory of ischemic strokes. Tissue plasminogen activator (t-PA) remains the only proven treatment for ischemic stroke. We hypothesized that pure cerebellar strokes are less often treated with t-PA. We aimed to determine what percent of cerebellar strokes are treated with t-PA and what are the main causes why patients with cerebellar strokes are not treated with t-PA. **Methods:** Retrospective chart review of patients was conducted from our stroke registry from 01/03 to 06/10. We evaluated consecutive patients with pure cerebellar ischemic infarcts. Patients with additional infarcts of the brainstem or cerebral hemispheres were excluded. We collected demographics, National Institute of Health Stroke Scale (NIHSS) on admission, rates of symptomatic intracerebral hemorrhage (sICH), neurological worsening, and discharge modified Rankin Scale (mRS) outcomes. **Results:** Among 48 patients, 8 patients (17%) received IV t-PA within 4.5 hrs of symptom onset. None of the patients had hemorrhagic transformation. However, two patients had neurological worsening; one of them died and the other required surgical intervention because of brainstem compression. Thirteen patients (27%) arrived within 4.5 hrs of symptom onset but were not treated because of either rapid improvement (31%), no deficits on NIHSS (46%) leading to misdiagnosis as TIA, or because of a t-PA contraindication (23%) such as elevated INR or petechial hemorrhage on CT. Of the 7 patients who had either rapid improvement or were misdiagnosed as a TIA, they presented with dysarthria (75%), dizziness (75%), nausea (100%) and/or vomiting (100%). In both of these groups, dysarthria resolved but they continued to have dizziness, nausea, or vomiting. Two (29%) of these patients had disabling deficits at discharge. Half (56%) of all cerebellar patients arrived outside the 4.5 hrs window. The vascular distribution of the non-treated infarctions was: 44% PICA, 33% SCA 4% AICA, 2% branch of PCA and 19% multiple territories. In the t-PA group; 13% were PICA, 25% SCA and 62 % were multiple territory. **Conclusions:** Our data indicate that most patients with acute cerebellar strokes tend not to receive IV t-PA because they arrived outside the 4.5 hrs window or had minimal or non-detectable deficits on NIHSS. However, the latter patients continued to have significant symptoms and some were disabled at the time of discharge. No instances of sICH were found in the t-PA treated group but the small sample number precludes drawing definitive conclusions about safety and outcome of t-PA for acute cerebellar ischemic strokes.

Table 1: Demographics, Risk Factors, Clinical Data and Outcomes

	tPA	No tPA	P Value
Demographics			
Mean Age (Years) ± SD	67±14	53±16	NS
Female Sex (%)	38	33	NS
Risk Factors			
Hypertension (%)	88	58	NS
Diabetes (%)	25	18	NS
AF (%)	25	5	NS
Smoking (%)	38	23	NS
Hyperlipidemia (%)	50	18	0.0459
Admission NIHSS (Median)	6	3	NS
Outcomes			
Median Discharge mRS ≤2 (%)	50	55	NS
Neurological worsening (%)	25	20	NS
Median LOS (days)	5	5	NS
sICH	0	1	NS

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Th P16

Intravenous Thrombolysis for Ischemic Stroke in Patients with ongoing Acute Myocardial Ischemia

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Background: Recent myocardial infarction (MI) is considered a contraindication for intravenous thrombolysis (IVT) for acute ischemic stroke (AIS) due to risks of hemopericardium and tamponade. The American Heart Association guidelines recommend fibrinolytic therapy for ST-elevation MI upto 12 hours from symptom onset and upto 24 hours with persistent symptoms and ECG changes if percutaneous coronary intervention is unavailable. Pericardial effusion (PEF) is common following MI. Thrombolysis in patients with MI doesn't increase the prevalence and severity of PEF. Clinical trials in AIS exclude patients with acute MI and many neurologists do not consider IVT in such situations. We report the incidence of patients with AIS with ongoing acute myocardial ischemia presenting within 4.5 hours of onset and the safety of IVT in this population. **Methods:** We identified all patients from our stroke database who received IVT from 1/1/2008 till 12/31/2009 within 4.5 hours of AIS onset and were found to have ongoing acute MI. Demographics, stroke characteristics, troponin levels, ECG and investigative findings, treatment modalities, and outcomes were collected. **Results:** Of 359 patients treated with IVT for AIS, we identified 4 (1.1%) patients found to have elevated cardiac enzymes at the end of rt-PA infusion. The diagnosis of non-ST elevation MI was made by the on-call cardiologists in view of rising troponin levels on serial assessment and new ECG changes and they were jointly involved in close cardiac monitoring and treatment. All patients received IV anticoagulation 24 hours after IVT and received warfarin, aspirin, statin, beta-blocker and ACE-inhibitor at discharge. Patient-3 developed hemorrhagic conversion of the infarct, so IV heparin was stopped. He also developed bradycardia, felt to be related to metoprolol use and received transvenous pacing. He was subsequently discharged on coumadin and underwent pacemaker placement after 1 month. Patient-4, who had prior severe CHF, underwent tracheostomy for pulmonary edema. There was no mortality and no clinical or echocardiographic evidence of pericardial effusion or tamponade. **Conclusions:** IVT administered under close supervision at specialized tertiary centers may be safe in AIS patients with concurrent acute sub-endocardial ischemia.

Table 1

	Patient 1	Patient 2	Patient 3	Patient 4
Admit NIHSS	**9**	**3**	**10**	**18**
Cardiac Complaints	**none**	**none**	**none**	**Chest discomfort**
Onset to IVT(min)	**95**	**115**	**190**	**116**
Admit ECG	AF with RVR (115/min) with PVC, left axis deviation, Q waves, T-wave inversion in leads 1, aVL.	sinus rhythm with PAC, T wave inversions in V3,4,5.	**NSR, RBBB, 3rd degree AV block**	**Sinus tachycardia (138/min), RBBB**
Peak Troponin (ng/ml)	**3.8**	**0.44**	**1.25**	**0.476**
Echo	**EF=55-60, No vegetation, normal prothetic Aortic valve**	LVEF 20% to 25%, LV thrombus, hypokinetic anterior wall, akinetic anteroseptal & inferior wall	**LVEF 25-30%, akinetic postinferior wall**	**LVEF<20%, LV thrombus, Akinetic anterior, anteroseptal and inferior walls**
CoronaryAngiogram	**Performed as outpatient, no significant disease**	**Triple vessel dis multiple stenotic lesions - PCI**	**2 vessel CAD, chronic LAD occlusion**	**No significant disease**
Discharge mRS	**1**	**0**	**3**	**5**
Adverse event during admission	**none**	**none**	**bradycardia**	**Pulmonary edema**
Symptomatic ICH	**N**	**N**	**Y**	**N**

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Th P17

Intravenous t-PA for Patients with Minor Ischemic Stroke: A Single Stroke Center Experience

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Background: Current guidelines do not recommend treatment with intravenous tissue plasminogen activator (IV-tPA) in patients with minor stroke. Minor stroke represents a common reason why patients after ischemic stroke are not treated with thrombolysis. However, there is no consensus definition of minor stroke and the outcome of patients with minor stroke is unknown. We compared clinical outcomes and safety in patients with minor stroke were, and those who were not, treated with IV t-PA. **Methods:** Patients with minor ischemic stroke presented within 3hrs form the stroke onset with 90 day modified Rankin Score (mRS) were selected from January 2004 to June 2010 using our prospective UCSD Stroke Center registry. Minor stroke was defined as patients with a National Institutes of Health Stroke Scale (NIHSS) score $\leq$5. The primary outcome was a 90 day mRS of 0-1. Secondary outcomes were Barthel index (BI) of 95 to 100 at 90 days, symptomatic intracranial hemorrhage (SICH) and death. Multivariable logistic regression was performed to determine the association between outcome (Day 90 mRS of 0-1 vs. 2-6, Day 90 BI of $<$95 vs. 95-100, 90-day mortality) and treatment group, adjusting for age, diabetes and initial NIHSS. Reasons for t-PA exclusion were obtained. **Results:** We identified 123 patients with minor ischemic stroke; 50 patients received IV-tPA (Group 1), 73 did not (Group 2). The reasons for treatment exclusion were: Rapid improving symptoms 33(45.2%); the patient or the family refused thrombolytic treatment 6(8.2%), patients were $>$3hrs at treatment time 5(6.8%), anticoagulation 5(6.8%), uncontrolled BP 1(1.4%), extreme glucose level 1(1.4%), stroke mimic 1(1.4%). Baseline characteristics (Age, gender, race, hypertension, A-fib, diabetes, tobacco use, pre stroke mRS) were similar in both groups with the exception of the initial NIHSS (mean$\pm$SD); Group 1: 3.44$\pm$1.36, Group 2: 1.92$\pm$1.33, p$<$ 0.0001. There were no statistically significant differences between IV-tPA and the untreated groups in 90-day mRS of 0-1 (50% vs. 68.5%; adjusted OR 0.68, 95% CI: 0.28-1.66, p=0.40) and BI of 95-100 (69.6% vs. 78.7%; adjusted OR 0.88, 95% CI: 0.31-2.45, p=0.81).There were 3 deaths (4.1%) in the untreated group and 3 deaths (6%) in the t-PA group (p=0.18). SICH was 6% in the treatment group. SICH was not recorded in the untreated group. **Conclusions:** Clinical and safety outcomes were similar between t-PA treated and untreated patients with minor stroke. A larger randomized clinical trial or observational study is needed confirm or reject these findings.

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Th P18

Outcome Of Intravenous rt-PA Treatment In Acute Stroke. Time To Administration And Baseline NIHSS Analysis

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Introduction: Previous studies have shown a worse rate of functional recovery and increased mortality in terms of greater baseline NIHSS score and a longer time window in the administration of IV rt-PA. It is unknown the cutoff NIHSS predictor of functional recovery and mortality, nor the effect of the combined variables of baseline NIH score and stroke onset to start treatment (OTT) outcomes. Objectives: To determine a baseline NIHSS value predictor for functional recovery and mortality in patients with stroke treated with rt-PA IV. To analyze the results by combining the baseline NIHSS variables and OTT and compared with the placebo arm of previous clinical trials. Patients/Methods: Prospective multicenter registry of IV rt-PA in five university hospitals with stroke unit. We included 967 patients with OTT $<$ 270 minutes. We collected demographic, clinical, hemorrhagic transformation rate, mortality and functional recovery (Rankin scale 3 months). We used the data published in the placebo arm of ECASS I-III studies, ATLANTIS and NINDS to study differences between treatment and placebo. ROC curves, Pearson and Mann-Whitney test were done in the analysis of the results with the program SPSS, version 15.0. **Results:** The sensitivity and specificity of baseline NIHSS were studied whit the ROC curves. The NIHSS value of 14 was obtained as the value that correspond to the largest area under the curve (0.77, P$<$0.01) in predicting functional recovery (Rankin 3months 0-2) (positive predictive value (PPV) 63.1%, negative predictive value (NPV) 79.3%, sensitivity 74.6%, specificity 69.1%) and mortality (area under the curve 0.8, P$<$0.01, PPV 78.3%, NPV 3.5%, sensitivity 43.9%, specificity 14.4%). Patients treated with NIHSS $\geq$ 14 and OTT $\leq$180 minutes did not show significant differences in recovery globally and mortality versus to the placebo group, and there was a worse recovery rates and higher mortality in the OTT $>$ 180 minutes compared to the placebo group (Mann-Whitney U, p=0.258 (0-90 minutes), p=0.066 (91-180 minutes), p=0.004 ($>$ 180 minutes), respectively. For OTT 91-180 minutes and NIHSS $\geq$ 14, 12.8% of patients were on Rankin 0 and 11.4% on Rankin 1 versus 40% and 22% respectively for NIHSS $<$14. Mortality 22.6% for OTT 91-180 minutes and NIHSS $\geq$ 14 versus 2.3% for NIHSS $<$14 (p$<$0.05)**Conclusions:** The baseline NIHSS $\geq$ 14 is a predictor of low recovery rate and high mortality in patients treated with IV rt-PA. Patients with the score greater or equal 14 points on the baseline NIH scale treated before 180 minutes after onset of symptoms did not obtain significant differences compared with the placebo arm, and do not benefit from treatment with IV rt-PA. Further studies are needed to confirm these findings.

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Th P19

Difference In Outcome For Patients With Ischemic Stroke Treated With Iv T-pa In Less Than 2 Hours Versus 2-3 Hours

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Objective: Intravenous tissue plasminogen activator (IV t-PA) is the only proven treatment for acute ischemic stroke but its efficacy diminishes with time. As a consequence, efforts are made to treat patients as quickly as possible. Data from the NINDS t-PA studies and subsequent pooled analyses showed that patients treated achieved better outcomes the earlier after stroke onset treatment was given. Many healthcare initiatives focus on treatment with IV t-PA in less than 2 hours. Our objective was to use the internal database at the University of California, San Diego Stroke Center to determine if patients treated before 2 hours achieved better outcomes than those treated between 2-3 hours. **Methods:** Using Fisher's Exact Test we compared 90 day modified Rankin Scales (mRS) in patients treated between 0-2 hours and 2-3 hours. Good outcome was defined as mRS 0 or 1 at 90 days. All patients received standard dose IV t-PA. We excluded patients who received adjuvant reperfusion therapy or were enrolled into clinical trials utilizing therapies other than IV t-PA. We adjusted for age, gender, hypertension, diabetes, personal history of stroke/TIA, prestroke mRS and baseline NIHSS. **Results:** Overall 209 patients (51% male, median age 75 years old) received IV t-PA. 88 patients were treated from 0-2 hours and 121 patients were treated between 2-3 hours. The early treatment group received treatment at a median of 105 minutes and the late treatment group at a median of 150 minutes (p$<$0.0001). The adjusted dichotomous 90-day mRS was not different between groups (p$<$0.9195, OR 1.05, CI 0.37-2.97). **Conclusion:** Despite prior evidence that treating patients earlier with IV t-PA is more effective, we could not demonstrate that patients treated between 0-2 hours achieved better 90 day functional outcomes than patients treated between 2-3 hours. Further studies with larger sample sizes are needed to prospectively investigate the relationship between outcome and time to treatment.

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Th P20

Estimated Peak Rarefaction Pressure Predicts Recanalization and Outcome in the Transcranial Ultrasound in Clinical SONothrombolysis (TUCSON) Trial

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Background&**Purpose:** The peak rarefaction pressure is the most dominant factor that influences both mechanical clot fragmentation and acceleration of enzymatic fibrinolysis. We sought to determine whether recanalization rate and functional outcomes in the Transcranial Ultrasound in Clinical SONothrombolysis (TUCSON) trial could be predicted by estimated in vivo peak rarefaction pressure. Subjects&Methods: We developed an acoustic attenuation model to estimate the in vivo peak negative pressures at the occlusion site within each subject of the TUCSON trial with CT scans eligible for measurements. Variables included temporal bone thickness, depths of occlusion location, and average attenuation of skin and brain tissues. Recanalization was defined as partial or complete using the Thrombolysis in Brain Infarction flow grades. Functional independence was assessed at three months using the modified Rankin Scale Score (mRS 0-1). **Results:** The peak rarefaction pressure was calculated in 20 acute ischemic stroke patients treated with sonothrombolysis (mean age 64$\pm$15 years, 65% men, median NIHSS score 13, interquartile range 6-17). The mean estimated peak rarefaction pressure was 30.2$\pm$15.5 kPa (range 8-68 kPa). A total of 6 patients (30%, 95%CI: 14%-52%) had peak rarefaction pressures less than 19 kPa which is considered the lower threshold for optimized microstreaming. Patients with persisting occlusion (n=6) tended to have lower peak rarefaction pressures (25.2+/-8.0 kPa) compared to patients with any recanalization (n=14, 13 complete, one partial; 32.3+/-17.7 kPa; p=0.228). Patients who were functionally independent (n=9) at three months tended to have higher peak rarefaction pressures compared to the rest (35.1$\pm$19.5 kPa vs. 25.9$\pm$11.2 kPa; p=0.217). After adjusting for baseline stroke severity, a 1 kPa increase in peak rarefaction pressure tended to be related to a higher likelihood of functional independence (OR: 1.05; 95%CI: 0.95-1.15; log OR: 0.4; p=0.360) at three months. After excluding patients with peak rarefaction pressures lower than 19 kPa, patients with functional independence had higher peak rarefaction pressures compared to the rest (45.7$\pm$14.0KPa vs. 30.7$\pm$9.6KPa; p=0.044). For the given effect size (log odds ratio of 0.4) a sample size of 110 patients would be needed to formally test this potential association with a power of 83% and a two-tailed alpha of 0.05. **Conclusions:** Our preliminary analysis underscores the importance of successful energy delivery above 19 kPA threshold to augment thrombolysis with 2 MHz ultrasound by demonstrating a trend towards higher peak negative pressures leading to recanalization and improved outcomes.

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Th P21

Safety And Efficacy Of Intravenous Thrombolysis In The Treatment Of Acute Basilar Occlusion: A Prospective Observational Study

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Background&**Purpose:** Randomised Controlled Trials (RCTs) have shown the safety and efficacy of intravenous thrombolysis (IVT) given within 4●5 h of the onset of the symptoms of acute ischemic stroke (IS). Unfortunately, the results of these RCTs do not directly apply to patients with acute basilar artery occlusions (BAO) given the limited number of these patients included in RCTs and the low incidence of BAO among IS patients. The best available data guiding treatment decisions in this specific stroke subgroup comes from the Basilar Artery International Cooperation Study (BASICS), a prospective international observational registry. We evaluated the safety and efficacy of IVT in consecutive patients with BAO treated either with IVT or antithrombotic therapy (AT) in two tertiary care centers. Subjects&Methods: Consecutive patients with acute (24 hours) BAO were prospectively recorded over a four-year period. BAO was diagnosed by ultrasound, MR angiography or CT angiography in all cases. Reversed BA flow was prospectively documented. Baseline stroke severity was evaluated by the NIH Stroke Scale Score (NIHSS). Demographics and stroke risk factors were recorded in a standardized fashion. IVT was administered according to AHA recommendations within 4.5 hours from stroke onset, while intra-arterial thrombolysis was not offered in any patient given the unavailability of interventional radiologists in both centers. Symptomatic intracranial hemorrhage (sICH) was defined according to the SITS-MOST definition. Poor functional outcome at three months was assessed using the mRS-score according to BASICS definition (4-6 points). **Results:** Among 86 patients with acute BAO (mean age 64±12years, 58% men, median NIHSS-score 14 points, IQR 9-22), a total of 31 (36%) received IVT (mean age 61±10years, 52% men, median NIHSS-score 15 points, IQR 12-24) while the remaining were treated with AT (mean age 66±12years, 62% men, median NIHSS-score 13 points, IQR 8-20). Patients treated with IVT were older ($p=0.034$), had higher admission NIHSS-scores ($p=0.041$) and a lower prevalence of diabetes mellitus ($p=0.007$) compared to AT patients. The two groups did not differ in terms of gender, remaining risk factors, admission blood pressure and blood glucose values, site of basilar occlusion (proximal vs. distal) and reversed BA flow. sICH occurred in 7% of patients in both groups ($p=0.886$). Poor outcome tended to be less frequent in IVT patients (26% vs 43%; $p=0.098$). In the multivariate logistic regression analyses the following three factors were independent predictors of poor outcome: NIHSS-score (OR per 1-point increase: 1.18; 95% CI: 1.08-1.30; $P<0.001$), BA flow reversal (OR: 0.06; 95% CI: 0.01-0.30; $p=0.001$) and IVT (OR: 0.15; 95% CI: 0.04-0.61; $p=0.008$)**Conclusions:** IVT appears to be equally safe and more effective than AT in patients with acute BAO.

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Th P22

Levels of Creatin Kinase in Blood are Predictors of Hemorrhagic Transformation in Patients Treated with rt-PA

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Objectives Creatine is a tripeptide which has been shown to be neuroprotective in cerebral ischemia due to its antioxidant properties. Hemorrhagic transformation (HT) after rt-PA is related to the endothelial damage which is due, amongst other mechanisms, to the release of free radicals, suggesting that antioxidant therapies may be used to avoid this complication. This study investigates the participation of creatine kinase (CK), an enzyme which acts on creatine, in the development of HT in patients receiving rt-PA. Patients and Methods Levels of CK were analyzed in 357 patients with ischemic stroke < 4.5 h of evolution treated with rt-PA. HT was assessed in the cranial CT performed at 24±12 h after the administration of treatment and was classified in accordance with the ECASS II criteria. Results Of the 357 patients, 255 (71.4%) did not have HT, 69 (19.3%) had hemorrhagic infarction (HI) and 33 (9.2%) had parenchymal hemorrhage. The levels of CK were higher in patients with HT (74 [53,96] vs. 86 [62,125]) ($p=0.04$). In the logistic regression model, levels of CK were independent predictors of HT after adjusting for the rest of the variables related to this complication in the univariate analysis (OR, x 10 U/L 0.9; CI 95%, 0.52-0.95; $p=0.04$). **Conclusions:** CK levels are predictors of HT in patients treated with rt-PA, supporting the participation of oxidative mechanisms in the development of HT in patients receiving thrombolysis.

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Th P23

Intravenous rt-PA and Outcome after a Mild Stroke

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Background and Objective: Randomized clinical trials of IV rt-PA have excluded patients with low NIHSS scores, yet several studies have shown a substantial percentage of these patients had poor outcomes when treatment was withheld. This study determined whether mild stroke patients who received intravenous (IV) rt-PA had decreased mortality and morbidity after consideration of their stroke characteristics during hospitalization. Methods We analyzed 176 cases of ischemic stroke eligible for IV rt-PA by time criteria with NIHSS score <8 admitted to Saint Luke's Stroke Center from March, 2006 through June, 2009. The NIHSS scores were further categorized as <4 and 4-7. Outcome was defined based on their discharge disposition. Discharge to home with or without home health or inpatient rehabilitation was defined as good outcome. Discharge to nursing homes or hospice homes or death were defined as poor outcome. Univariate analysis including t-test, Chi-square, and Fisher Exact test was used when appropriate. Relative risk regression was used to examine the effect of rt-PA and clinical characteristics that predisposed patients for not going home. Results One hundred and seventy six mild ischemic strokes (male to female: 1.7:1 and a median age of 68 yrs ranging from 30 to 95 yrs) were included in this study. Percent of patients treated with IV rt-PA was 46% and 14% for those with NIHSS 4-7 and NIHSS 0-3, respectively. Patients who did not received rt-PA had higher mortality (5%) then those who received it (4%) ($p>0.05$). In the untreated group, more patients were discharged to nursing homes (15% vs 2%, $P<0.05$) and fewer patients were discharged to inpatient rehabilitation units (12% vs 28%, $P<0.05$). Admission NIHSS score, prior to stroke mobility function, and recurring stroke during hospitalization were significant factors determining discharge disposition. **Conclusion:** IV rt-PA treatment in mild strokes is associated with lower mortality and morbidity. This patient population is worthy of a randomized controlled trial testing the safety and efficacy of IV rt-PA.

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Th P24

Evaluation Of Patients Treated With IV tPA At Regional Stroke Centers vs. Community Hospitals: Is There Opportunity For A Wider Stroke Population To Be Treated?

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Background and Purpose: It is not known whether community hospitals (CH) and regional stroke centers (RSC) treat similar patients with IV tPA, and if the outcome of these patients is the same. The purpose of our study was to compare the baseline characteristics and outcomes of patients treated at CHs and then transferred to RSCs with those of patients initially treated at the RSCs. **Methods:** We performed a retrospective review of prospectively collected data from the NINDS Stroke Branch Registry of consecutive ischemic stroke patients treated with IV tPA at a RSC or referring CH who were admitted to one of two RSCs between January 2005 and October 2009. Patients' demographics, pre-treatment imaging modality, hemorrhage rates, and clinical outcomes were compared using univariate and multivariate logistic regression analyses to control for baseline variables. **Results:** Of 285 patients identified, 68% were treated with IV tPA at a RSC and 32% at a CH. Baseline stroke risk factors were similar between the two groups. Of patients treated at a RSC, 84% were screened with MRI compared to 4% of the patients treated at a CH. All the patients treated at a RSC but only 90% of those treated at a CH had a discharge diagnosis of ischemic stroke ($p<0.0001$). Patients treated at a RSC, compared with those treated at a CH, were older (mean age 71 vs. 64 years, $p=0.0004$), had longer symptom onset to treatment times (157 ±24 vs. 146 ±39 minutes, $p=0.0217$), and higher NIHSS scores (mean 13.5 vs. 11.3, $p=0.0593$). The rate of PH2 hemorrhagic transformation was similar for patients treated at the RSCs and CHs (7.2% vs. 7.7%, $p=0.8860$). Functional outcome at discharge (mRS
1: 23% vs. 29%, $p=0.3603$) and discharge disposition ($p=0.8473$) were also similar between the two groups. **Conclusions:** Though patients treated with IV tPA at RSCs and CHs had similar outcomes, patients treated with IV tPA at RSCs were older and had more severe strokes than patients treated at CHs. Patients treated at CHs were more likely to have a non-stroke etiology for their symptoms. Access to neurologists with expertise in stroke and the use of MRI as a screening tool may explain the more inclusive and accurate administration of IV tPA at these regional stroke centers.

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Th P25

Stroke Complicating Trans-Catheter Aortic Valve Implantation

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Background: Trans-catheter aortic valve implantation (TAVI) is an alternative to open heart valve replacement but carries an undefined risk for periprocedural stroke. Furthermore, the risk factors associated with stroke the attributes and outcome of these strokes are not known. Patients and**Methods:** All patients undergoing TAVI were included in a prospective database. Strokes complicating TAVI in the first 5 days following the procedure were documented and the differences between patients with and without stroke were studied. **Results:** Forty patients (17 men, mean age 79.3±7.1) underwent TAVI and were included. Of these, 6 (15%) had focal neurological deficits in the peri-procedural period (3 TIA, 3 stroke of which 2 were minor and one was major). Patients with stroke/TIA didn't differ from those without cerebral ischemia in baseline criteria or procedural variables. Five of the events were believed to be embolic resulting from dislodgement of calcific material from the aortic valve and one TIA was secondary to hypoperfusion during severe bradycardia. All patients with cerebral ischemia had involvement of the posterior circulation. One patient with basilar occlusion died but the

remaining 5 patients survived and all had a modified Rankin score of 2 or less at 90 days post stroke. None of these patients had a recurrent stroke during the follow up period. **Discussion:** Peri-procedural cerebral ischemia following TAVI is not uncommon. There was no particular pre-TAVI or procedural risk factor profile that increased the risk for peri-procedural stroke. Further studies are needed to examine whether patients that are at higher risk for developing stroke after TAVI can be identified.

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Th P26

Pre-existing Statin Use Predicts Early Reperfusion in Hyper-Acute Ischemic Stroke

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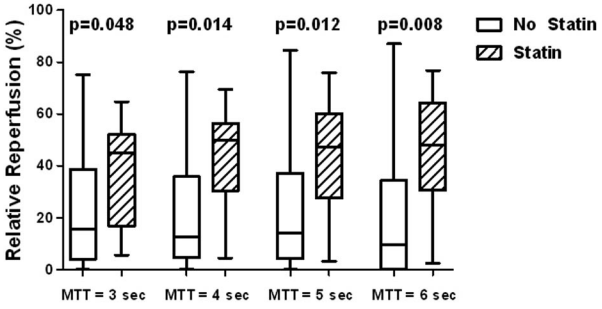
Background: Pre-existing statin use has been associated with improved neurological outcomes in ischemic stroke patients. Although several potential mechanisms have been examined in animal models, few have been examined in humans. We hypothesized that early reperfusion is enhanced in ischemic stroke patients taking statins at stroke onset. **Methods:** Acute ischemic stroke patients underwent two MR scans: within 4.5 (tp1) and at 6 hours (tp2) after stroke onset. Mean transit time (MTT) maps were generated to measure regions of perfusion deficit at tp1 and tp2. Regions of reperfusion were defined by perfusion deficits at tp1 which normalized at tp2. Four different thresholds were used to define "perfusion deficit" (MTT $>$ 3, 4, 5, or 6 secs longer than the contralateral mean) to ensure that results were not spuriously based on an arbitrary threshold. Baseline characteristics, relative reperfusion, and change in NIH Stroke Scale between tp1 and 1 month follow-up (ämNIHSS) were compared between patients taking statins on admission and those not taking statins. Wilcoxon Rank Sum was used for group comparisons unless D'Agostino test confirmed normality, in which case, t-tests were used. Two forward-selection multivariable linear regression models identified which clinical variables (of 10 considered) most strongly predicted: (1) relative reperfusion and (2) ämNIHSS. **Results:** Thirty-one acute stroke patients were prospectively enrolled; 12 were taking statins, while 19 were not. Baseline characteristics did not differ between the two groups except more patients in the statin group had coronary artery disease ($p=0.03$). Pre-existing statin use resulted in significantly greater reperfusion compared to the untreated group across all MTT thresholds (Fig, A). For the 4-sec MTT threshold, median reperfusion was 50% (IQR 30%, 56%) in the statin group vs. 13% (IQR 5%, 36%) in the untreated group, $p=0.014$. Of 10 baseline clinical variables, the best-fitting model for prediction of reperfusion included: (1) pre-existing statin use ($p=0.021$), (2) volume of perfusion deficit at tp1 ($p=0.024$), and (3) admission mean arterial pressure ($p=0.040$). Patients taking statins had greater ämNIHSS (8.8 points) at one month compared with untreated patients (4.4 points), $p=0.028$ (Fig, B). The best-fitting model for prediction of ämNIHSS included only two variables: pre-existing statin use ($p=0.010$) and age ($p=0.015$). **Conclusion:** Statin use prior to ischemic stroke onset is associated with early reperfusion and improved outcome. This raises the hypothesis that statin use may improve clinical outcome by enhancing early reperfusion.

A



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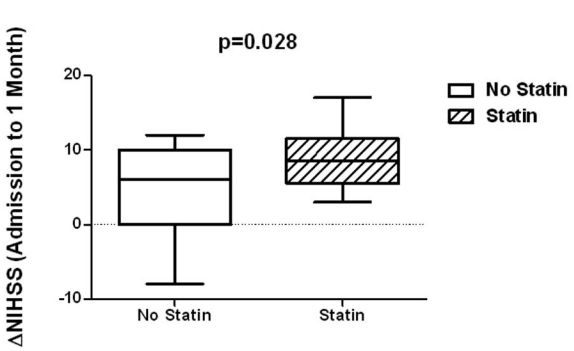

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Th P27

Heavy Alcohol Consumption: A Novel Predictor of Symptomatic Intracerebral Hemorrhage After IV t-PA?

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Background and Significance: Hemorrhagic transformation (HT) is a well known complication of intra-venous tissue plasminogen activator (IV t-PA) treatment. Parenchymal hematoma (PH2) transformation post IV t-PA is the most severe and is associated with increased morbidity and mortality. Several predictors of PH2 transformation have been reported, but few have focused on baseline alcohol consumption. **Methods:** We reviewed the NINDS Stroke Branch Registry, which contains clinical and radiologic data, for all IV t-PA patients admitted to our facilities between January 2005 and November 2009. The NINDS Stroke Program is a multi-center, regional stroke program. Comparisons between putative stroke risk factors and HT subtypes were performed using univariate and multivariate regression analyses. Baseline alcohol intake was determined on admission and categorized as $\leq$ 2 drinks or $>$ 2 drinks per day. MRI and CT consensus readings performed within 1 week of t-PA treatment were used. **Results:** During this 5-year period, 285 patients were admitted to our hospitals after IV t-PA treatment. Demographically, 30.9% were $\geq$ 80 years; their mean age was 68.8 $\pm$ 15.83; 53.3% were women, 59.3% white; 36.5% black; and 4.2% other. In terms of risk factors, 71.9% had hypertension; 24.6% diabetes; 41.4% hyperlipidemia; 26% coronary artery disease; 24.2% atrial fibrilliation; 18.9% previous stroke; and 16.8% were current smokers. In terms of alcohol use, 87% drank $\leq$ 2 drinks per day and 13% $>$ 2 per day. Twenty-one patients had PH2, 14 PH1, and 64 "any other" HT. In univariate and multivariate regression analyses, intake of $>$ 2 drinks per day was associated with PH2 transformation ($p=0.0341$; $p=0.0083$ after adjusting for NIHSS). No significant association was noted for PH1 alone or the combined of PH1, PH2 and "any other" HT. **Conclusion:** Heavy alcohol consumption is a well established risk factor for ischemic and hemorrhagic stroke. This study suggests that heavy alcohol consumption may also be associated with severe hemorrhagic transformation (PH2) after IV t-PA treatment.

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Th P28

High-density Lipoprotein Cholesterol Level is a Predictor of Outcome after Intravenous Recombinant Tissue Plasminogen Activator Therapy for Acute Stroke: The Stroke Acute Management with Urgent Risk-factor Assessment and Improvement (SAMURAI) rt-PA Registry

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Background and Purpose: Recent studies showed that statin improved clinical outcome of ischemic stroke, but the effect of lipid levels on the outcome is controversial. We investigated whether baseline lipid levels were associated with clinical outcome at 3 months after IV recombinant tissue plasminogen activator (rt-PA) therapy for acute ischemic stroke. **Methods:** Six-hundred consecutive patients who received IV rt-PA at ten stroke centers were registered in the SAMURAI rt-PA Registry. We assessed lipid levels on emergent visit; total cholesterol, triglyceride, high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol. The primary outcome was favorable outcome at 3 months corresponding to the modified Rankin scale $\leq$1. The secondary outcome was any intracranial hemorrhage (ICH) within the initial 36 hours. We examined whether each lipid profile was predictive of these outcomes. **Results:** Of 600 patients, those with a premorbid modified Rankin scale $\geq$2 or those who had lack of any lipid profiles or initial MRI were excluded. Of 408 included patients (140 women, 70.9 $\pm$ 11.1 years old), 48 patients used statins prior to stroke. One-hundred and fifty-eight patients (38.7%) had favorable outcome. HDL-C level in patients with favorable outcome was higher than in those with unfavorable outcome (1.40 $\pm$ 0.40 mmol/l versus 1.32 $\pm$ 0.37 mmol/l, $p=0.025$), whereas other lipid levels or frequency of prior statin use were not different between two groups. The patients with favorable outcome were gradually increased with HDL-C levels divided into tertiles (32.1%, 39.1%, 44.9%). After multivariate analysis, HDL-C level was only independently related to favorable outcome among lipid profiles (OR 1.89; 95%CI 1.02-3.50 per 1-mmol/L, $p=0.043$). For 164 non-cardioembolic patients, HDL-C level was also independently related to favorable outcome (OR 2.95; 95%CI 1.11-7.83, $p=0.030$), although it was not for 244 cardioembolic patients. Any ICH occurred in 76 patients (18.6%).

There were no significant associations between ICH and any lipid profiles. **Conclusions:** Baseline HDL-C level was associated with favorable outcome at 3 months after IV rt-PA therapy for acute ischemic stroke.

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Th P29

Interspecies Differences of Chemokine Receptor and Ligand Expression in Neural Stem Cells and their Implications for Neuroregenerative Medicine

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Introduction: Recent studies show the potential of intravascular stem cell therapies for the treatment of stroke. Neural stem cell(NSC) homing in intravascular stem cell therapy and subsequent intraparenchymal migration relies on NSC expression of chemokines and their receptors. As these therapies come closer to clinical trials, it is essential to understand the interspecies differences of chemotaxis related receptor and ligand expression to expedite the transition from rodent research to human application. Here we use RT-qPCR to compare human neural stem cell (hNSC) and mouse neural stem cell (mNSC) chemokine receptor and ligand expression at basal levels. Furthermore, we compare hNSCs and mNSCs after exposure to MCP-1 to test the response of NSCs to a chemokine shown to be upregulated in the microenvironment of the ischemic brain. Finally, we explore the implication of these differences on cell migration. **Methods:** Human and mouse cells were grown as monolayers in their respective growth media. In pretreated cell groups, MCP-1 (20ng/mL) was introduced to cell media 1 hour prior to RNA extraction. RT-qPCR was performed on extracted RNA using microarray technology for chemokine receptors and ligands. The Boyden chamber migration assay was used to determine migration to SDF-1 at concentrations 0ng/mL, 100ng/mL, 500ng/mL, 1000ng/mL, and 1500ng/mL. **Results:** Analysis of baseline expression demonstrated that 18% of analyzed factors were different between hNPCs and mNPCs ($p<0.001$). The five factors with the largest fold regulation difference between hNSCs and mNSCs are CCL2, CCL7, CXCL12, CMLKR1, and CXCR4. After treatment with MCP-1 there was a 1.61% change in factor expression between human and mouse chemokine. Of the mRNA transcripts upregulated above 3 fold regulation, ligands accounted for 6 of 6 factors in mNPCs and 1 of 1 in hNPCs. Of the mRNA transcripts downregulated below -3 fold regulation, receptors accounted for 5 of 5 factors in mNPCs and 1 of 3 in hNPCs. Migration of hNSCs compared to mNSCs in response to SDF-1 was greater by 2.46 fold ($p< 0.01$), consistent with the greater expression of CXCR4 on hNSCs than mNSCs. **Conclusion:** Baseline chemokine receptor and ligand expression between human and mouse NSCs was significantly different, possibly resulting in interspecies differences in NSC response to the ischemic brain microenvironment. In the context of cell therapy for stroke, the implications of interspecies distinctions should be strongly considered when conclusions drawn from rodent research are translated to human treatment.

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Th P30

Interleukin-6 Promoter Polymorphism Predicts Stroke Severity and Outcome in Acute Ischemic Stroke Patients from North India

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Introduction: Interleukin-6 (IL-6) plasma levels and function are genetically influenced. In particular, a guanine/cytosine substitution occurring in position -174 of IL-6 gene promoter changes the expression of IL-6 circulating proteins. IL-6 is known to be involved in the pathogenetic mechanisms of acute ischemic stroke. Studies in stroke, however, report conflicting data regarding the association of the frequency of GG/GC/CC genotypes and risk of stroke. Further, it is not known whether this gene polymorphism correlates with the severity and prognosis of stroke.Hypothesis:We studied the occurrence of IL-6 -174 G/C polymorphism in patients of acute ischemic stroke and correlated it with stroke severity and outcome. **Methods:** 59 patients with acute ischemic stroke and 120 age and sex-matched healthy controls were studied. IL-6 genotypes were evaluated by polymerase chain reaction and restriction enzyme analysis. Stroke was categorized by Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification. Severity was assessed clinically by National Institute of Health Stroke Scale (NIHSS) and by infarct volume on Diffusion Weighted Imaging on MRI. Outcome measures included mortality, Modified Rankin Scale (MRS) and Barthel index at 3 months. Serum levels of IL-6 were assessed in stroke patients (during acute phase) and in controls by ELISA. **Results:** Frequency of GG, GC and CC genotypes did not differ significantly between cases and controls [GG 63 % vs 71 %, ($p=0.99$), GC 22 % vs 21 %, ($p=0.25$) and CC 15 % vs 18 % ($p=0.25$)]. Of the two alleles, G allele was more common in both cases (73.7%) and control groups (81.2%). Patients with GG ($r=0.263$, $p=0.04$) and GC ($r=0.258$, $p=0.04$) genotypes had more severe stroke clinically. However, there was no radiological correlation. Serum levels of IL-6 following acute stroke (mean 4.4 $\pm$ 1.6; median 4 days) were higher in cases than controls (14 pg/ml vs 2pg/ml) but did not correlate with presence of any genotype. No specific association was seen between frequency of genotypes and stroke subtypes. Only the patients with GC genotype were found to have significant worse outcome on MRS at 3 months ($p=0.02$). Of the patients with GG genotype, 3 patients died at 3 months [3/32 patients (9.3%)] compared to those with GC [4/13 patients (31%)] and CC [3/8 patients (37%)] genotypes. This difference was statistically significant($p=0.03$). **Conclusions:** Frequency of IL-6-174 G/C promoter polymorphism did not differ between acute ischemic stroke patients and normal controls. Patients with GC genotype had worse outcome on MRS at 3 months. Patients with GG genotype had decreased mortality at 3 months when compared to those with GC and CC genotype which thus appears to be protective.

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Th P31

Brain Plasticity Changes In Patients With Vascular Lesions

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Background: Brain plasticity is influenced by many factors in patients with lesions (e.g. tumor, vascular lesion). Age, gender, handedness, lesion location and volume are few of the putative factors that have been implicated. The proximity of lesions to functional cortex is also a significant factor influencing brain plasticity changes[1]. **Objective:** We investigated whether vascular lesions altered cortical language representation in right handed individuals. In a majority of normal right-handed subjects, the language function is lateralized to the left hemisphere[2]. However, this left hemispheric dominance for language has been known to shift depending on distance of lesion from functional areas involved in language [1,2]. **Methods:** We retrospectively analyzed data from right handed patients with vascular lesions ($N = 67$, 38 females) who underwent preoperative functional imaging to locate their dominant language hemisphere. Vascular lesions were either AVMs, ($N = 42$) or cavernomas ($N = 23$) or other ($N=2$). Forty-six patients had lesion in the left hemisphere. Functional changes were characterized using BOLD fMRI acquisition during the antonym word generation, letter word generation and text reading tasks. Lateralization Index (LI) was determined for Broca's and Wernicke's areas by measuring area of activation in left(L) and right(R) homologous brain regions and calculated using the formula (L-R)/(L+R). **Results:** Distance from lesion to center of Wernicke's activation was significantly associated with language lateralization ($p < .05$). Patients with distance less than 10 mm had language lateralized to the right hemisphere. Distance from lesion to center of Broca's activation was not significantly associated with language lateralization. No significant associations were found between demographic variables such as age, gender or handedness. No significant associations were found between lesion characteristics such as volume, lesion type, and lesion location. **Conclusions:** These results suggest that patients with vascular lesions such as AVMs or cavernomas show a shift in hemispheric dominance for language with the homologous regions in the right hemisphere playing a greater role in language processing than is commonly observed in most healthy right handed normals. References: 1. Yetkin, F.Z., Swanson, S., Fischer, M., Akansel, G., Morris, G., Mueller, W., & Haughton, V. (1998). Functional MR of frontal lobe activation: Comparison with Wada language results. American Journal of Neuroradiology, 19, 1095-1098. 2. Springer JA, Binder JR, Hammeke TA, Swanson SJ, Frost JA, Bellgowan PS, Brewer CC, Perry HM, Morris GL, Mueller WM. Language dominance in neurologically normal and epilepsy subjects: a functional MRI study. Brain, 122, 2033-46, 1999.

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Th P32

Metabolic Profile Of Motor Cortex In Stroke

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Non-invasive detection of sensitive metabolic markers could broaden our understanding of pathophysiological processes underlying post-stroke plasticity linked to neuronal-glial interactions. The goal of this study was to investigate whether certain metabolites, which are specific to neurons, glial cells, or the neuronal-glial neurotransmission system, in spared (radiologically normal-appearing) primary and non-primary motor areas in either the ipsilesional or contralesional hemisphere, are altered in stroke, and whether these alterations correlate with clinical motor severity. Survivors of a first ischemic stroke located outside the primary and non-primary motor areas and age- and sex-matched healthy controls were included. N-acetylaspartate, myo-inositol, and glutamate/glutamine were measured by using proton magnetic resonance spectroscopy (1H-MRS) in spared gray matter of the hand representation area, identified by functional MRI, in the primary motor cortex (M1), dorsal premotor cortex (PMd), and supplementary motor area (SMA), bilaterally measured. Studies were carried out during the chronic stage (>six months post-onset), and differences in metabolite concentrations relative to those of healthy controls were evaluated, as well as analyses of metabolite correlations within each region of interest. Relationships between metabolites concentrations and arm motor impairment were also evaluated. Primary findings revealed significant

metabolite differences across hemispheres and regions of interest between stroke and controls for N-acetylaspartate and myo-inositol, but not for glutamate/glutamine. In the ipsilesional hemisphere, we found decreased N-acetylaspartate along with stronger correlations between N-acetylaspartate and glutamate/glutamine within M1, increased myo-inositol within PMd, and decreased N-acetylaspartate and stronger correlations between all metabolites within SMA. In the contralesional hemisphere, we found significant changes only within M1, i.e., increased ml and stronger correlations between N-acetylaspartate and glutamate/glutamine. Ipsilesional N-acetylaspartate and glutamate/glutamine within M1 and N-acetylaspartate within PMd were positively correlated with arm motor impairment while contralesional N-acetylaspartate with time post-stroke. Our preliminary results demonstrated that in chronic phases of stroke, significant alterations of the neuronal-glial interactions occur in primary and non-primary motor areas, with the largest changes occurring in the ipsilesional hemisphere. The 1H-MRS approach proposed here can be used as a valuable tool in the study of metabolite concentrations and metabolic connectivity patterns within spared motor areas post-stroke.

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Th P33

MR Spectroscopic Analysis Of Stroke Patients Treated With Autologous Mononuclear Cells Shows Increased NAA/Cr Suggestive Of Neurogenesis

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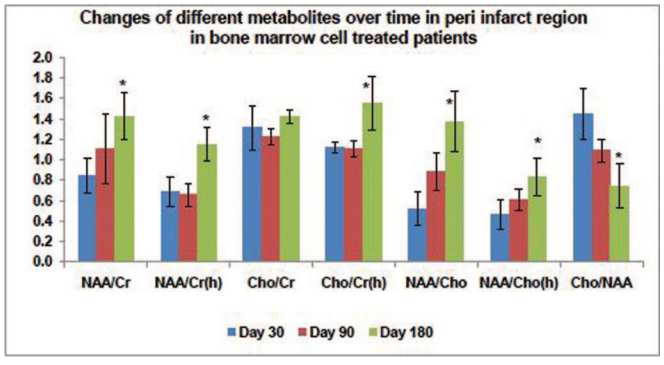
Background and Purpose: N-acetylaspartate (NAA) is a potential marker of neurons, on Magnetic Resonance Spectroscopy (MRS) of the brain. Studies have found that NAA decreases in the peri-infarcted regions of the brain within 2 weeks after stroke followed by a continued, slow decline in NAA during the chronic stages over years. Animal models of stroke suggest that bone marrow mononuclear cells (MNCs) reduce infarct lesion maturation, promote neurogenesis, and improve neurological outcome. We are conducting a safety and feasibility study of autologous MNCs administered to stroke patients within 24 to 72 hrs after symptom onset. We are conducting serial MRS imaging on all study patients in order to identify potential biological activity that MNCs may exert within the brain. We analyzed our MRS data to address the hypothesis that MNCs reduce neuronal death and/or promote neurogenesis in the peri-infarct area after stroke. **Methods:** As part of a clinical trial, 10 ischemic stroke patients underwent bone marrow harvest and intravenous transplantation of autologous mononuclear cells within 24 to 72 hrs after symptom onset. Single voxel proton Magnetic resonance spectroscopy on a 3T scanner at baseline and on days 30, 90, 180 were performed to measure different metabolites such as NAA, Choline(Cho), and Creatinine in the peri infarct region. **Results:** Figure 1 shows the mean changes of various metabolite ratios in the peri-infarct region for all the enrolled patients. There was a significant increase in NAA/Cr and NAA/Cho from day 30 to day 180 whereas the Cho/NAA showed a significant decrease during this period. We were not able derive base line data for most of the enrolled patients for this study and could not address if MNCs reduce neuronal death within 30 days after stroke. **Conclusion:** Our preliminary results demonstrate that autologous bone marrow MNCs administered in the subacute stages of stroke might prevent neuronal loss and might promote neurogenesis or repair in the peri-infarct area after 30 days. These findings potentially may confirm animal studies that mononuclear cells could be cytoprotective and/or enhance neurogenesis. However, it remains unproven that NAA/Cr or other spectroscopic metabolites can be used as a marker to investigate neuroprotection or neurogenesis. These findings may also reflect recovery of neuronal metabolism, restoration of function of existing neurons, or possibly increased dendritic sprouting or synaptogenesis. These results are preliminary and limited by the small sample size.



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Th P34

Suppression Of Infarct Expansion In Stroke Patients Administered Autologous Bone Marrow Mononuclear Cells

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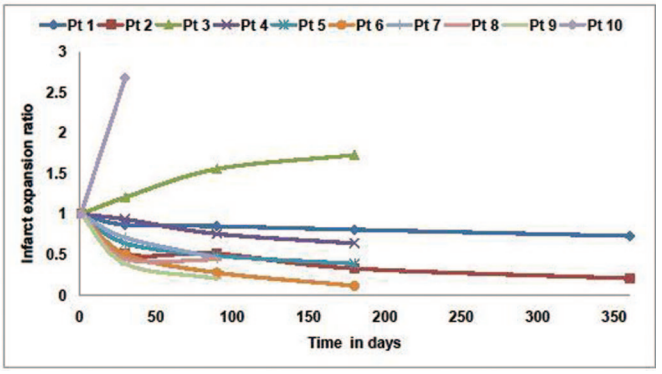
Background and Purpose: Animal studies suggest that bone marrow mononuclear cells when administered in the first few days after stroke improve neurological outcome by reducing infarct maturation. We therefore studied the changes in lesion volume in patients with acute ischemic stroke enrolled in a clinical trial testing the safety of autologous bone marrow mononuclear cells. **Methods:** As part of a clinical trial, 10 patients with MCA ischemic strokes underwent bone marrow harvest and transplantation of autologous mononuclear cells within 24 to 72 hrs after symptom onset. Multimodal MRI on a 3T scanner with T1/T2, DWI, FLAIR and perfusion imaging are being performed at baseline and on days 30, 90, 180, and 360 to assess for structural changes. Over the same time period, 10 patients with MCA ischemic stroke meeting inclusion criteria for our study were retrospectively selected as controls from our prospectively collected stroke database for which the baseline DWI was performed at 24 hrs after stroke and a T2/FLAIR was performed at 30 days after stroke. 31 lesion volumes from 9 study patients and 20 lesion volumes from 10 control patients were calculated using a published method of hand drawn region of interests (ROI) multiplied by the slice thickness by a single rater with extensive experience in neuroimage data processing to avoid inter-rater variability. The infarct expansion ratio (IER) was calculated as the ratio of the lesion volume on FLAIR at 30 days compared with the initial DWI lesion volume at baseline. **Results:** Fig 1 shows the lesion volume changes to date of all the patients enrolled ($n=10$) in the bone marrow study. Except for two patients who underwent elective hemicraniectomy 4 days after stroke (patient 3 and 10), none of the study patients showed infarct expansion. However, the stroke patients that were retrospectively collected from our database had expansion of the lesion volume at 30 days. The mean IER at 30 days in the these "control patients" was 1.6 ± 0.4 and in the cell treated patients was 0.9 ± 0.2 ($p<0.05$). **Conclusions:** Our preliminary results demonstrate that in patients with subacute stroke receiving autologous bone marrow mononuclear cells, the lesion volume does not expand but even decreases over time. These findings suggest that autologous bone marrow mononuclear cells may suppress infarct expansion and may confirm animal studies reporting that mononuclear cells are cytoprotective and reduce infarct maturation. The results are limited by their preliminary nature and the small sample size.

Fig 1.



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Th P35

Alternation of Functional Connectivity after Corticospinal Tract Infarction -A Longitudinal Case-control Functional MRI study-

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Background: The physiological process during motor recovery after stroke still remains uncertain. The aim of this study was to characterize the alternation of functional connectivity compensating the motor dysfunction in stroke patients. **Methods:** Ten right-handed patients with pure motor hemiparesis due to supratentorial corticospinal tract infarction of first-ever stroke (9 men, mean age of 72.7 years) were prospectively examined and compared with 10 matched controls. The patients underwent serial functional MRI of finger tapping tasks with a 3T-MRI scanner at 3 time points; within 2 weeks (Scan1), at 1 month (Scan2) and at 3 months (Scan3) after stroke onset. Chronological and case-control comparisons of each of conditional (rest vs. task) analyses and psychophysiological interaction (PPI: functional connectivity) analyses were conducted in a voxelwise manner. **Results:** In conditional analyses of paretic hand task, in Scan1 of patients, both sides of supplementary motor areas (SMA), contralesional primary motor area (M1), dorsal premotor area (PMd), ventral premotor area (PMv) and ipsilesional PMd showed greater activity than controls, and in Scan2 and Scan3 of patients, activity of both sides of SMA, ipsilesional PMd, PMv, contralesional cerebellum became greater. In PPI analyses, functional connectivity between ipsilesional M1 and PMd become greater

during the course. Contralesional motor related areas ,such as M1, PMd, and PMv, acquired greater functional connectivity with ipsilesional PMd, not directly with ipsilesional M1 in the first 2 weeks, and this functional coupling decreased during the later course of recovery. **Conclusions:** These results indicate that cortical reorganization compensating impaired motor network dynamically occurs through acute and chronic phases, and this alternation is not in an unidirectional manner over time. Staged rehabilitative intervention according to time course after stroke may contribute to effective achievement of successful motor recovery.

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Th P36

Axonal Outgrowth And Myelination In The Cortical Peri-infarct Area After Human And Experimental Stroke

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Background & **Purpose:** Axonal remodeling is critical to brain repair after stroke. Phosphorylated neurofilament (pNFH) participates in axonal growth. We analyzed the pNFH levels and myelination in ischemic rat and human brains after stroke. **Methods:** Adult rats subjected to middle cerebral artery occlusion (MCAO) were sacrificed at 7, 28, and 56 days after stroke (n=5/group). Sham operated rats (n=4) were used as a control group. Human brain samples of acute (n=3) and chronic (n=2) ischemic cerebral infarction were also studied. The pNFH and myelin basic protein (MBP, a marker of oligodendrocytes) expression were measured immunohistologically. The percentages of axonal density within the total areas were calculated using Image J. In vitro, a Standard Neuron Device, which separates axons from neuronal cell bodies, was used to measure axonal changes in rat cortical neurons challenged by oxygen-glucose deprivation (OGD) (n=3). Co-culture of neurons with differentiated N20.1 cells, an oligodendrocyte progenitor cell line, was employed for analysis of axonal myelination. **Results:** Analysis of confocal images revealed that sham-operated rats exhibited pNFH (33±14%) immunoreactivity in the cortex and the majority of pNFH was myelinated as measured by co-localization with MBP. Stroke in rats decreased pNFH to 25±11% and MBP immunoreactivity in the cortical ischemic boundary at 7 days ($p<0.01$). However, 56 days after stroke, pNFH density levels reached 33±13%, which was concurrent with an increase of MBP immunoreactivity compared with 7 days after stroke (78±6% vs 50±12%, $P<0.01$), indicating that these axons are remyelinated. In vitro, neurons challenged by OGD exhibited a reduction of axons at 24h (3.4, $P<0.01$), whereas regrowth of axons (2.7, $P<0.01$) and an increase in pNFH protein levels (2.7, $P<0.05$) were detected at 96h after OGD. In addition, these axons were myelinated by oligodendrocytes. Furthermore, in human brains, pNFH substantially increased in peri-infarct areas of chronic infarction compared to acute infarction (42±10% vs 23±6%, $P<0.01$). Many of pNFH axons detected in chronic infarction were co-localized to MBP immunoreactivity. **Conclusions:** The present study indicates that during stroke recovery, axonal outgrowth and myelination occur in the ischemic boundary regions of rodent and human ischemic brains.

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Th P37

Direct Generation Of Neurosphere-like Cells From Human Dermal Fibroblast

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Background and Purpose: Although a number of experimental evidences have shown that transplantation of neural stem cells (NSCs) can promote neurologic recovery after stroke, the lack of autologous NSCs prevented clinical trials so far. Reprogramming of human fibroblast by delivering four factors (Oct3/4, Sox2, Klf4, and c-Myc) generate pluripotent stem cells (iPS) resembling embryonic stem cells (ESCs). Currently, developing non-tumorigenic alternative methods for the induction of iPS and controlling its differentiation are the key issues. However, the direct generation of NSCs from human fibroblast has not been successful. Here we describe a direct induction of neurosphere-like cells from human fibroblast without genetic manipulation. **Methods:** Primary human fibroblasts were cultured from skin tissues, and immortalized human NSCs were prepared from human fetal telencephalon cultures via a retroviral vetor encoding v-myc. We generated iNS by transfecting proteins from the human NSCs into human fibroblasts, and by maintaining the cells in neurosphere culture conditions. The cells were used for various in vitro and in vivo validations, and were further differentiated into neurons. **Results:** The fibroblasts were transformed into sphere morphology and generated secondary and tertiary neurospheres. These induced neurosphere-like cells (iNS) expressed NSC markers, such as Sox2 and musashi1, and had full demethylations of Sox2 regulatory regions, which has been observed in NSCs. Genetic fingerprints and chromosomes of iNS were identical to those of the skin donor. iNS were differentiated to express neural and glial markers spontaneously, and expressed sodium channels in a forced differentiation into neuron. However, iNS still had some genetic characteristics of fibroblast as determined by the gene expression profiles, and thus were likely to be partially-reprogrammed. **Conclusion:** Our results provide a novel concept for the direct generation of autologous neurosphere-like cells from human skin tissue. After further studies to optimize the reprogramming method, iNS can be used to regenerate the damaged brain after stroke.

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Th P38

Stroke Survivors Employ Different Stiffness Control Strategies during Learning of Reaching Movements in a Dynamic Environment

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Background: Performing reaching movements in a dynamic environment requires accurate control of endpoint stiffness. With learning, significant changes occur in the orientation and the area of the endpoint stiffness ellipse. Stroke results in sensorimotor abnormalities that can affect control of such movements. The purpose of this study, supported by the AHA (#0820136Z), was to determine if endpoint stiffness control during learning of reaching movements in a dynamic environment is affected by stroke. **Methods:** Chronic stroke subjects performed reaching movements using Inmotion2 robotic system (Interactive Motion Tech Inc., MA). Reaching movements were performed with the affected arm in a velocity-dependent force field that deviated the movement perpendicular to the direction of motion. All subjects received actual feedback of their movement. The effect of the learning period (baseline, early and late dynamic training) was tested for each of the eight targets (located at 90°, 135°, 180°, 225°, 270°, 315°, 0° and 45° with respect to the positive x-axis). The dependent variables were the stiffness ellipse orientation and area. **Results:** A significant effect of the learning period was revealed for the stiffness area for the targets at 270° ($p=0.021$) and 315° ($p=0.020$). Post-hoc tests revealed that for the target at 270°, dynamic training increased the stiffness area while at 315°, it reduced the stiffness area. A significant effect of learning period was revealed for the orientation for the targets at 270° ($p=0.022$) and 315° ($p=0.020$). Post-hoc tests showed that for target at 270°, dynamic training caused the stiffness orientation to shift towards the perturbation axis while at 315°, the shift was towards the movement direction. **Conclusions:** Stroke survivors demonstrated significant stiffness control for learning movements towards themselves than away from the body. This is expected because the effects of stroke symptoms like muscle weakness and spasticity are higher for movements away from the body than towards. During learning of reaching movements in dynamic environments, stroke survivors employ different stiffness control strategies for different directions probably because the direction of muscle activations are affected by the stroke symptoms. In some directions, learning is achieved by increasing the amount of stiffness (increased area) and directing the stiffness towards perturbation while in others, learning is achieved by reducing stiffness and directing it towards the direction of motion. These results provide useful information for designing specific force fields for stroke rehabilitation.

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Th P39

Study of NTx®-265: Human Chorionic Gonadotropin (hCG) and Epoetin Alfa (EPO) in Acute Ischemic Stroke Patients (REGENESIS Trial)

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Introduction: Preclinical studies suggest that certain growth factors given in the early days after stroke can improve long-term behavioral outcome. An earlier study ("BETAS trial") found that 3 doses of b-hCG followed by 3 doses of erythropoietin was safe. The current trial (NCT00938314) examined this sequential growth factor study in a Phase IIa, placebo-controlled, double-blind, randomized trial. **Methods:** Entry criteria included NIHSS 8-20, supratentorial ischemic stroke, 24-48 hr post-stroke at start of therapy; tPA administration was an exclusion criterion. Patients received 3 QD doses of SQ b-hCG (10,000 IU) followed by 3 QOD doses of IV erythropoietin (EPO). There were 3 equally sized cohorts, each randomized to active:placebo in a 3:1 ratio: in Cohort 1, EPO dose=4,000 IU; Cohort 2, 12,000 IU; Cohort 3, 20,000 IU. Primary outcome measure was change in NIHSS from enrollment to d90. Secondary outcome measures included modified Rankin Score (mRS) and Barthel Index at day 90, plus an array of exploratory assessments. Due to financial constraints, enrollment was reduced to 96 patients and moved to India (18 sites). **Results:** A total of 8 patients died during the trial, the distribution of which did not differ by treatment assignment. All but 4 living patients received all 6 study doses as planned. Patients were 65 M/21 F, mean (SD) age = 58 (12) yr. At least one 15 minute session of post-stroke OT was provided to 25% of patients; PT, to 81%; and ST, to 29%. Median NIHSS at baseline, prior to therapy, was 12.7, decreasing to 7.9 at d30 and 6.0 at d90. There was no significant difference between active therapy and placebo in any endpoint, whether the 3 Cohorts were examined separately or together. Among those patients who received OT, both the change in NIHSS and the mRS were significantly better among those receiving active therapy as compared to placebo. **Discussion:** The current trial did not find that sequential growth factor therapy initiated 24-48 hours after stroke onset was associated with improved outcome at 90 days based upon the primary outcome measure. The current trial did demonstrate that, in the setting of moderate to severe acute ischemic stroke, sequential hCG and EPO are safe at the EPO doses examined. Future studies might restrict enrollment to those subjects likely to receive physiotherapy.

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Th P40

Difference In Platelet Activation Pattern Between Patients With Ischemic Stroke And Those With Obstructive Sleep Apnea Syndrome

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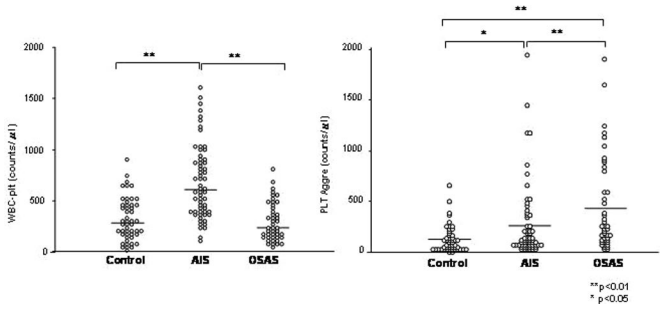
Difference in platelet activation pattern in stroke and sleep apnea **Background:** Platelets play a crucial role in the pathogenesis of acute ischemic stroke (AIS). Obstructive sleep apnea syndrome (OSAS) is also associated with platelet hyperaggregability, resulting in high cardiovascular morbidity and mortality. However, state of platelet activation in OSAS is not fully understood and may be different from that in AIS. **Purpose:** The aim of the present study is to assess platelet function in AIS and OSAS with the use of flow cytometry and to determine the difference in the pathogenesis between the two diseases. **Methods:** Sixty three AIS patients (M/F 40/23, 67±16 y/o, Subtype atherothrombosis, 2-23 days after onset), 47 OSAS patients (M/F 41/6, 50±12 y/o), and 50 non-AIS/non-OSAS controls (M/F 21/29, 53±14 y/o) were studied. Platelet activation was detected for white blood cells-platelet aggregates (WBC-plt) and platelet-platelet aggregates (Plt aggre) by using 3 color flow cytometry. **Results:** Amount of WBC (median(25-75%) counts/μl in blood) in each group was 4905(4000-6075)in controls, 7300(5800-8400) in AIS, 5700(4900-6450) in OSAS, respectively. WBC counts in both AIS and OSAS increased significantly compared to those in controls. Circulating WBC-plt increased in AIS, however those in OSAS did not. Plt aggre in both AIS and OSAS increased significantly compared to those in controls. The magnitude of the increase in Plt aggre in OSAS was significantly higher than AIS. **Conclusion:** The results indicate that process of platelet activation in OSAS is different from that in AIS, and suggest that platelet activation in OSAS is not due to vascular inflammation and atherosclerotic changes observed in AIS. Platelet activation in OSAS might be due to increased plasma catecholamine levels resulting in vascular contraction during apnea.



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Th P41

Genome-wide Search for Ischemic Stroke Genes: The Siblings with Ischemic Stroke Study (SWISS)

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Introduction: Genome-wide association studies of stroke have failed to yield any findings that consistently replicate across studies. However, family based designs have yielded estimates of heritable risk suggesting there are genetic factors involved in the etiology of ischemic stroke. The goal of SWISS is to further refine family based studies of stroke by employing an affected sibling-pair (ASP) design to attempt to discover novel loci for ischemic stroke, as well as for specific stroke subtypes (using TOAST criteria). These results are based on a recruitment of 300 ASPs. Materials and**Methods:** Probands were recruited at 65 US medical centers and 5 Canadian medical centers including adult (>18 years old) men and women presenting with a neurologist-confirmed ischemic stroke. Stroke-affected siblings of the probands (concordant siblings) were recruited using proband-initiated contact. DNA was extracted from peripheral blood. A total of 286 cases and 93 controls were successfully assayed using Illumina Linkage III panels. Standard genotyping quality control was conducted prior to analyses, and yielded a total of 5,699 SNPs. Transmission disequilibrium (sib-TDT) test based on clustered-analyses of sibship concordance and discordance of phenotypes incorporating the Cochran-Mantel-Hantzel procedure were used to compare within and between clusters of participants. We estimated the Bonferroni corrected threshold for significance at 8.78×10^{-6}. **Results and Conclusions:** In these preliminary results, we did not detect any results passing Bonferroni correction, although we have identified candidate loci that we will pursue as part of a sequencing effort to identify familial/rare variants associated with stroke. Currently, we are adding over 412 samples as recruitment is ongoing for the genetic component of SWISS, allowing for the pursuit of more evasive risk variants with an increased sample size yielding greater statistical power.

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Th P42

Results of NOTCH3 Sequencing in Siblings with Ischemic Stroke Study Probands

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Background: Mutations within the NOTCH3 gene are responsible for the disorder cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL). NOTCH3 contains 33 exons; however, mutations causing CADASIL appear to be restricted to the first twenty-four exons and result in the gain or loss of a cysteine amino acid. The role of common exonic NOTCH3 variation and mutations in exons 25-33 in stroke remains unresolved. **Methods:** All 33 exons of NOTCH3 were sequenced in 275 probands from the Siblings With Ischemic Stroke Study (SWISS). SWISS is an affected sibling pair study in which probands were enrolled across the US and Canada. SWISS participants were excluded from enrollment if they were known to have had CADASIL on clinical grounds. **Results:** One of 275 probands (0.4%) was identified as carrying a known CADASIL mutation (p.R558C). This was a case of a 57-year-old Caucasian man with a TOAST subtype of small-artery occlusion. Nine novel non-synonymous variants were identified in exons both before and after exon 24. One of the novel variants in exon 4 results in a histidine-to-arginine substitution (p.H170R) that is adjacent to known CADASIL mutants (p.R169C and p.G171C). The p.H170R mutation occurred in a 75-year-old Caucasian woman with a TOAST subtype of 'other determined etiology'. She had an extensive medical history consisting of more than three ischemic strokes, bilateral carotid endarterectomies, diabetes mellitus, and coronary artery disease. **Conclusion:** Variants outside the first 24 exons of NOTCH3 and those that do not alter a cysteine residue deserve further study in relation to ischemic stroke. Novel variants are being screened in other affected siblings in SWISS and in a 'sporadic' case-control series. The results of this sequencing in familial patients, assessed pathogenicity of the novel variants and the association of common variation at the NOTCH3 locus with ischemic stroke will be presented.

Table. NOTCH3 sequence variants in SWISS Study Probands. Known pathogenic mutation is highlighted.

Exon	Genotype	rs#	Amino Acid
4	A>G	N/A	H170R
9	C>T	rs11670799	P496L
9	C>T	N/A	S497L
11	C>T	N/A	R558C
18	C>T	N/A	H981Y
19	G>C	rs35769976	A1020P
19	G>T	N/A	W1028L
21	C>A	N/A	H1133Q
22	G>A	rs10408676	V1183M
25	C>G	N/A	L1547V
28	G>A	N/A	G1710D
32	G>A	N/A	V1952M
33	C>T	N/A	P2033L
33	G>T	N/A	G2081V
33	C>T	rs1044009	A2223V

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Th P43

Image analysis of participants in the Siblings With Ischemic Stroke Study (SWISS)

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Background: White matter hyperintensity (WMH), or leukoaraiosis, is a radiographic marker of small cerebral vessel disease associated with lacunar stroke and intracerebral hemorrhage in stroke-affected populations. Limited data are available on WMH burden in families with symptomatic cerebrovascular disease. We sought to characterize WMH volume (WMHV) in participants in SWISS. **Methods:** SWISS is a pedigree-based study recruiting adults with confirmed ischemic stroke and their stroke-affected and unaffected siblings. Clinical images from participants are centrally adjudicated with MRI scans converted to Analyze format using MRIcro software (University of Nottingham School of Psychology, UK). Axial FLAIR images were used for computer-assisted volumetric analysis of WMH. DWI was used to measure acute infarct volumes. WMHV was calculated by doubling WMHV from the stroke-unaffected hemisphere for supratentorial infarcts and summating WMHV from both hemispheres for infratentorial infarcts. All WMHV measurements were adjusted to head size. Two readers blinded to clinical data evaluated each study. A radiologist reviewed a subset of scans and compared to the readers' values for estimates of inter-rater reliability. **Results:** A total of 26 sibling pairs and 148 individuals without a scan from a sibling pair were analyzed. Correlations for volumetric estimates across readers (r=0.96-0.97) as well as with the radiologist (r=0.96-0.98) were excellent. The table includes summary data for the 26 sibling pairs. Infarct and WMH volumes were not normally distributed. After log transformation, acute stroke volumes in probands and concordant siblings showed strong correlation (r=0.79-0.84). Across the cohort, WMHV significantly differed by stroke subtype (p=0.00013). Median WMHV for those with cardioembolic mechanism was 1.93 cm^3, large artery atherosclerosis 2.06 cm^3, small vessel disease 2.87 cm^3, and undetermined = 3.36 cm^3. For concordant siblings, 20/44 (45%) had undetermined stroke subtype compared with 36/154 (23%) probands. **Conclusions:** The SWISS imaging repository expands the exploratory potential of this unique genetic database in relationship to complex cerebrovascular phenotypes. Using a validated, semi-automated method with high inter-rater correlation estimates, we demonstrated that acute infarct volumes are highly correlated in siblings with stroke, likely attributable to heritability of specific mechanisms of cerebral ischemia. The novel finding of a within-family correlation of acute infarct volume requires replication.

Table:

	Probands (paired)	**Concordant Siblings**
Intracranial area [median (IQR)]	14816 (14354, 15596)	14389.26 (14058, 14992)
WMH [mean]	6.70	7.42
WMH [median (IQR)]	4.27 (1.40, 10.53)	3.52 (1.54, 8.93)
Acute stroke volume [mean]	5.19	10.24
Acute stroke volume [median (IQR)]	0.50 (0, 1.89)	0.28 (0, 5.70)
	Probands (paired)	**Discordant Siblings**
Intracranial area[median (IQR)]	15421 (15333, 15633)	1622 (15458, 16483)
WMH [mean]	4.87	0.91
WMH [median (IQR)]	0.91 (0.42, 11.60)	0.86 (0.82, 1.11)
Acute stroke volume [mean]	7.67	N/A

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Th P44

Ischemic Stroke Exome Pilot Study

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Background and Purpose: The genetic architecture of ischemic stroke is complex and likely to include rare or low frequency variants with high penetrance and large effect sizes. Such variants are likely to provide more important insights into disease pathogenesis compared to common variants with very small effect sizes. Because a significant portion of human functional variation may derive from the protein-coding portion of genes we undertook a pilot study to identify variation across the human exome (i.e., the coding exons across the entire human genome) in 10 ischemic stroke cases. **Methods:** To maximize the genetic contribution to stroke risk, 10 cases were selected based upon their early age-of-onset, a positive family history of stroke, and the presence of no (or minimal) standard stroke risk factors. These cases included 8 African-Americans and 2 Caucasians; and 5 lacunar, 2 cryptogenic, 2 dissection, and 1 cardioembolic subtypes. Agilent SureSelect technology was used to capture all predicted human exons after constructing 75bp paired-end Illumina sequencing libraries. The fragments were then sequenced using the Illumina Genome Analyzer IIx platform and aligned to UCSC Human Genome build 18 (NCBI build 36.1) using Burrows-Wheeler Aligner. **Results:** Each sequenced sample generated an average of 3.8Gbp over 25.5 million read pairs with 97% of the reads aligning uniquely and 71% mapping to +/- 200bp of the targeted regions. After applying quality filters, African-Americans showed greater variation with an average of ~24.5K variants compared to ~22.4K for Caucasians, as expected from the literature; the number of novel variants (not in dbSNP) was 2839 (11.6%) vs.1105 (4.9%), respectively. Pursuing the hypothesis that stroke susceptibility genes may be enriched for novel variants across cases, we identified 70 genes where each African-American case had at least one rare variant but only 48 when the 2 Caucasian cases were included. Under a double-hit hypothesis of two novel variants in the same gene, only 6 genes were identified. Three of the six genes are involved in carbohydrate and/or lipid metabolism, and of these, one was previously associated with diabetes. Of the three remaining genes, one is involved in the inflammatory response, one is solely expressed in the CNS, and the function of the last is unknown. **Conclusions:** We obtained high capture efficiency and excellent coverage of the exome in our 10 case samples. African-Americans had greater coding diversity than Caucasians as expected. We identified 48 genes where each case had at least one-novel variant and 6 genes with at least two. Exome sequencing will be a valuable tool for uncovering rare coding variants contributing to stroke risk.

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Th P45

Genome-wide SNP Association For Cerebral Vasospasm In Subarachnoid Hemorrhage Patients

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Objectives: In the United States, 10 per 100,000 people a year suffer from an aneurysmal subarachnoid hemorrhage (aSAH). aSAH is a destructive disease that occurs primarily in women and is associated with a 30% mortality and 30% morbidity rate. Cerebral vasospasm (CV) is a common and serious complication involving the constriction of cerebral arteries after aSAH. Brain damage from secondary ischemic deficit due to this vasospasm can lead to cerebral infarction and may cause poor outcomes. Despite therapies targeted toward the primary mechanisms associated with CV, controversy continues regarding the underlying pathogenesis of this condition; hence an effective therapy remains elusive. We examined an association of genetic variants across the entire human genome in aSAH patients to decipher the molecular-genetic mechanisms of altered cerebral blood flow velocity. **Methods:** Genotyping with Affymetrix SNP 6.0 array was performed at the National Institutes of Health with 279 patients with aSAH (197 females and 81 males, 53.1 $\pm$ 11.4 years old) recruited from University of Pittsburgh. This microarray-based technology allows whole genome screening with 1 million single nucleotide polymorphisms (SNPs) without specific functional genetic hypotheses prior to undertaking analysis. Clinical data was prospectively collected, including severity of injury (admission Hunt and Hess and Fisher scores), measurement of cerebral blood flow with the first 14 days of injury [cerebral angiography, daily transcranial Dopplers, mean flow velocity and lindegaard ratio (LR) and CT scans], and clinical evidence of neurological deterioration. Data potentially representing the CV were tested in association with genotypes. **Results:** The strongest significant associations were between rs10279206 in chromosome 7q36.3, rs6760279 and rs16865932 in chromosome 2p25.1 ($p=1.46 \times 10^{-2}$, $p=4.56 \times 10^{-2}$ and $p=4.99 \times 10^{-2}$ respectively) with LR with the multiple test corrections of Bonferroni threshold < 0.05. **Conclusion:** Despite the relatively small sample size used in this study, significant genetic loci of chromosome 7q36 and 2p25 were associated with an increased cerebral blood flow velocity detected by the LR in aSAH patients. This result implicates the role of genetics in altered cerebral blood flow velocity, which can influence on the prognosis of aSAH.

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Th P46

Prediction of Stroke and Ischemic Heart Disease by Carotid Intima-Media Thickness in Japanese Urban Cohort: The Suita Study

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Introduction: Carotid intima-media thickness (IMT) has been increasingly a subclinical marker for cardiovascular disease. However, few studies have examined the association of IMT with stroke and ischemic heart disease (IHD) in Asia. We assessed the hypothesis that carotid atherosclerosis was a predictor for stroke and IHD events in a general urban Japanese population. **Methods:** We studied 5,331 Japanese individuals (mean age 55.3 years, without stroke or IHD) who completed a baseline survey and carotid atherosclerosis in the Suita Study, and were then followed for 8.7 years on average. Carotid atherosclerosis was evaluated by high-resolution ultrasonography with atherosclerotic indexes of IMT in the common carotid artery (CCA), carotid artery bulb, and internal and external carotid arteries. Mean IMT was

defined as the mean of the IMT of the proximal and distal walls for both sides of the CCA at a point 10 mm proximal to the beginning of the dilation of each carotid artery bulb. Max-CCA and Max-IMT were defined as the maximum IMT in the CCA and the entire scanned area, respectively. Low-density lipoprotein cholesterol (LDL) was estimated using the Friedewald formula. The risks of stroke and IHD across carotid atherosclerosis were compared by the use of multivariable-adjusted Cox proportional-hazards model. **Results:** In 46,561 person-years of follow-up, we documented 124 cerebral infarctions, 49 hemorrhagic strokes, 12 unclassified strokes, and 125 IHD events. The multivariable-adjusted hazard ratios (HRs; 95% confidence intervals, 95% CI) in the fourth quartile (≥0.95 mm) of the mean IMT for all strokes, cerebral infarction, and IHD were 2.48 (1.12 to 5.52), 3.66 (1.05 to 12.70), and 2.94 (0.99 to 8.70), respectively, compared with the first quartile (≤0.75 mm). The adjusted HRs (95% CI) in the fourth quartile (>1.70 mm) of Max-IMT for all strokes, cerebral infarction, and IHD were 1.93 (1.09 to 3.41), 1.79 (0.87 to 3.69), and 2.29 (1.12 to 4.69), while those in the fourth quartile (>1.15 mm) of Max-CCA were 1.67 (1.01 to 2.76), 2.15 (1.07 to 4.32), and 2.41 (1.24 to 4.69), respectively, compared with the first quartile (<1.0 mm for Max-IMT and <0.9 mm for Max-CCA). The adjusted HRs (95% CI) for all strokes, cerebral infarction, and IHD were 3.32 (1.01 to 10.76), 2.17 (0.52 to 9.04), and 13.7 (3.90 to 48.2) in 0.1mm of mean IMT, while they were 1.32 (1.03 to 1.68), 1.42 (1.07 to 1.87), and 1.61 (1.30 to 1.99) in 0.1mm of Max-CCA, respectively. The HRs (95% CI, P value) of cerebral infarction and IHD combined in 0.1mm of Max-CCA were 2.39 (0.89 to 6.40, P=0.1) with the use of an antihypercholesterolemic drug (statin in almost all cases), 1.47 (1.08 to1.98, P=0.01) with LDL≥130 mg/dL and a non-antihypercholesterolemic drug, and 1.56 (1.21 to 2.01, P=0.002) with LDL**Conclusions:** Carotid IMT, especially Max-CCA is a strong predictor for stroke, cerebral infarction, and IHD in Asia.

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Th P47

B-Type Natriuretic Peptide Level is a Better Predictor of Stroke Risk in Patients with Atrial Fibrillation

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Background: Nonvalvular atrial fibrillation (AF) is the most common cardiac dysrhythmia. It is well known that left atrial appendage thrombus (LAAT) is the most frequent source of embolic stroke (ES) in AF patients. Currently, the CHADS2 score is widely utilized to predict stroke risk. We observed that left ventricular diastolic dysfunction (DD) is prevalent among patients with risk factors constituting CHADS2 score (cardiac failure, hypertension, age, diabetes, stroke). It is plausible that DD with subsequent elevation of left ventricular filling pressure (LVFP) mediates blood stasis and the formation of LAAT. We evaluated whether BNP, a surrogate for LVFP, is a better predictor of LAAT than the CHADS2 score. Hypothesis: BNP level is superior to- and independent of the CHADS2 score in predicting LAAT. **Methods:** We conducted a retrospective cohort study of 275 consecutive nonvalvular AF patients who underwent transesophageal echocardiography (TEE) to exclude LAAT. Pre-TEE data was collected, including CHADS2 score, BNP level and use of aspirin or warfarin. A 2-sided T-test was used to compare mean BNP levels in LAAT(+) vs. LAAT(-) patients. A multivariate logistic regression analysis (MVLRA) was used to demonstrate whether BNP predicts LAAT independent of known confounders. An ROC curve was used to identify a cutoff value for BNP, below which LAAT is highly unlikely. **Results:** Among 275 subjects, 23 (8.3%) were LAAT(+) by TEE and 67% of patients had BNP levels available for analysis. Baseline characteristics in LAAT(+) and LAAT(-) patients were similar; including CHADS2 score (2.53 vs. 2.3, p=NS), antiplatelet use (73% vs. 70%, P=NS) and warfarin use (87% vs. 70%, p=NS). Mean BNP levels were significantly higher in LAAT(+) than LAAT(-) subjects (2082 vs. 457, P =0.02). MVLRA demonstrated that BNP is predictive of LAAT independent of the CHADS2 score and its individual components (p=0.009), as well as the use of antiplatelet and warfarin. The ROC curve showed that BNP has a higher discriminatory capacity in predicting LAAT than the CHADS2 score (AUC 0.94 vs. 0.54) and that none of the patients with BNP < or =450 pg/dl had LAAT, regardless of the CHADS2 score [LR (-) = 0]. **Discussion:** These preliminary data suggest that BNP is both independent of- and superior to the CHADS2 score in predicting the formation of LAAT. Our study is limited by a low LAAT event rate, retrospective design and unavailability of BNP data from all subjects. If proven by a prospective controlled outcome study, BNP has the potential to replace or complement the CHADS2 score in predicting stroke risk and determining the need for anticoagulation therapy. Furthermore, it may be possible to identify a cutoff value for BNP (< or = 450 pg/dl) below which LAAT formation and ES are highly unlikely, eliminating the need for anticoagulation in many patients.

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Th P48

Newly Diagnosed Atrial Fibrillation among Different Subtypes of Ischemic Stroke and Transient Ischemic Attack

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Background and Purpose: Newly diagnosed atrial fibrillation (NDAF) i s the atrial fibrillation (AF) detected after ischemic stroke (IS) or transient ischemic attack (TIA) in patients with previous sinus rhythm. Most studies on NDAF are limited to patients with cryptogenic events (TOAST group 5). However, NDAF can also occur in other subtypes of IS or TIAs. Our objective was to assess the frequency of detection of NDAF in the 5 TOAST subtypes of IS and TIA. Methods We assessed every patient admitted with IS and TIA between 01/01/2007 and 12/31/2009. We excluded periprocedural events (n = 103) because of the known relationship between surgery and the occurrence of NDAF, hemorrhagic strokes (n = 16), and patients with known AF (n = 45). We classified the remaining TIA and IS cases into TOAST subtypes. Every patient underwent continuous electrocardiographic monitoring for at least the first two days after admission. We compared the frequency of NDAF between the 5 groups (÷2, P < 0.05). As this is a descriptive study, not intended to infer causality between TOAST subtypes and occurrence of NDAF, we did not compare risk factors and other variables between TOAST subtypes. We described age, gender, frequency of diabetes and the severity of stroke according to the NIH stroke scale in the five groups. Results We assessed 172 patients with IS or TIA without prior AF, 103 men (64.4%), aged 68±14 years. We detected 19 NDAFs (11.0%, 95%CI 7.2-16.6). The frequency of NDAF in the five TOAST subgroups were: large vessel disease: 5/37 cases (13.5%), non-AF cardioembolic: 6/31 cases (19.4%), small vessel disease: 0/32 cases (0.0%), other causes: 3/13 cases (23.1%), and cryptogenic: 5/59 cases (8.5%), P = 0.32. We found no gender differences (P = 0.27) between the five groups. Age (P = 0.001), frequency of diabetes (P = 0.002), and severity of stroke (P = 0.009) were different in the 5 groups: large vessel disease 69±11, 17.7% and 6.5±6.6; cardioembolic 61±15, 34.1% and 7.8±6.9; small vessel disease 66±11, 15.2% and 2.5±2.0; other causes 58±16, 6.1% and 7.2±5.9, cryptogenic 72±11, 26.8% and 6.2±6.1, respectively. **Conclusions:** NDAF was detected in every TOAST subgroup with the exception of small vessel disease. We suggest that NDAF screening with continuous electrocardiographic monitoring should not be limited to cryptogenic IS and TIA.

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Th P49

Stroke Risk in Persons with Heart Failure: The REGARDS Study

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Introduction: Heart failure (HF) is the second most frequent cause of cardioembolism after atrial fibrillation (AF) and affects 5 million US persons. In AF, risk factors for stroke are well established and this allows the use of risk stratification tools to help identify those most likely to benefit from warfarin. In HF, risk factors for stroke are not well known and no similar risk stratification tool exists, although up to 28% of persons with HF in sinus rhythm take warfarin. We examined demographic and clinical factors in HF, looking for predictors of high incident stroke risk. **Methods:** The REasons for Geographic And Racial Differences in Stroke (REGARDS) study is a population based study of US adults aged ≥45 years. Participants were characterized as having HF (by digoxin use or both paroxysmal nocturnal dyspnea and orthopnea, excluding AF), AF (by self report or electrocardiogram and including participants with both HF and AF), or neither HF nor AF. Stroke incidence rates were computed following event adjudication, and a log-rank test used to show differences in time to stroke. Among participants with HF, age, sex, systolic blood pressure (SBP), hypertension, diabetes (DM) and history of prior stroke/transient ischemic attack (TIA) at baseline were compared between those with and without incident stroke using t-tests or chi-square tests. Cox models were used to compare the stroke risk among HF participants, for different levels of significant risk factors. **Results:** Of the 30,239 REGARDS participants, 1,397 were excluded because of missing essential variables. Of the remaining 28,842, 1,360 (5%) had HF, 2,538 (9%) had AF, and the remainder had neither. The stroke incidence rate was 0.69/100 patient years (95% CI 0.49,0.93) in participants with HF. After multivariable adjustment, participants with HF were 1.3 times (95% CI 0.92,1.9) more likely, to experience a stroke than those with neither HF nor AF. Among participants with HF, SBP (p=0.046), DM (p=0.03) and prior stroke/TIA (p=0.0004) increased the risk of stroke. HF participants with prior stroke/TIA and diabetes were more likely to have stroke than those with diabetes alone (table). Hazard ratio and stroke incidence among those with HF without AF

	Hazard ratio for stroke (ref=HF alone)	Stroke incidence per 100 patient years
All HF		0.69 (0.49,0.93)
HF+DM	1.9 (0.82,4.5)	0.72 (0.24,1.2)
HF+prior stroke/TIA	3.5 (1.3,9.5)	1.3 (0.47,2.5)
HF+prior stroke/TIA+DM	6.4 (2.7,15.1)	2.4 (1.1,4.0)

Conclusions: Prior stroke/TIA is the strongest risk factor for stroke in persons with HF. DM is also a stroke risk factor in HF. Stratification of persons with HF into levels of increasing risk for stroke is feasible and should allow the development of risk stratification tools to help define a subgroup of HF persons in whom the benefits of anticoagulation outweigh the risks.

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Th P50

Left Ventricular Dysfunction is associated with Cerebral Grey Matter Injury: Results of an in-vivo Brain MRI Segmentation Study

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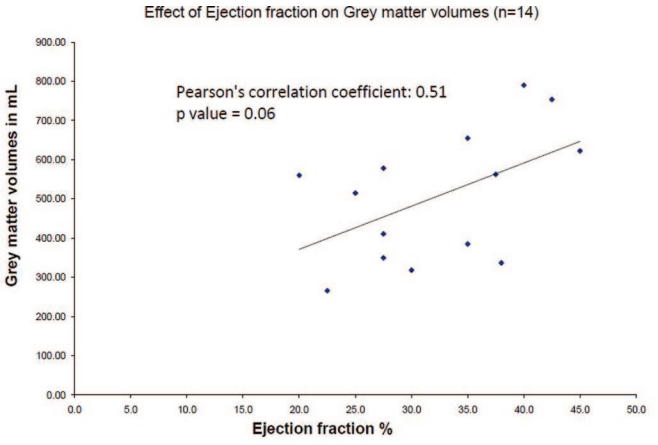
Introduction: Patients with poor systolic function experience varying degrees of cognitive deficits although the underlying mechanisms remain poorly understood. White matter

hyperintensities are common in patients with heart failure. However, not much is known about the relationship between heart failure and cerebral gray matter injury. Chronic cerebral hypoxia may have pathologic and clinical consequences that are not fully elucidated. **Objective:** To quantify cerebral gray and white matter volumes in patients with low left ventricular ejection fraction (LVEF) compared to unaffected, age-matched controls with normal LVEF. **Methods:** This was a cross-sectional pilot study. Subjects with low LVEF (<50%) and normal LVEF (>50%), demonstrated on transthoracic echocardiogram, were included in the study. All patients had brain MRI scans as part of transient ischemic attack evaluations. MRI scans demonstrating restricted diffusion or old stroke were excluded. T1-weighted spin-echo axial sequences were used for brain extraction, volume calculation and segmentation of gray and white matter; using a fully automated brain volume and segmentation program SIENAX (v2.2). Analyses were performed blinded to the subjects' LVEF status. **Results:** 28 subjects including 14 cases with low LVEF (mean EF 34.2 ±7.7) and 14 controls with normal LVEF were examined. Baseline demographics were well-matched in both group. The median grey matter volume was 537.5 ml (mean 507.4 ± 166.3; range 265.7-790.2) in the low LVEF group and 542.0 ml (mean 541.3 ± 167.2; range 317.8-795.4) in the control group (p=0.57). The median white matter volume was 941.8 ml (mean 966.7 ± 203.3; range 536.3-1313.7) for the low LVEF group and 843.5 ml (mean 916.1 ± 206.2; range 600.0-1284.4) in the normal LVEF (p=0.40). There was a positive correlation between grey matter volumes and low LVEF: [Pearson's correlation coefficient: 0.51; p value 0.06] (Figure) not seen with white matter volumes or in the control group. Further analysis using regional gray matter voxel-based morphometry is ongoing to delineate regional gray matter areas that may be more susceptible to injury in patients with low LVEF. **Conclusion:** These preliminary observations indicate that low LVEF may lead to preferential injury of the cerebral gray matter compartment. This may have significant clinical implications and also assist in designing interventions to reduce grey matter injury. Larger studies including multi-modal MR imaging and neuropsychological assessments are warranted to explore this potential mechanism of gray matter injury in patients with low LVEF.



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Th P51

Frequency and Progression of Cerebral Microbleeds among Patients with Stroke Due to Endocarditis

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Background: Cerebral microbleeds (CMBs) are most commonly ascribed to microvascular injury of hypertension or amyloid angiopathy, but also may arise from other bleeding prone angiopathies. Although isolated reports have described CMB in endocarditis, the risk of hemorrhage with such findings has not been detailed. Our objective was to describe CMBs in a large case series of stroke patients with endocarditis and to identify whether they had an increased risk for hemorrhage compared to those without CMBs. **Methods:** Patients admitted or referred to the stroke service at a tertiary care center from January 2002 to June 2010 were reviewed to identify those who were diagnosed with endocarditis - infective or marantic and who underwent at least one MRI with a gradient refocused echo (GRE) sequence. All available MRI scans at presentation and thereafter were analyzed for presence, number, and location of CMBs. **Results:** Among 57 patients with endocarditis, 43 had MRIs with GRE sequences. In these 43 patients, average age was 58.3, range 14-91, and 55.8% were female. Presenting clinical diagnoses were ischemic stroke in 86.0%, intracerebral hemorrhage in 9.3%, transient ischemic attack in 2.3%, limb ischemia in 2.3%, and narcolepsy in 2.3%. One patient presented with an ischemic stroke and a subdural hematoma. Among the ischemic stroke patients, 73.0% had no hemorrhagic transformation (HT) of the ischemic field at the time of first MR imaging and 27.0% did have HT at first imaging. Overall, CMBs were found in 28 patients (65.1%). 27 patients (62.8%) had at least one CMB present on first MR imaging. Among patients with CMBs, the mean number of CMBs was 4.5 (range 1 - 26). Patients with CMBs had 1 or more in the following locations: cortical gray-white junction region - 78.6%, subcortical white matter - 39.3%, cerebellum - 32.1%, thalamus - 10.7%, basal ganglia - 10.7%, pons - 3.6%, and medulla - 3.6%. Among patients with any CMB at first imaging, 11.1% developed HT and 3.7% developed subsequent intracerebral hemorrhage, while among those without any CMB at first imaging, 12.5% developed subsequent HT and 0% developed subsequent intracerebral hemorrhage. Ten of the patients with CMBs at first imaging had at least one subsequent MRI with GRE performed and 6 (60%) developed new microbleeds on subsequent scans. **Conclusion:** MRI GRE-imaging is useful to assess and monitor the evolution of bleeding-prone cerebral angiopathy in endocarditis. Cerebral microbleeds are common at presentation, present in nearly two-thirds of patients, with the cortical gray-white junction region the most common site. Among patients with CMBs at presentation, over half will develop additional CMBs over subsequent days.

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Th P52

High Incidence of Vascular Risk Factors and Small Vessel Disease in Young Patients with Stroke

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Objective: Ischemic strokes in the young can be devastating to patients, families, and clinicians alike. Historically, stroke in the young has been attributed, in large part, to cryptogenic, genetic, autoimmune, and cardiac etiologies. Recently at our center, we have seen in younger patients many vascular risk factors that traditionally develop in older patients. We aimed to review epidemiological data from ischemic stroke patients 45 years old and younger (young), versus those over 46 (old), to identify specific trends in vascular risk factors and classic TOAST etiologies in young patients. We hypothesized that within our large metropolitan stroke center, young stroke patients share more in common with older patients with respect to etiologies and risks than previously known. **Methods:** Using our stroke registry (07/04 - 06/10), we retrospectively identified patients with ischemic strokes treated at our institution. Demographics and risk factors were collected. Young and old patients were further subdivided by gender, ethnicity, and stroke etiology (using TOAST criteria). **Results:** 2409 patients were identified, 170 within the young group. Subgroup analysis is shown in table 1 between young and old patients. The percentage of small vessel disease in the young was identical to that found in the older group. Given the unexpected percentage of small vessel disease in the young, we further investigated this group (Table 2). There were a higher percentage of African American and Hispanic stroke patients in the younger age group, especially small vessel stroke patients (25% and 23%, respectively). Smoking was seen in a higher percentage within the young stroke population, particularly with young Caucasian patients. Over half of the young patients had hypertension, more so within the young African American patients. Diabetes and coronary artery disease disproportionally affect African American patients as well. Further analysis has also shown an increase over the years in the incidence of small vessel strokes in the young. **Conclusion:** Young stroke patients at our center have high incidences of traditional stroke risk factors. In support of these findings, the percentage of young patients with small vessel strokes is particularly striking, considering that this is a sign of end-organ damage from vascular disease. Our data call for stronger educational programs and primary care aimed at reducing modifiable risk factors for stroke in young patients, particularly minorities but also amongst Caucasians.

Table 1

Demographics and Risk Factors	Old (n=2239)	Young (n=170)	P Value
Mean Age (Range)	69 (46-100)	38 (13-45)	
Male Sex %	52%	56%	NS
Atrial Fibrillation %	22%	4%	<.0001
Hypertension %	79%	51%	<.0001
Coronary Artery Disease %	25%	9%	<.0001
Diabetes %	34%	21%	.0007
Smoking %	25%	36%	.0027
Hyperlipidemia %	31%	17%	<.0001
Ethnicity			
African American %	33%	45%	.0014
Caucasian %	52%	35%	<.0001
Hispanic %	13%	18%	.05
Etiology by TOAST			
Large Artery %	34%	17%	<.0001
Cardio-embolic %	43%	34%	.017
Small Vessel %	20%	20%	NS
Other %	3%	29%	<.0001

Table 2

Demographics and Risk Factors	African American	Hispanic	Caucasian
Atrial Fibrillation %	1%	1%	3%
Hypertension %	69%	37%	31%
Coronary Artery Disease %	15%	7%	3%
Diabetes %	28%	20%	12%
Smoking %	33%	30%	41%
Hyperlipidemia%	9%	23%	20%
Etiology by TOAST			
Large Artery %	21%	17%	12%
Cardio-embolic %	35%	33%	36%
Small Vessel %	25%	23%	6%
Other %	19%	27%	46%

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Th P53

Severity of Leukoaraiosis in Large Vessel Atherosclerotic Disease

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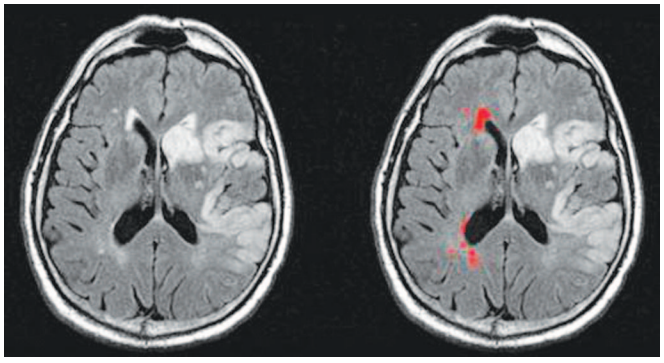
Background. Burden of leukoaraiosis, or MR-detectable white matter hyperintensity (WMH), reflects severity of diseased cerebral vasculature. In stroke patients, WMH burden is strongly

linked to small vessel disease; however, long-term impairment of cerebral perfusion due to significant extracranial (EC) and intracranial (IC) atherosclerosis may affect the severity of leukoaraiosis. We sought to determine whether, independently of stroke subtype, burden of WMH is associated with the radiographic evidence of EC or IC atherosclerosis in patients with acute ischemic stroke (AIS). **Methods:** We retrospectively identified 141 prospectively enrolled AIS subjects with CT angiogram (CTA) of head and neck and a brain MRI on admission from 2008-2009. EC was defined as evidence of ≥ 50% stenosis in the extracranial internal carotid artery, and IC as ≥ 50% stenosis in either the middle, anterior, or posterior cerebral arteries on CTA, contralateral to the side of AIS. WMH volume (WMHV) was determined using validated, semi-automated protocol. To avoid confounding by the presence of focal white matter damage caused by the index stroke, total WMHV was measured from the hemisphere unaffected by AIS (Figure). Multiple logistic regression was used to assess the relationship between WMHV and radiographic evidence of EC/IC atherosclerosis. **Results:** There were a total of 71 patients with EC and 70 patients with IC in this group (mean age 70.2 years, 54% women), with 24 (18%) demonstrating evidence of both. Median WMHV was 13.7 cc in subjects with EC, 9.8 cc in subjects with IC, and 7.9 cc in subjects with both. In univariate analysis, age ($p<0.0001$), diagnosis of hypertension (HTN), ($p=0.01$), hyperlipidemia ($p=0.004$), IC ($p=0.009$) but not EC ($p=0.12$) independently predicted WMHV. In multivariate regression model including EC, only age ($p<0.0001$) and HTN ($p = 0.025$) demonstrated independent effects on WMHV. Evidence of IC showed a significant trend towards association with higher WMHV (coefficient: 0.35, Standard Error: 0.20) after adjustment for age and history of HTN; however, this effect was not statistically significant ($p = 0.07$). **Conclusions:** Only HTN determined severity of leukoaraiosis measured as WMHV in patients with EC admitted for evaluation of AIS. Whereas EC was not associated with WMHV, the trend towards association between IC and WMH burden warrants further investigation in a larger group of subjects to maximize the power. Understanding the role of atherosclerosis in chronic cerebrovascular injury presenting as MR-detectable WMH may offer novel preventive and management strategies in the future.



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Th P54

The Cream&Sugar Study: Elevated Glucose Levels, But Not Triglycerides, Are Associated With More Severe White Matter Disease In Acute Ischemic Stroke Patients

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Introduction: The Berlin Cream&Sugar Study is the first prospective observational study in acute ischemic stroke patients that aims to determine if parameters of postprandial glucose and triglyceride (TG) metabolism predict recurrent stroke. MRI imaging of Cream&Sugar participants revealed that cerebral white matter disease (WMD) was frequently present after acute ischemic stroke. Hypothesis: This substudy of the Berlin Cream&Sugar Study tests the hypothesis that fasting and postprandial TG and glucose levels are associated with WMD. **Methods:** We performed a combined oral triglyceride (OTTT) and glucose tolerance test (OGTT) in 36 patients within 3 to 7 days after first ischemic stroke to simultaneously determine postprandial glucose and triglyceride tolerance under standardized testing conditions. Glucose and triglyceride levels were measured before, during, and 5 hours after the test. Severity of WMD was assessed on fluid attenuated inversion recovery sequences of a 3T MRI scanner using Wahlund scores. Patients were stratified into two groups according to their Wahlund scores, high (above median Wahlund score) and low (equal or below median). We performed a non-parametric test to compare levels of glucose and triglycerides between both strata. **Results:** Of 36 patients (mean age 66 years, SD 12.66, median NIHSS 2.5, IQR 0-11), the median Wahlund score was 5 (IQR 2 - 8). Fasting glucose levels differed significantly between 21 patients with high and 15 patients with low Wahlund scores (median 113 mg/dl, IQR 70 - 145 mg/dl vs. median 88 mg/dl, IQR 71 - 128 mg/dl; Mann-Whitney-U Test, $P<.05$). Moreover, median glucose levels 2 hours after the OGTT differed significantly between patients with high and low Wahlund scores (189 mg/dl , IQR 145 - 198 mg/dl vs.142 mg/dl, IQR 124 - 160 mg/dl; Mann-Whitney-U Test, $P<.05$). In contrast, fasting TG and TG levels 5 hours post-OTTT did not significantly differ between patients with high and low Wahlund scores. **Conclusion:** In conclusion, both elevated fasting and non-fasting glucose, but not TG levels are associated with more severe WMD in patients with ischemic stroke.

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Th P55

Soda Consumption and Risk of Vascular Events in the Northern Manhattan Study

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Previous studies have shown a positive association between diet soda consumption and risk of the metabolic syndrome and diabetes, which are important vascular risk factors. The goal of this study is to examine the association between soda consumption and risk of stroke, myocardial infarction (MI), or vascular death. The study population included participants from the Northern Manhattan Study, a multi-ethnic population-based cohort study to examine the incidence and risk factors for stroke, with data on soda consumption available (N=2564, 36% men, mean age 69 ± 10 years, 20% white non-Hispanic, 23% black non-Hispanic, 53% Hispanic). Diet and regular soda consumption were assessed by self-report using a semi-quantitative food frequency questionnaire at baseline, and were examined categorically: no soda (<1/mo) (N=901, referent), moderate regular only (1/mo-6/wk) (N=761), daily regular only (N=286), moderate diet only (N=214), daily diet only (N=116), moderate diet and any (1+/mo) regular (N=239), daily diet and any regular (N=47). Cox models were used to examine the association between soda consumption and incident vascular events (stroke, MI, or vascular death) controlling for sociodemographics and vascular risk factors. During a mean of 9.3 years of follow-up, 559 vascular events accrued. After controlling for age, sex, race/ethnicity, smoking, physical activity, alcohol consumption, and calories consumed per day, a 61% increased risk of vascular events was observed among those who drank daily diet soda only as compared to those who drank no soda (95% CI 1.13-2.30), and this association persisted after additionally controlling for the metabolic syndrome, peripheral vascular disease, and cardiac disease history (RR=1.48, 95% CI 1.03-2.12). A marginally significant increased risk of vascular events was also observed among those who consumed diet soda daily and regular soda once or more per month (adjusted RR=1.74, 95% CI 0.96-3.16). There was no significant increased risk of vascular events among those who consumed moderate or daily regular soda only (vs. no soda: moderate regular only adjusted RR=0.93, 95% CI 0.74-1.16; daily regular only adjusted RR=1.20, 95% CI 0.91-1.59). This study suggests that diet soda is not an optimal substitute for sugar-sweetened beverages, and may be associated with a greater risk of stroke, MI or vascular death than regular soda. Further studies are needed to explore potential mechanisms for the association between diet soda consumption and vascular events.

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Th P56

Subclinical Stroke Symptoms and Diabetes in the REasons for Geographic And Racial Differences in Stroke (REGARDS) Study

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Introduction: Individuals with diabetes are at increased risk of CVD events, which are not always clinically recognized, hampering optimal secondary prevention efforts. We examined the prevalence of stroke symptoms that had not been diagnosed by a physician as stroke (subclinical stroke symptoms) for participants with diabetes, pre-diabetes and neither in a large national cohort study. **Methods:** The REGARDS study includes 30,239 participants recruited between 2003-7 who are being followed prospectively. The community-dwelling sample was age ≥45 years at baseline and designed to be balanced on race and sex; the final sample was 55% female and 41% black. Participants were examined for prevalence of stroke symptoms using 6 validated questions (sudden weakness, numbness, painless loss of vision in one/both eyes, loss of half vision, loss of ability to understand people, and loss of ability to express oneself verbally/in writing). Diabetes was defined by report of physician diagnosis, receipt of diabetes medications, fasting glucose ≥126 mg/dL, or random glucose ≥200 mg/dL. Pre-diabetes was defined as fasting glucose 110-126 mg/dL or random glucose 140-199 mg/dL among those without diabetes. On those free of stroke or TIA at baseline, we calculated multivariable adjusted odds ratios (OR) for subclinical stroke symptoms associated with diabetes and pre-diabetes compared to neither, adjusting for sociodemographics and baseline stroke risk factors. **Results:** Of the 25,696 participants included in the analysis, 23.6% had diabetes and 15.6% had pre-diabetes. Subclinical stroke symptoms were reported among 22.7% of those with diabetes, 15.6% of those with pre-diabetes, and 14.9% of those with neither. After adjustment, participants with diabetes still had a 32% higher OR for reporting clinically unrecognized stroke symptoms than those with pre-diabetes or neither (Table). **Conclusion:** Nearly one in four diabetic individuals with no recollection of a stroke diagnosis nevertheless reported symptoms suggestive of stroke. A better understanding of the mechanisms leading to residual excess stroke risk after controlling for stroke risk factors in individuals with diabetes is needed, and interventions to improve stroke detection in persons with diabetes may be warranted.

Table. Prevalence and odds ratios (95% CI) for reporting subclinical stroke symptoms, by diabetes status.			
	Diabetes status		
	Neither (n=15615)	Pre-diabetes (n=4011)	Diabetes (n=6070)
N with stroke symptoms (%)	2323 (14.9%)	624 (15.6%)	1380 (22.7%)
Crude	(ref)	1.05 (0.96 – 1.16)	1.68 (1.56 – 1.81)
Age and sex adjusted	(ref)	1.06 (0.97 – 1.17)	1.70 (1.57 – 1.83)
+ Race	(ref)	1.03 (0.94 – 1.14)	1.56 (1.45 – 1.69)
+ Socioeconomic factors	(ref)	1.03 (0.93 – 1.13)	1.43 (1.33 – 1.55)
+ Stroke risk factors	(ref)	1.00 (1.00 – 1.10)	1.32 (1.22 – 1.43)
Socioeconomic factors: income, education, health insurance, geographic region of residence, urban/rural residence. Stroke risk factors: systolic blood pressure, smoking status, history of cardiovascular disease, history of atrial fibrillation, and left ventricular hypertrophy.			

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Th P57

Prestroke Glycemic Control Predicts Functional Outcome in Ischemic Stroke: The Fukuoka Stroke Registry (FSR)

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Introduction: Recent studies have shown that intensive glycemic control failed to reduce cardiovascular risk in diabetic patients, while hyperglycemia in acute phase of stroke is detrimental to outcome. Hypothesis: We assessed the hypothesis that prestroke glycemic control (PSGC) may affect outcome in patients with acute ischemic stroke. **Methods:** FSR is a multicenter stroke registry of acute stroke patients admitted to seven stroke centers in Fukuoka, Japan. From June 1999 to March 2010, 6653 patients were enrolled. Among them, the patients who fulfilled the following criteria were included in this analysis: (1) first-ever stroke, (2) ischemic stroke, (3) hospitalization within 24 hours after onset, (4) HbA1c measured at admission, (5) no impairment of ADL before onset. PSGC state was categorized into four groups according to the Japan Diabetes Society guidelines, excellent (HbA1c$<$5.8%), good (5.8%$\leq$HbA1c$<$6.5%), fair (6.5%$\leq$HbA1c$<$8%) and poor (8%$\leq$HbA1c). Neurological severity was evaluated by NIHSS, which was divided into quartile. We defined "neurological worsening" when NIHSS at 3 weeks became worse than admission NIHSS, and "good recovery" when NIHSS improved more than 4 during 3 weeks in patients with admission NIHSS$\geq$5 or when NIHSS at 3 weeks was 0 in those with admission NIHSS$\leq$4. Functional outcome was assessed using modified Rankin Scale (mRS) and mRS$\geq$2 was defined as dependent. **Results:** A total of 3248 patients were studied. Admission NIHSS was not different among PSGC groups (P$=$0.14), whereas NIHSS at 3 weeks was higher in poorer PSGC groups (P$=$0.01). As PSGC became worse, the frequency of neurological deterioration was high ($p<0.001$) and that of good recovery was low ($p<0.001$). Functionally dependent patients were more prevalent in poorer PSGC groups ($p<0.001$). Multivariate-adjusted logistic regression analysis revealed that PSGC state was independently associated with functional outcome. Poor PSGC group showed increased risk of functional dependence at 3 months (Odds Ratio, 3.36; 95% CI, 1.91-5.94; $P<0.001$) compared with excellent PSGC group. **Conclusions:** The neurological improvement and functional outcome are significantly poor after ischemic stroke in patients with poor glycemic control before onset.

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Th P58

Consciousness Impairment in a Consecutive Series of 1436 Acute Ischemic Strokes

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Background and objectives: Decreased level of consciousness (LOC) at ischemic stroke onset is infrequent and associated with a poor prognosis. Its causes and mechanisms are insufficiently understood. We aimed at finding predictors and topographic correlations for such strokes. Methods : In an acute hospital based registry of consecutive acute ischemic strokes admitted within 24 hours after last proof of wellbeing(Acute STroke Registry and Analysis of Lausanne, ASTRAL), decreased level of consciousness was defined as a value of $\geq$ 1 on the corresponding NIHSS item on initial neurological assessment. Acute status epilepticus was excluded by EEG if suspected. Demographic, clinical, etiological, radiographic, arterial imaging and outcome factors were considered. Poor prognosis was defined as a modified Rankin Scale score of $\geq$ 2 at 3 months. In a first multivariate logistic regression analysis of predictors of decreased LOC, we entered all significant variables except initial NIHSS. The second multivariate logistic regression analysis considered only significant variables concerning anatomical localisation and arterial territories. Results : In 1'436 acute ischemic strokes, 139 (9.7 %) had a decreased LOC on admission, of whom only one was attributable to early mass effect. These patients showed significantly poorer prognosis (OR 7.8, 95% CI 5.09-11.84) and higher mortality rate at three months (OR 4.67, 95% CI 3.15-6.92). On multivariate analysis, they had more frequently one or more previous strokes (OR 5.1, 95% CI 2.79-9.31), more frequently early ischemic changes on radiology (OR 1.74, 95% CI 1.10 - 2.75) and a higher frequency of arterial stenosis or occlusion in the ischemic territory (OR 2.87, 95% CI 1.6 -4.91). Lacunar mechanism (OR 0.11, 95% CI 0.04 - 0.36) and stroke with an uncertain cause (OR 0.37, 95% CI 0.18-0.71) were less frequent. Regarding localisation, patients with pure basilar strokes (OR 1.83, 95% CI 1.15-2.90), bilateral (OR 2.05, 95% CI 1.00-4.19), mixed supra- and infratentorial strokes (OR 6.11, 95% CI 3.02-12.35), large hemispheric infarction, and involvement of midbrain simultaneous with at least one other posterior circulation structure (OR 4.99, 95% CI 2.13-11.65) showed decreased LOC. Limiting the multivariate analysis to stroke localization, LOC was more frequently normal in left sided infarctions (OR 0.56, 95% CI 0.36 - 0.88) and in supratentorial strokes without cortical involvement (OR 0.23, 95% CI 0.10 - 0.54). **Conclusion:** Decreased level of consciousness at ischemic stroke onset is related to the presence of previous strokes, current stroke mechanism, early ischemic changes on acute imaging and acute arterial occlusions. Lesions have to be distributed in specific patterns and widespread in infra- and supratentorial structures in order to decrease LOC, suggesting distributed networks for its maintenance.

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Th P59

Predictors of Short Term Clinical Outcome Following Stroke in the Young: Data from a Tertiary Care Center in the US "Stroke Belt"

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Introduction: Few studies have looked at predictors of clinical outcomes of stroke in young adults residing in the Stroke Belt (Southeastern US). Subjects and**Methods:** We retrospectively abstracted baseline predictor and discharge data on all stroke patients aged 18-45 seen at a tertiary hospital in Alabama from October 2007- March 2010. Outcome was assessed by the discharge modified Rankin Score (mRS). Predictors of outcome were assessed using general linear models (regression), predicting the mean discharge mRS. Backwards stepwise regression was employed to develop a most parsimonious multivariable model. **Results:** Among 1453 consecutive stroke patients, 327 were young adults (22.5%). Ninety subarachnoid hemorrhages and 19 transient ischemic attacks were excluded from the analysis. Outcome data were available on 215 stroke patients - 153 ischemic and 62 intracerebral hemorrhagic (ICH) infarcts (M:F 119:94) 52% White; with median admission NIH Stroke Scale (NIHSS) of 6 (interquartile range: 2 to 15) - who were relatively uniformly dispersed over the 0-to-6 range of mRS at discharge. Univariately, admission NIHSS was the most significant predictor of discharge mRS ($p<0.0001$). In addition, the discharge mRS was related to admission glucose, stroke subtype, use of illegal drugs, renal disease, history of coronary artery disease (CAD), current smoking and the presence of carotid artery plaques (Table).The discharge mRS was not affected by age, sex, race, hypertension, diabetes, obesity, hypercholesterolemia, obesity, atrial fibrillation, congestive heart failure, systolic blood pressure, or admission creatinine ($p>0.05$). Only history of CAD persisted as a significant predictor after adjustment for baseline NIHSS. **Discussion:** These data suggest that after adjustment for stroke severity, history of CAD is the most potent predictor of functional outcome at discharge. We hypothesize that factors such as the use of illegal drugs or the presence of renal disease have their effect on stroke outcome though a pathway of presenting as a more severe stroke event. In contrast, CAD, which is often associated with left ventricular dysfunction with altered systemic perfusion, appears to have an effect on stroke outcome independent of the stroke severity.

Table 1. Multinomial Logistic Regression Analysis on Intra-Atherosclerosis and Extra-Atherosclerosis Group

Variables	OR for Intra-Atherosclerosis		OR for Extra-Atherosclerosis	
	OR	95% CI	OR	95% CI
Total Cholesterol	0.881	(0.670, 1.158)	1.434	(1.081,1.904)
LDL Cholesterol	0.952	(0.703,1.289)	1.464	(1.074,1.996)
HDL Cholesterol	0.590	(0.253,1.377)	1.290	(0.541,3.073)
Triglyceride	0.931	(0,796,1.089)	1.014	(0.873,1.177)
Non-HDL Cholesterol	0.922	(0.692, 1.229)	1.434	(1.072,1.918)
TC/LDL	1.161	(0,745,1.811)	0.663	(0.315,1.396)
TG/LDL	1.056	(0.931,1.198)	0.922	(0.720,1.182)
LDL/HDL	1.140	(0.891, 1.458)	1.181	(0.920,1.515)

* Non-LAA group as a reference group.
† Each lipid index was added individually to the model.
‡ Adjusted for gender, age, hypertension, diabetes, dyslipidemia, smoking, history of stroke, history of heart disease, hemoglobin, Hb A1C, Systolic blood pressure,
LDL = Low Density Lipoprotein, HDL = High Density Lipoprotein, TC = Total Cholesterol, TG = Triglyceride

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Th P60

Mortality Prediction Across Stroke Type: Does Including CT Findings for ICH Cases Improve Model Performance?

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Background: Ischemic stroke (IS) and intracerebral hemorrhage (ICH) are distinct diseases, yet these two stroke types are often combined in outcome studies. CT findings, such as ICH volume, location, and intraventricular hemorrhage (IVH), are key predictors of mortality in ICH. However, CT findings for ICH are often unaccounted for in studies of mixed stroke type as they have no correlate in IS and are unavailable in administrative datasets. We investigated the impact of adding CT data for ICH cases on multivariable model performance for mortality prediction in a population of mixed stroke type. **Methods:** All cases of first ICH or IS (2000-2003) in Nueces County, Texas were identified from the population-based Brain Attack Surveillance in Corpus Christi (BASIC) project. Logistic regression models were developed to predict 30-day mortality. All-cause mortality was determined from state and national databases. The base model covariates (Model 1) included National Institutes of Health Stroke Scale (NIHSS) and a stroke type indicator (ICH or IS). Model 2 added CT data (ICH volume in cc; IVH yes/no; infratentorial ICH yes/no) using interaction terms with stroke type. This method accounted for the CT data in ICH cases only and avoided the need for separate models stratified by stroke type. Model performance was assessed with area under the curve (AUC) and an alternate test of model fit, the unweighted sum of squared residuals (S). AUC and S were corrected for overfitting with multiple bootstrapped samples. **Results:** A total of 1,296 cases were included (IS 1,088 (84%), ICH 208 (16%)). Mean age was 71.0 (SD 12.5), 52% were female, 53% were Mexican American, 68% had hypertension, 35% had diabetes, and 29% had coronary disease. Median NIHSS was 4 (inter-quartile range (IQR) 2, 8) overall; 3 (IQR 1, 7) for IS; and 9.5 (IQR 3, 21) for ICH. Thirty-day mortality was 16% overall; 11.3% for IS; and 39% for ICH. AUC and S for the two models are shown in the Table. Adding CT findings to the model resulted in no significant change in AUC or S when all stroke types were included. Even when the analysis was restricted to ICH only, there was no change in model performance with addition of CT data, though there was a trend toward increased AUC. **Conclusions:** In this mixed cohort of IS and ICH, addition of CT data for ICH cases did not improve model performance for 30-day mortality prediction over a simpler method using NIHSS and stroke type as predictors. These findings have implications for the design of studies that combine IS and ICH, suggesting that the resources needed to obtain CT data for ICH cases may not be needed to improve mortality prediction.

TABLE: 30-day Mortality Model Performance

	Model	AUC (95%CI)	S (95%CI)
All Cases (N=1,296)	Model 1: NIHSS and stroke type	0.83 (0.77, 0.88)	112.8 (91.1, 134.6)
	Model 2: Model 1 plus interaction terms for CT findings (stroke type*ICH volume; stroke type*IVH; stroke type*infratentorial); and stroke type*NIHSS	0.83 (0.78, 0.88)	107.8 (86.8, 129.8)
	Change in parameter Model 2-Model 1 (95% CI)	0.005 (-0.013, 0.02)	-4.9 (-11.2, 1.4)
ICH cases only (N=208)	Model 1: NIHSS	0.84 (0.75, 0.92)	27.5 (19.9, 35.6)
	Model 2: Model 1 plus CT findings (ICH volume, IVH, infratentorial)	0.89 (0.82, 0.96)	22.5 (14.5, 30.9)
	Change in parameter Model 2-Model 1 (95% CI)	0.05 (-0.015, 0.13)	-5.0 (-11.6, 1.5)

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Th P61

Association Between Cerebral And Peripheral Artery Atherosclerosis In Patients With Ischemic Stroke

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Background Peripheral arterial disease (PAD) in patients with acute ischemic stroke is associated with recurrent vascular events and high cardiovascular mortality. However, PAD in stroke patients is often underdiagnosed due to asymptomatic clinical features. Ankle brachinal index (ABI) is a simple and efficient method in identifying both symptomatic and asymptomatic patients with PAD. Objective We investigated the frequency of PAD and relationship between cerebral atherosclerosis and PAD in terms of location and burden of cerebral artery atherosclerosis in ischemic stroke patients. Methods Among 2273 patients who were registered to the single hospital-based stroke registry between January 2007 and May 2010, there were 1461 patients with acute cerebral infarction or transient ischemic attack who were free of potential cardio-embolic sources of embolism and other rare causes of stroke. Of them, 938 patients (64.2%) undertook ABI examination. After excluding two patients who did not have cerebral angiography and five patients with ABI $>$1.3, 931 patients were included for the analysis. An ABI $=<$0.9 was considered as the presence of PAD. Results Demographic characteristics were not different between patients with ABI performed and those without except higher frequency of previous cerebral infarction history in the latter group. Of 931 patients, 81 patients (8.7%) were found to have PAD. Cerebral atherosclerosis, which was defined as arterial stenosis $>=$50% were found in 551 patients (59.2%). The presence of PAD was associated with that of cerebral atherosclerosis (OR:3.04, 95% CI:1.73-5.35). The number of cerebral arteries with atherosclerosis was greater in patients with PAD than those without($p<0.001$). In the multivariate analysis, patients with PAD were older and more likely to have low body mass index, diabetes mellitus, hypercholesterolemia, previous cerebral infarction, coronary artery disease and the number of cerebral arteries with atherosclerosis when comparing with those without PAD. Among cerebral arteries, atherosclerosis of the extracranial internal carotid artery was associated with PAD (OR:3.49, 95% CI:2.02-6.04). Twenty six percent of patients with atherosclerosis of the extracranial internal carotid artery had PAD. **Conclusions:** The presence of PAD was associated with that of cerebral atherosclerosis. Acute ischemic stroke patients with cerebral atherosclerosis, particularly of the extracranial internal carotid artery, should be closely examined and screened for the presence of PAD.

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Th P62

Low Ankle-brachial Index Is A Predicting Factor For Initial Severity Of Acute Ischemic Stroke

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Backgroud & objective : Ankle-brachial index (ABI) is a simple and non-invasive method to evaluate atherosclerotic stenosis or occlusion in peripheral arteries of the lower extremities. A Low ABI is predictive of the presence of peripheral arterial occlusive disease (PAOD). Patients with PAOD demonstrate higher cardiovascular mortality during follow-up than those without. However, reasons of the association between poor clinical outcome and PAOD remain unknown. Initial stroke severity is a strong predictor of long-term outcome in stroke patients. We investigated whether a low ABI is associated with initially severe stroke presentation in patients with acute ischemic stroke. Methods : The subjects for this study were consecutive ischemic stroke patients who underwent ABI measurements during admission from January 2007 to May 2010. All subjects had a brain infarction of less than 7 days after symptom onset. All ischemic strokes were subtyped based on the Trial of ORG 10172 in Acute Stroke Treatment classification. ABI values, which were lower than 0.90, were considered abnormal. According to the ABI values, patients were categorized into the normal ($\geq$9) and the abnormal ($<$0.9) groups. Demographic characteristics and initial National Institutes of Health Stroke Scale (NIHSS) scores at admission were compared between the groups. We also compared initial NIHSS scores between the groups within each subtype of stroke. Results : Of the 1346 patients enrolled, ABI was abnormal ($<$0.9) in 129 (9.6%) patients.. When comparing with the normal group, the abnormal group was older, had lower body mass index (BMI) and more frequent histories or illnesses of previous ischemic stroke, previous coronary artery disease, diabetes, and atrial fibrillation. Mean initial NIHSS score was higher in the abnormal group (6.99 $\pm$ 6.69, $P<0.001$) than the normal ABI group ((4.43 $\pm$ 4.95, $P<0.001$). Median NIHSS scores were higher in the abnormal group in the stroke subtypes of large artery atherosclerosis (4 vs 3, $p=0.038$), cardioembolism (5 vs 3, $p=0.017$), and undetermined etiology due to more than two causes identified (4 vs 2, $p=0.001$). In the multivariate analysis using multiple linear regression, low BMI ($p<0.001$), abnormal ABI ($p<0.001$), no diabetes ($p=0.018$), no smoking history ($p=0.027$), large artery atherosclerosis ($p<0.001$) and cardioembolsim ($p<0.001$) were associated with the higher NIHSS scores. **Conclusion:** A low ABI was an independent factor associated with severe stroke at admission. Although the mechanism of association between ABI and stroke severity is uncertain, previous observations of poor clinical outcome in patients with PAOD may be partly explainable by severe stroke in them.

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Th P63

Reversed Robin Hood Syndrome Is Associated with Early Risk of Stroke Recurrence

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Background&**Purpose:** Reversed Robin Hood syndrome (RRHS) was recently identified as one of the mechanisms of early neurological deterioration in acute ischemic stroke (AIS) related to arterial blood flow steal from ischemic to non-affected brain. We hypothesized that this acute, symptomatic hemodynamic compromise could also predispose to stroke recurrence. Subjects&Methods: Consecutive patients with AIS or transient ischemic attack (TIA) affecting the anterior circulation were prospectively evaluated with serial NIHSS assessments and bilateral transcranial Doppler (TCD) monitoring with breath-holding test. RRHS was defined according to previously validated criteria as the documentation of intracranial steal phenomenon during voluntary breath-holding on TCD coupled with neurological deterioration by $>$2

NIHSS points. The outcome-event of interest was recurrent stroke during the follow-up period with brain imaging being mandatory to support the clinical diagnosis of recurrent stroke. **Results:** A total of 364 patients (185 women, mean age 62±15years) had an ischemic stroke (80%) or TIA (20%) in the anterior circulation, and 32 (9%) had RRHS. During a mean follow-up period of 6 months (range 1-24) a total of 18 (5%) recurrent strokes (17 ischemic; 1 hemorrhagic) were documented. The cumulative recurrence-rate was higher in RRHS patients (25%; 95%CI:6%-43%) compared to the rest (14%; 95%CI:1%-27%; P<0.001 by log-rank-test). All recurrent strokes in RRHS patients were ipsalateral cerebral infarcts to the index event anterior circulation vascular territory. The underlying mechanism of recurrent stroke in all RRHS patients was large vessel atherosclerotic infarction. The mean elapsed time between the index and the recurrent stroke tended to be shorter in RRHS patients (1.0±1.5months) compared to the rest (4.9±6.5months; p=0.075). The 1-month stroke recurrence rate was six-fold higher in RRHS (19%; 95%CI:3%-35%) compared to the rest (3%; 95%CI:1%-5%; P<0.0001 by log-rank test). After adjusting for demographic characteristics, vascular risk factors and secondary prevention therapies RRHS was independently associated with a higher stroke recurrence risk (HR: 6.25; 95%CI:1.94-20.14; p=0.001). **Conclusions:** RRHS was associated with a higher risk of early stroke recurrence among patients with the anterior circulation cerebral ischemia independently of demographic characteristics, vascular risk factors and secondary prevention therapies. This recently described vascular steal phenomenon may constitute a novel risk factor for recurrent stroke in AIS patients.

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Th P64

Stroke Incidence, Usage Rate Of Iv T-pa, And In-hospital Mortality Of 474,415 Citizens In Kurashiki-city, Japan

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Background and Purpose: In Japan, we are uncertain of the precise data of stroke incidence and community-based thrombolytic therapy after governmental approval on 2007. Thus, our aim is to investigate the stroke incidence, usage rate of IV t-PA, and in-hospital mortality in middle size city of Japan. **Methods:** All patients suffering acute stroke in Kurashiki-city (population of 474,415, age ≥40 years of 254,628) have been admitted into 10 hospitals from March 2009 to February 2010. Clinical backgrounds including stroke subtype, treatment, and in-hospital prognosis were prospectively recorded. After all registration sheet were send to central office, we adjusted the data by the standard-population model of world health organization (WHO). As using the Japanese standard-population model (population of 120,287,000), we estimated the number of stroke patients per a year in Japan. **Results:** The number of stroke patients (age ≥40 years) who were hospitalized in the 10 facilities was 896 (496 men). There were 624 (70%) patients with cerebral infarction, 213 (24%) with intracerebral hemorrhage, and 59 (6%) with subarachnoidal hemorrhage. Incidence rate per 100,000 for all stroke was 352 (95% CI; 329-374) in Kurashiki-city and 240 (95% CI; 210-271) in WHO model. Regarding cerebral infarction, incidence rate was 245 (95% CI; 226-265) in Kurashiki-city and 159 (95% CI; 134-183) in WHO. Cerebral infarction cases admitted to hospitals within 3 hours of onset were 191 of 624 (31%). Thrombolysis were given for 30 (16%) patients. Usage rate of thrombolysis per 100,000 was 12 (95% CI; 8-16) in Kurashiki-city and 8 (95% CI; 3-14) in WHO. Total 57 patients were dead during their hospitalization, and in-hospital mortality per 100,000 was 24 (95% CI; 17-29) in Kurashiki-city and 13 (95% CI; 6-20) in WHO. Concerning Japanese population model, estimated number of patients suffering stroke was 177,420/year. **Conclusion:** In the urban Japanese city, stroke incidence per 100,000 was 352 and in-hospital mortality was 24. Thrombolysis were given for 16% of hyper-acute stroke patients. Stroke seems to occur to approximately 180,000/year in Japan.

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Th P65

Association of Fish Consumption Factors with Stroke Mortality in The Multiethnic Cohort Study

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Background and Purpose: Fish consumption has been found to be protective against cardiovascular disease in some studies. However, Japanese, whose diets are rich in fish, have a relatively lower heart disease rate but a higher stroke incidence than other ethnic groups. The purpose of the present study is to use the unique data of the Multiethnic Cohort to study how fish consumption factors contribute to the observed differences in these diseases among African-Americans, Whites, Japanese, Native Hawaiians, and Latinos. **Methods:** We examined the relationship of fish consumption to the risk of stroke mortality, overall and by subtype, through the end of 2005 in 89,052 men and 109,090 women aged 45-75, residing in Hawaii and Los Angeles and free of stroke at recruitment between 1993 and 1996. Using Cox regression, we calculated relative risks (RRs) overall and by sex and ethnicity for the intake of total dietary ù3 fatty acids (ù3), fish, and preparation methods, adjusting for known risk factors including hypertension at baseline. **Results:** There were 1,789 stroke deaths during an average of 11.9 years of follow-up. Overall, ù3 was inversely associated with stroke mortality (4th vs. lowest quintile: RR = 0.74, 95%CI = 0.58-0.94), as was canned tuna fish (3rd vs. lowest tertile: RR=0.84, 95%CI=0.77-0.99). Baked, boiled and raw fish had inverse relationships in all groups (3rd vs. lowest tertile: RR = 0.84, 95%CI = 0.72-0.97), except for Japanese men with an interaction p-value of 0.0014. Salted and dried fish was positively related to hemorrhagic but not ischemic stroke mortality (eaters vs. non-eaters: RR=1.41, 95%CI=1.06-1.87). Among men, although no effect from total fish was observed, fried fish (eaters vs. non-eaters: RR=1.18, 95%CI=1.00-1.38) were positively associated with stroke risk. Among women, total fish (4th vs. lowest quintile: RR=0.75, 95%CI=0.58-0.98) was inversely associated with stroke death. **Conclusion:** Dietary ù3 may have a protective effect against stroke mortality. Consumption of fish with high salt content was related to a higher risk of stroke, especially hemorrhagic stroke. Perhaps the high salt use in fish preparation led to Japanese men not exhibiting the protective effect for fish seen in other groups.

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Th P66

Smoking Is The Most Difficult Risk Factor To Manage In Stroke; 5 Years Follow Up Study

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Background: To prevent the stroke recurrence, proper risk factor management is important. We investigated the management status for the stroke risk factors five years after ischemic stroke. Method: We recruited subjects who admitted in Inha University Hospital due to acute ischemic stroke or transient ischemic attack. On admission, baseline data about demographic features and risk factors were registered. Five years later, two trained research nurses investigated the patients' management status of the stroke risk factors and smoking through telephone interview and medical records. **Results:** We analyzed 651 consecutive patients from September 2003 to February 2005. Among them, the information of 499 (74.8%) patients could be collected by telephone survey or medical record if also available. The mean interval between discharge and follow-up were 4.8 years. Upon investigation, 115 patients (23.0%) were identified to expire during the follow up period. We could contact with 384 (77.0%) patients on the telephone or medical records. The mean age on admission was 61.9±11.1 and the male was 199 (51.8%). At the time of follow up investigation, 312 patients (81.3%) were taking antithrombotics; 265 (69.0%) antiplatelets, 39 (10.2%) anticoagulants, and 8 (2.1%) combination of both. Among 303 patients with hypertension, 277 (91.4%) were taking antihypertensive agent, 113 of 125 (90.4%) with diabetes were taking oral hypoglycemic agent or insulin, and 155 of 188 (82.4%) with dyslipidemia were taking lipid lowering agent including statin. Contrary to the other risk factor management status, only 57 of 123 smokers (46.3%) on admission stopped smoking after stroke (ex-smokers) and 40 patients (32.6%) were still smoking until recently. Among 40 current-smokers, 12 smokers (9.8%) tried but failed to maintain smoking cessation, and most of them restarted smoking three or four years after stroke (mean interval to resmoke, 3.4 years). **Conclusion:** Our results suggest that many patients with ischemic stroke did not manage their risk factors actively, particularly for smoking. There is a need for more vigorous effort for secondary prevention and education for patients and their family, and more active smoking cessation program is needed for the stroke patients.

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Th P67

Baseline Smoking Level Increases the Long-Term Risk of Death or Non-Fatal Vascular Event in People with Stroke: a 10-Year Survival Analysis

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Background: Patients with stroke have a greater risk of death or non-fatal vascular events. This risk is exacerbated by smoking. Aims: We aimed to determine the 10 year risk of death or non-fatal vascular events suffered by patients with stroke based on their smoking status at baseline. **Methods:** 1589 cases of first-ever and recurrent stroke were recruited between 1996 and 1999 within a defined geographical region in North East Melbourne. Both hospital and non-hospital cases were included. Over a 10 year period, all deaths, recurrent stroke events and acute myocardial infarctions that were reported at follow up interviews were validated using medical records. Cox proportional hazards was used to assess factors associated with death, acute myocardial infarction or recurrent stroke. The model was adjusted for age, sex and socioeconomic status. **Results:** Smoking at baseline was associated with poorer outcome (Hazard Ratio [HR]: 1.51, 95% Confidence Interval [CI]: 1.21-1.89, P<0.001). Patients who were ex-smokers at baseline (HR: 1.17, 95% CI: 0.99-1.37, p=0.059) also appeared to have poorer outcome. Patients who were smoking at baseline had poorer outcome than those who were ex-smokers (ratio of HR: 1.29, 95% CI: 1.04-1.61, p=0.021). **Conclusions:** Patients with stroke who continue to smoke have poorer outcomes in the long term than those who quit smoking. This further highlights the potential benefits of ceasing smoking, even among those who have suffered a stroke.

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Th P68

Population Attributable Risk for Major Risk Factors of Ischemic Stroke in Korea

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Background: Stroke is the first-leading cause of death in Korea. With the rapid aging of our society, it is very important to reduce burden of stroke to us, and prevention is the most important strategy to accomplish this goal till now. However, we do not know how much each of major risk factors of stroke contributes to its incidence in our society. This study aimed to estimate the magnitude of major risk factors' association with ischemic stroke and the population attributable risk (PAR) for each risk factor. **Methods:** In this case-control study, a consecutive series of 3,629 patients who were hospitalized due to acute ischemic stroke within 7 days of onset between April 2008 and September 2009, were collected from 9 centers participating in the 'Clinical Research Center for Stroke' program sponsored and funded by the Korean government. Each case was age (+- 3 years) and sex-matched to each control. Control data were obtained from the Korean National Health & Nutrition Examination Survey (KNHANES), which was designed to represent the Korean population. We calculated adjusted odds ratios (ORs) with a conditional logistic regression model and PARs for the major risk factors of ischemic stroke. **Results:** The adjusted ORs (95% CI) were 2.11 (1.87~2.37) for hypertension, 2.26 (1.97~2.60) for diabetes mellitus, 1.25 (1.08~1.44) for hyperlipidemia, 2.83 (2.46~3.26) for current smoking, 4.63 (3.78~5.68) for history of stroke, and 1.84 (1.46~2.33) for history of ischemic heart disease. The PARs were 15.8~22.8% for hypertension, 7.3~11.4% for diabetes, 0.7~3.9% for hyperlipidemia, 27.9~37.5% for current smoking, 3.6~6.0% for stroke history, and 0.8~2.4% for ischemic heart disease. Both body mass index (BMI) or obesity (BMI$\geq$25kg/m^2) did not show significant association with ischemic stroke. **Conclusion:** This study is the first one to report the magnitude of relationships between major risk factors of stroke and ischemic stroke in the Korean population. With respect to prevention of stroke in the society level, the burden of smoking is relatively high in Korea compared to other well-known risk factors of stroke.

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Th P69

Stroke Among The New Zealand Workforce: A Prospective Study Of Middle-aged Employees

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Aims: To examine the association between ethnicity and incident cerebrovascular disease among middle-aged employees. Methods and**Results:** Four thousand four hundred and eighty-five subjects from the New Zealand workforce (3239 men and 1246 women), aged 40-78 years who were free from stroke and worked full time at baseline (1989-1991), were followed an average of 9 years. The outcome measure was incident fatal stroke or clinically verified non-fatal stroke (a total of 185 events). Kaplan-Meier analysis demonstrated that increased age, Pacific Islander ethnicity, current smoker, high blood pressure, increased waist measurement and diabetes were significant predictors of stroke ($p<0.05$). Cox proportional hazard models adjusted for sociodemographic and clinical risk factors measured did not reduce the estimate for Pacific Islander ethnicity (HR 1.77, 95% CI 1.16-2.81). **Conclusion:** In this population, Pacific Islander ethnicity is related to increased risk of stroke independent of demographic and clinical risk factors. Further research is needed to examine geographic variation and different stroke types (acute ischemic stroke, intracerebral hemorrhage, subarachnoid hemorrhage, transient ischemic attack) in this population.

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Th P70

Comparison of baseline characteristics of strokes between China and Canada: results from the China National Stroke Registry and the Registry of the Canadian Stroke Network

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Objective Stroke is a major global health problem in both developing and developed countries. We aimed to compare baseline characteristics, treatments and outcomes for stroke or transient ischemic attack (TIA) in China with those in Canada. Methods The China National Stroke Registry (CNSR) consecutively recruited 21,902 patients with acute stroke or TIA from 132 hospitals across China between September 2007 and August 2008. We analyzed data from the CNSR and compared the results with the published report from Ontario Stroke Audit of the Registry of the Canadian Stroke Network, which contains data of stroke or TIA patients (n=4,913) from 153 hospitals in Ontario, Canada between April 2004 and March 2005. Results Patients in China were younger that those in Canada (Mean$\pm$SD of age in years: 63.8$\pm$12.9 vs. 73.0$\pm$13.4, $P<0.001$) and were more likely to be male (61.2% vs. 48.8%, $P<0.001$). Chinese patients presented at a younger age than Canadians. Intracerebral hemorrhage and ischemic strokes were more common in China (23.7% vs. 7.1%, $P<0.001$; 66.3% vs. 46.0%, $P<0.001$), and TIA and undetermined strokes were more common in Canada (6.2% vs. 33.8%, $P<0.0001$; 0.6% vs. 9.8%, $P<0.0001$, respectively). There were no significant difference in subarachnoid hemorrhages between China and Canada (3.4% vs. 3.3%, $p=0.74$). Compared with Canadian patients, based on self-report disease histories, Chinese patients were more likely to smoke (38.9% vs. 14.1%, $P<0.001$) and more likely had hypertension (63.2% vs. 61.6%, $p=0.04$), but less likely had diabetes (17.7% vs. 23.7%, $P<0.001$), hyperlipidemia (9.7% vs. 30.2%, $P<0.001$), arterial fibrillation (5.5% vs. 13.9%, $P<0.001$) and previous stroke (30.9% vs. 34.1%, $P<0.001$). **Conclusion:** There are substantial differences in demographics, subtypes of stroke and risk factors between China and Canada. The proportion variation in stroke subtypes may be partly related to the ethnic differences between the two countries. Awareness of the key risk factors (e.g., smoking, hypertension) may be helpful in improving the stroke control and prevention strategies in China. The differences in treatments and outcomes after stroke remain to be determined in further analyses.

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Th P71

Strokes and Tias in the Out-Of-Hospital Setting: Incidence and Temporal Trends

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Introduction: Stroke incidence in the US population has been typically addressed by population-based studies using data obtained predominantly through the inpatient setting. However, a substantial number of stroke cases are diagnosed in care facilities or outpatient clinics, as there has been a trend towards managing care in the outpatient setting. Ignoring these events can lead to a significant underestimate of incidence. We examined strokes and TIAs ascertained in the out-of-hospital setting, collected from three study periods of the Greater Cincinnati/Northern Kentucky Stroke Study (GCNKSS). We hypothesized that the rate of out-of-hospital events has been increasing over time. Methods The events were ascertained during three one-year study periods (July1993-June1994, 1999, and 2005) among residents of the 5 counties that comprise the largely biracial study population of 1.3 million. We analyzed stroke events screened in all area hospital-based and health department clinics, as well as in a randomly selected sample of nursing homes and primary care physician settings. Cases were cross referenced with all events captured in the hospital setting in our study to prevent double counting. Events ascertained in physician offices and nursing homes were weighted to account for the sampling methodology. Results Incidence rates for out-of-hospital ascertained strokes and TIAs are shown in the table. Accounting for sampling methodology, using appropriate weighting, the out-of-hospital events accounted for 10.1% of stroke/TIA events within our population in 1993-94, and then increased to 24.5% in 1999 and 19.7% in 2005. **Conclusion:** The proportion of out-of-hospital cases in 1999 and 2005 was substantially higher than 1993-1994. We cannot rule out that the results may be related to subtle methodologic drift or random variability between periods. However, we speculate that the observed trend for more out-of-hospital management from the early 1990s to 2005 has been driven by the increasing financial pressures to manage medical issues in the outpatient setting, in order to reduce health care costs. Regardless, out-of-hospital ascertainment captures a substantial proportion of strokes and TIAs in our population, demonstrating that this methodology is crucial for understanding the true incidence of stroke. Table: CGNKSS Out-of-hospital Stroke/TIA Incidence rates (per 100,000; adjusted to 2000 US Census)

	1993/94	1999	2005
Stroke	30 (26, 33) [n=50] [weighted n=260]	86 (80, 92) [n=81] [weighted n=782]	55 (51, 60) [n=60] [weighted n=543]
TIA	22 (18, 25) [n=36] [weighted n=179]	38 (34, 42) [n=38] [weighted n=346]	33 (29, 36) [n=32] [weighted n=316]

–incidence rates include 95% confidence interval, n = number of out-of-hospital cases ascertained, weighted n = number of cases considered for incidence rate after adjusting for sampling methodology

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Th P72

Sex Differences in Blood Pressure Control 6 Months after Ischemic Stroke

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Introduction: Overall, women over the age of 65 have been shown to be more likely than men to have uncontrolled hypertension. Whether this gender difference is also present after ischemic stroke, when the indication for blood pressure control is particularly compelling, is unknown. **Methods:** We utilized data from QUISP, a randomized quality improvement trial focused on secondary stroke prevention that included all patients admitted with ischemic stroke from 2004 through 2006 to 14 hospitals in a Northern California integrated health care plan. For this study, we included only those with hypertension (defined as prior history, discharge diagnosis, or active prescription for antihypertensive medications) who were discharged alive and not to hospice care. Extensive electronic records were supplemented with chart abstraction on a sample of patients to determine living and marital status, socio-economic status, insurance, pharmacy coverage, and number of antihypertensive medications prescribed at discharge, post-discharge, and blood pressure (BP) control ($<$140/90 mmHg) 6+/-2 months after stroke. We examined the relationship between gender and uncontrolled BP, adjusting for factors predictive of BP control and those significantly different by gender. All analyses were conducted using mixed logistic models with hospital as random effect. **Results:** We included 1346 patients with ischemic stroke who met entry criteria. Women comprised 53.6% of the cohort. Six months after stroke, 54% of women compared to 64% of men had controlled blood pressure (OR 0.66, 95% CI 0.53-0.82, P$<$0.0001), a difference that persisted when adjusted for both age and race (OR 0.69 95% CI 0.55-0.86, p=0.001). Women were significantly older than men, twice as likely to live alone, three times as likely to be widowed or divorced, had higher mean systolic BP at discharge, and were less likely to be current alcohol users or have diabetes. However, none of these factors explained the difference in blood pressure control: female sex remained independently associated with being less likely to have controlled blood pressure at 6 months (OR 0.70 95% CI 0.55-0.89, p=0.004) even with adjustment for these covariates in a multivariable model. No differences were observed in prescribing patterns of antihypertensives either at discharge (p=0.60) or at six months (p=0.72) or in adherence with post-stroke visits (p=0.57). **Conclusion:** Hypertension is less well controlled in women compared to men after ischemic stroke. Aggressiveness of drug therapy, adherence with follow-up care, and social factors do not appear to account for this difference. Drug potency or physiological differences are possible explanations but further studies are required.

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Th P73

Use of a Regional Health Information Exchange (HIE) to Facilitate Outcomes Epidemiology

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Introduction: The Greater Cincinnati/Northern Kentucky Stroke Study is a periodic (1993-94, 1999, 2005, and now 2010), study of stroke incidence and case fatality in a 5-county region of 1.3 million. An outcomes arm, involving interviews of 500 acute ischemic stroke subjects at baseline and 3 months, was added for 1999 and 2005. For 2010, we partnered with HealthBridge, an HIE containing regional healthcare information, to study whether HIE use improves efficiency of participant identification. As an HIE, HealthBridge mobilizes healthcare information electronically across all adult hospital systems in our study region (except the VA hospital), and facilitates health information delivery to all providers involved in a patient's care. **Methods:** In 2005, finding subjects with possible stroke involved screening hospital admission records' chief complaint terms. Some facilities securely transmitted daily electronic admission log data to us, while other facilities required travel to examine logs on site. Study nurses were then dispatched to review medical records of potential cases, but due to uncertainty about whether stroke had occurred, significant on site medical record review was often required to confirm subject eligibility. For 2010, our University of Cincinnati (UC) Informatics group established a secure interface between UC and HealthBridge to receive real-time Health Level 7-formatted Admission/Discharge/Transfer (ADT) data feeds and populate a dedicated database with likely stroke subjects' data, including admit date, chief complaints, demographics, facility, and room number, for further study team review. We also remotely accessed facilities' electronic medical records via HealthBridge to review imaging and admission notes, to increase likelihood of ischemic stroke before dispatching nurses to consent subjects. Person-hours of effort from both periods were captured, and the data were descriptively analyzed. **Results:** For 2005, recruitment of 502 subjects required an average of 14 coordinator and 26 study nurse hours daily over 12 months; 42 subjects were excluded as non-strokes after physician review. During the first 5 months of 2010, recruitment of 250 subjects required an average of 10 coordinator and 21 study nurse hours daily; only 1 case was excluded as a non-stroke. Thus, daily effort hours were reduced by 22.5% in 2010, and recruitment over the first 5 months was 16.8% higher than expected based on 2005 estimates. **Conclusion:** Use of an HIE can enable access to and review of real-time healthcare data across a region in a secure fashion. It allowed for greater efficiency and accuracy of study subject identification and recruitment than traditional approaches in this pilot study. HIE-based approaches have the potential to greatly facilitate population-based epidemiology and outcomes studies, and further study of their potential is needed.

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Th P74

Stroke and the Stars of Hollywood: Analysis of the Burden of Stroke Among Oscar Nominees

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Background: Hollywood stars shape and reflect American society, including the frequency and impact of disease. The 2011 International Stroke Conference, the first to take place in Los Angeles/Hollywood, is an appropriate occasion to investigate the frequency and impact of stroke among leading Hollywood actors. **Methods:** We compiled a list of all nominees for the Best Actor/Actress Oscars since award inception in 1927 through 2009. Lifetime reports of nonfatal and fatal stroke and myocardial infarction were identified by internet search of public records and of prior medical studies of all-cause mortality among Oscar nominees. Impact of stroke and MI occurrence upon career and productivity was investigated by analysis of film and TV appearance frequencies before and after event, as listed in the Internet Movie Database (IMDb). **Results:** During 82 years of Oscar competition, 409 actors/actresses have been nominated for Best Actor/Actress Awards and 140 (34.2%) have won at least once. Nonfatal or fatal strokes have been reported in 30 (7.3%), MIs in 39 (9.5%), and stroke or MI in 65 (15.9%). The average age at which nominees with stroke were first nominated was 35.6 and age at first stroke 67.8. Women were more likely to develop stroke than men [18/30 (60%)]. Stroke severity was fatal in 6 (20%), nonfatal in 24 (80%). Career productivity was impaired by vascular events. Annual number in movies/TV in the 3 years post-event, compared with the 3 years pre-event, was reduced by 73% after first stroke and 69% after first MI. Strokes were equally frequent in nominees who won a Best Actor Oscar, vs non-winners, but occurred longer after first nomination among winners (mean 31.1 vs 26. 8 yrs, p $<$ .002). Exemplar nominees (N) or winners (W) from each decade who experienced stroke include Mary Pickford (W 1929), Bette Davis (N 1934, W 1935), James Cagney (N 1938, W 1942), Cary Grant (N 1942), Kirk Douglas (N 1950), Richard Burton (N 1954), Grace Kelly (W 1954), Elizabeth Taylor (N 1957, W 1960), Patricia Neal (W 1963), Liza Minnelli (N 1970, W 1973), Dudley Moore (N 1982), James Garner (N 1985), and Sharon Stone (N 1995). **Conclusions:** Stroke and cardiovascular disease have exacted an enormous toll upon Hollywood stars, as upon Americans generally, with loss of career productivity and loss of life. These findings may be useful to promote healthier, disease-avoiding lifestyle behaviors among influential film actors and actresses and their worldwide public.

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Th P75

Simultaneous Detection Of NR2 Peptide And Antibody Differentiate Ischemic Stroke And Reveal Intracerebral Hemorrhage Accompanied With Ischemic Complications Within 4.5 Hours Of Hyper-acute Stroke

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Introduction: To speed up ruling in or ruling out of patients assignment for thrombolytics using a blood test combined with CT imaging in the Emergency Department could be extremely beneficial in this critical treatment window. European multicenter trials (Dr.C. Foerch, PI, Goethe University, Frankfurt am Main, Germany)were conducted to evaluate diagnostic accuracy of NR2 peptide and antibody biomarkers for rapid differentiation of cerebral ischemia *vs* intracerebral hemorrhage. **Methods:** Plasma specimens collected at 13 clinical sites (NCT00916864) were tested using NR2 peptide and NR2 antibody assays. Of 186 patients recruited between June 2009 and January 2010, 94 had acute and 43 had prior and/or multiple ischemic stroke. To define tissue-based evidence of injury, all patients had CT. Blood samples were drawn within 0.5-4.5 hours of acute hemispheric stroke onset. **Results:** In this 186-patient cohort, prevalence of intra-cerebral hemorrhage by CT was 25%. In adult patients $>$18 years old NR2 peptide measurements $>$ 0.5 ng/mL indicates acute hemispheric ischemic stroke within 4.5 h of onset.NR2 peptide showed sensitivity of 88% and specificity of 99% within 3.0-4.5 hours of hyper-acute stroke. Detection of NR2 antibody (cut off of 2 .0 ng/mL) determines prior and/or multiple ischemic events with sensitivity of 97% and specificity of 98%.Patients suffered intracerebral hemorrhage accompanied with ischemic complications (10.7%) had elevated both NR2 peptide and antibodies. **Conclusion:** The NR2 peptide and antibody brain biomarkers provide reliable measurements of stroke across a broad, clinically important range and should prove useful in urgent situations. Simultaneous detection of NR2 peptide and antibodies in patients with hyper-acute hemispheric stroke (i) improves diagnostic certainty of cerebral ischemia, (ii) helps to rule-out intracerebral hemorrhage, and (iii) reveals group of intracerebral hemorrhage accompanied with ischemic complications. The latter group of patients might be assigned for low doses thrombolytic therapy.

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Th P76

Recanalization and Collaterals Predict Outcome in Proximal MCA Occlusion, but neither Penumbra nor Core of Stroke

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Abstract ISC 2011 Recanalization and collaterals predict outcome in proximal MCA occlusion, but nor penumbra nor core of stroke. **Introduction:** Data on new predictors of outcome include

penumbra core or collaterals. **Objective:** To test the predictive value of recanalization, collaterals, penumbra and core of ischemia for functional outcome in a large group of patients with MCA occlusion. Method: Consecutive events included prospectively in the Acute Stroke Registry and Analysis of Lausanne from April 2002 to April 2009 with an acute stroke due to proximal MCA occlusion (M1) were considered for analysis. Acute CTA were reviewed to grade the collaterals (dichotomized in poor $<=$50% or good $>$50% compared to the normal side) and localization of M1 occlusion (proximal or mid-distal). Acute CTP were reviewed and reconstructed to determine penumbra, core and stroke index (penumbra/penumbra+core) of brain ischemia. Good outcome was defined by mRS 0-2 at 3 months. **Results:** Among 242 events (115 male, mean NIHSS 18.1, SD 5.8, mean age 66, SD 15), 42% were treated with intravenous thrombolysis, and 3% with intraarterial thrombolysis. Collateral status was rated as poor in 53% of events and proximal M1 occlusion was present in 64%. Recanalization determined at 24 hours with CTA was complete in 26% events and partial/absent in 54%.CTP was available for 212 events. Mean penumbra was 88.6 cm^3 (median 84.4, SD 53.8), mean core was 54.1 cm^3 (median 46.2, SD 45.7) and stroke index was 64% (median 68%, SD 25%). Good outcome was observed in 87 events (36%) and was associated in multivariate logistic regression with thrombolysis ($p=0.02$, OR=2.5, 95% CI 1.2-5.4), recanalization ($p<0.001$, OR=4.1, 95% CI 1.9-8.9), lower NIHSS ($p<0.001$, OR=0.84, 95% CI 0.78-0.91), male gender ($p=0.01$, OR=2.8, 95% CI 1.3-5.9), mRS prior to stroke ($p=0.02$, OR=0.5, 95% CI 0.28-0.9) and good collateral status ($p=0.005$, OR=3, 95% CI 1.4-6.4). Nor penumbra, nor core, nor stroke index were significant in the multivariate model, even if an association was present in the univariate model between good functional outcome and penumbra ($p=0.004$, OR=1.008, 95% CI 1.003-1.01), core ($p<0.001$, OR=0.98, 95% CI 0.976-0.99) and strokeindex ($p<0.001$, OR=16.7, 95% CI 4.6 59.9). **Conclusion:** MCA recanalization is the best predictor for good functional outcome, followed by collateral status. CTP data did not predict the functional outcome in our large group of M1 occlusion.

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Th P77

Prediction of Recurrent Vascular Events Following Transient Ischemic Attack: DWI, PWI and Serum Biomarkers of Brain Ischemia

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Background: Transient ischemic attack (TIA) patients are at increased stroke risk, but clinical assessment alone is unreliable and new techniques of risk prediction are urgently needed. We hypothesised that Stroke MRI and serum brain ischemia biomarkers could predict recurrent vascular events following TIA and minor stroke, with 12 months of follow-up. **Methods:** Sixty-four eligible, consecutive TIA/minor stroke patients (NIHSS$\leq$3) prospectively received DWI, PWI, MRA and FLAIR within 48 hours of symptom onset. A 41 patient subset had acute measurement of four serum brain ischemia biomarkers: BNP, D-dimer, S100β and MMP-9. Follow-up included day 90 FLAIR imaging and clinical assessment at 30, 90 days and 12 months. Imaging assessment was independently performed by three experienced readers, including one neuroradiologist. The primary outcome measure was recurrent vascular events at 12 months. Statistical methods included Kaplan-Meier survival and Cox regression analysis. **Results:** TIA (n=47) and minor stroke (n=17) patients were recruited. Males comprised 42/64 (65%). Median age was 66.5y (IQR 55.5-75.3). Acute DWI lesions, 40% multiple, were found in 32/64 (50%) and in 19 (40%) of TIA patients; intracranial vascular lesions in 18/58 with available MRA (31%); PWI lesions in 13/36 (30%). New FLAIR lesions occurred in 12/56 (21%). There were 24 clinical outcome events, but only 3% of patients had a stroke. For every 5mL increase of DWI volume, the hazard ratio (HR) for recurrent event was 1.12 (95%CI 1.04-1.19; P=0.002). DWI positivity and intracranial vascular lesions were associated with an increased risk of recurrent vascular events at 1 year (HR 4.8, 95%CI 1.4-16.7; P=0.01), independent of clinical risk ($ABCD^2$ score). PWI positivity (HR 3.47 (95% CI 1.28-9.4, P=0.012) and D-dimer increment (1000ng/mL) (HR 1.6, 95%CI 1.04-2.45, P=0.03) were also associated with increased risk of recurrent event when considered in isolation. **Conclusions:** DWI positivity and intracranial vascular lesions predict increased risk of vascular events following TIA/minor stroke, beyond clinical risk scores. These results suggest that MRI findings are integral to prognosis after TIA/minor stroke. In addition, PWI and serum brain ischemia biomarkers have potential application in risk stratification of TIA patients.

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Th P78

Predictors and Accuracy of Abnormal CT Perfusion in 1296 Consecutive Acute Ischemic Stroke Patients

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Introduction: Diagnosis, localization and acute treatment of acute ischemic stroke is most frequently based on noncontrast cerebral CT (NCCT). CT perfusion (CTP) may improve the performance of NCCT. We aim to describe prevalence and predictors of pathological CTP in a large series of consecutive stroke patients and to determine its accuracy in predicting infarction on follow-up imaging. **Methods:** All consecutive patients arriving within 24 hours in our hospitals and then admitted to the stroke unit and/or intensive care were entered in a prospective registry (Acute STroke Registry and Analysis of Lausanne, ASTRAL). All patients with a good quality CTP (usually 4 or 16 slices) performed within 24 hours from January 2003 to March 2010 were included in the present analysis. Demographic, clinical, radiological and follow-up imaging (CT and/or MRI $>$ 24h after initial imaging) were analysed. We used univariate logistic regression analysis to test the association of different factors associated with focal hypoperfusion on CTP. Significant predictors (at P$<$20%) were used to fit a multivariable model. **Results:** Of 1296 patients undergoing acute CTP, 455 (35%) had early ischemic changes on NCCT, and 943 (73%) had a focal hypoperfusion on CTP. Initial NIHSS, aphasia and neglect, cardioembolic stroke mechanism, bilateral carotid territory strokes, other non-lacunar supratentorial territories, increased glucose level, quicker time from symptoms onset to CT, early ischemic changes on NCCT, presence of silent infarcts, and presence of significant arterial pathology were independently associated with a positive CTP. The calculated sensitivity of CTP with regards to an infarction on follow-up imaging was 80.5% and the specificity was 51.3% . **Conclusion:** Focal hypoperfusion on CTP is frequent in acute ischemic stroke and is predicted by higher NIHSS, earlier imaging, non-lacunar cardiogenic supratentorial infarcts, increased glucose levels, and the presence of arterial pathology in the ischemic territory. Sensitivity for subsequent infarct is high, and specificity moderate. Adding CTP to acute CT-based imaging may improve recognition of stroke and its localization, interpret arterial pathology, and therefore improve stroke management.

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Th P79

Persistence of Hyperdense Middle Cerebral Artery Sign on Follow-up CT Scan is Associated with Poor Outcome in Ischemic Stroke Patients Treated with Intravenous Thrombolysis

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Background- Significant numbers of acute ischemic stroke (AIS) patients recover with optimal care and timely-administered intravenous thrombolysis with tissue plasminogen activator (IV-TPA). However, the rates and extent of recovery remain highly variable. Considering the scarce and costly resources, early identification of reliable predictors for functional outcomes is important for planning interventions and rehabilitation strategies. Hyperdense middle cerebral artery sign (HMCAS) on pre-treatment unenhanced CT scan represents the presence of thrombus, often associated with severe neurological deficits and poor clinical outcome. However, it is reliable only in AIS patients managed conservatively. In thrombolyzed patients, it may disappear (representing clot dissolution) or persist (persisting clot) on the follow up CT scan. We aimed at evaluating whether disappearance or the persistence of HMCAS on follow-up scan can predict the final outcome. Methods- Data from consecutive AIS patients treated with IV-TPA, in a standardized protocol, from Jan2007 to March2010 were included in the prospective thrombolysis registry at our tertiary care center. For this evaluation, posterior circulation strokes were excluded. HMCAS was assessed by 2 independent stroke neurologists, blinded to the patient data or outcomes. Functional outcomes assessed by modified Rankin Scale (mRS) at 3-months were dichotomized as good (mRS 0-1) and poor (mRS 2-6). The data were analyzed for the early predictors of function outcome with SPSS version 16 for Windows. **Results:** Of the total of 1918 AIS patients admitted to our center, 189 (9.9%) eligible cases were treated with IV-TPA during the study period. Baseline data included mean age 64$\pm$13 years; 102 (59%) males; mean onset-to-treatment time 157$\pm$38 minutes and median NIHSS 16 points. Hypertension was the commonest vascular risk factor in 144 (76%) while 63 (33%) patients suffered from atrial fibrillation (AF). HMCAS was observed on the pre-treatment scan in 95 (50%) patients and persisted in 47 (50%) of them. Overall, 96 (51%) patients achieved good functional outcome (mRS 0-1 at 3 months). On the univariable anlaysis, age, atrial fibrillation, pre-TPA NIHSS score and HMCAS on the follow-up CT scan were associated with poor functional outcome. However, only pre-TPA NIHSS score (OR1.09;95%CI 1.04-1.16,p=0.001) and HMCAS on the follow-up CT scan (OR 22.93;95%CI 8.81-54.52,p **Conclusion:** Persistence of hyperdense middle cerebral artery sign on the follow up CT scan in acute ischemic stroke patients treated with IV-TPA can be used as an early predictor of poor functional outcome.

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Th P81

Prognostic Value of Whole Brain Volume Perfusion CT in Acute Stroke $<$6h after Symptom Onset

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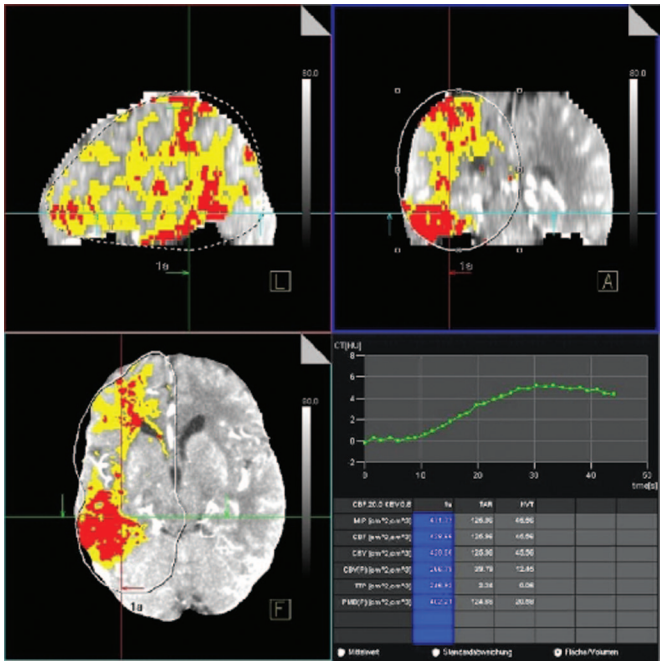
Purpose: In acute ischemic stroke rapid diagnosis and efficient treatment is indispensable for the patient's outcome. Aim of this study was to evaluate the prognostic value of infarct lesion volumes according to whole brain volume perfusion CT in acute stroke within the first six hours after symtom onset. **Method and Materials:** Patients were included in this prospective study, if they had been admitted to our department within the first 6 hours after symptom onset of

acute stroke. A total of 28 patients first received a non-contrast CT of the brain to exclude intracerebral hemorrhage. After that, whole brain volume perfusion CT was performed. Lesion volumes were determined manually on colour coded 3D parameter maps of cerebral blood flow (CBF) and cerebral blood volume (CBV). Volumes of reduced CBF (<20 ml/100ml/min) were determined automatically. Final infarct volume was identified on follow up non enhanced CT 72 h later. Absolute lesion volumes were analyzed using multiple regressions and Mann-Whitney-U-tests. **Results:** Mean value of manually determined CBF lesions was 70.4 cc, mean value of manually determined CBV lesions was 55.4 cc. Automatical delineation of lesions with CBF < 20 ml/100 ml/min resulted in a mean volume of 63.2 cc. Mean final infarct volume was 66.4 cc. For manually defined lesion volumes, positive correlation was found both for CBF (correlation coefficient R2=0.72) and for CBV (R2=0.75). Automatically determined lesion volumes of reduced CBF (< 20 ml/100 ml/min) also showed high correlation with final infarct volumes (R2= 0,74). Age, sex and stroke severity (NIHSS) had no significant influence on correlation quality. **Conclusion:** In acute stroke whole brain perfusion CT has a high prognostic value regarding final infarct volumes. Both manually and automatically delineated lesion volumes determined from volume perfusion CT showed high correlations with final infarct volumes, the highest predictive value was found for manually defined CBF lesions according to colour coded 3D maps (y=1.0335x).



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Th P82

Combination of Neurovascular Imaging Modalities for Evaluation of Patients with Stroke

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Background: A combination of two non-invasive tests, MR imaging/MR angiography (MRA) and CT/CT angiography (CTA), may reduce the need for conventional digitial subtraction angiography (DSA) for diagnosis of cerebrovascular disease among patients with stroke. **Objective:** To ascertain the effectiveness of a combination of two non-invasive tests in preventing the need for DSA in patients with stroke. **Methods:** All consecutive stroke patients from two comprehensive stroke centers from January 2008 to July 2010 were analyzed. Findings of CTA, MRA, and DSA were abstracted from chart review. We estimated the value of combination of two non-invasive tests to provide definitive diagnosis judged by the treating vascular neurologist either by definitely excluding or determining the need for surgical or endovascular treatment without any DSA. **Results:** A total of 700 patients (344 [49%] men) were studied in this cohort with a mean age of 63 years ± 16. There were a total of 241 patients who had at least two imaging modalities, 81 patients with CTA /MRA combination, 69 patients with CTA/DSA combination, 65 patients with MRA/DSA combination, and 26 patients with all three modalities. Among the 107 patients who underwent a CTA and MRA, a DSA was still required for diagnostic purposes in 26 (24%) of the patients. **Conclusion:** In current practice, a combination of two vascular imaging studies is frequently used. In our experience, the findings derived from CTA and MRA combination still require confirmation with DSA in one-quarter of the patients.

Table: Imaging Modalities

CTA	266	CTA only	90
MRA	331	MRA only	159
DSA	81	DSA only	71
CTA+MRA only	69		
CTA+DSA only	65		
MRA+DSA only	65		
CTA+MTA+DSA only	26		
Atleast two imaging modalities	241		
No Imaging	139		

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Th P83

CT Assessment Of Blood Brain Barrier Permeability And Risk Of Haemorrhagic Transformation In Ischaemic Stroke

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Introduction: Haemorrhagic Transformation (HT) is a potential complication of ischaemic stroke treatment associated with increased morbidity and mortality. CT perfusion (CTP) can be used to derive permeability maps which may reflect reduced blood brain barrier integrity. We investigated whether increased permeability could be predictive of HT in acute ischaemic stroke in addition to known predictors of HT. Methods Imaging and clinical data from patients with ischemic stroke who underwent plain computed tomography (CT) and CTP within 6hrs of symptom onset were reviewed. Non-contrast CT was assessed for the extent of early ischaemic changes using the Alberta Stroke Programme Early CT Score (ASPECTS). ASPECTS scores were evaluated on perfusion maps of cerebral blood volume (CBV), cerebral blood flow (CBF) and mean transit time (MTT), in addition to permeability maps of surface areas product (PS) and extraction ratio (E). Regions of interest (ROI) corresponding to ASPECTS were drawn on each map and mean values for each parameter were calculated. The same ROIs were assessed for HT according to the Safe Implementation of Treatments in Stroke (SITS) criteria, as well as infarction and normal /abnormal tissue on follow-up imaging at 24-72 hours. Binary logistic regression and ROC analysis were performed to identify predictors of HT. Results Imaging on 30 patients was reviewed, 9 of whom proceeded to HT. CBV and CBF were the only parameters able to predict an outcome of HT over infarction for a ROI (p=0.026 and p=0.002 respectively). ROC analysis revealed modest predictive values for HT with CBV and CBF with an area under the curve (AUC) of 0.67 for both. Extraction ratio was a more accurate predictor of infarction compared to conventional infarct markers CBF and CBV (AUC= 0.792, 0.692 and 0.627 respectively). Atrial Fibrillation was associated with HT (p=0.01). Non significant associations included increased blood glucose (p=0.176), previous stroke (p=0.69), early ischemic change on baseline CT (p=0.121), and increasing extent of baseline permeability and perfusion abnormalities (p=.0.097 and 0.177) **Conclusion:** Permeability Surface Area Product and Extraction Ratio did not identify tissue destined to haemorrhage after stroke. CBF and CBV did predict HT, but predictive value was limited for both. Extraction Ratio may be useful in predicting extent of infarct core.

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Th P84

Does Threshold Based Segmentation of MRI Correlate with Visual Reading of Ischemia and Perfusion Deficit in Acute Scans?

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Introduction: Threshold based segmentation (TBS) of MRI scans has the potential to automate the identification of ischemic and penumbral areas without lengthy processing and reader expertise. The objective of this study was to test specific Apparent Diffusion Coefficient (ADC) and perfusion Tmax thresholds for identification of ischemic and penumbral areas in acute stroke patients. **Methods:** LESION is a multicenter, prospective study of imaging in acute stroke. Patients were included in this TBS study if they had an acute MRI (1.5T or 3T scanners) with high quality DWI and PWI images based on visual inspection, had presented within 3 hours from onset, were scanned prior to acute intervention, had a diagnosis of definite acute ischemic cerebrovascular syndrome (AICS), and were enrolled between 2000-09. All MRI scans were reviewed by an experienced reader blinded to the qualitative reads to determine presence of ischemia, perfusion deficit, and evidence of mismatch. TBS of MRI scans were determined by generating the perfusion maps in Perfscape™ (Olea Medical) and then measuring the ADC and Tmax volumes in Neuroscape™ (Olea Medical) using an ADC value of 615 mm^2/seconds and Tmax value of > 6 seconds. A mismatch definition of Tmax - ADC volume > 60 cc was used. The TBS decisions of ADC positive = yes/no, Tmax positive = yes/no, and mismatch = yes

/no were compared to the qualitative reads. The agreement between the TBS and qualitative decisions were determined along with the positive predictive values of the TBS decisions. **Results:** Ninety patients (68±15 years, 43 females) met the inclusion criteria. Patients had a median NIHSS of 9 (IQR 5-18) and median onset to MRI time of 129 minutes (IQR 89-175). ADC threshold decisions were in agreement with the qualitative read of ischemia in 74% (64/86) of the scans with a positive predictive value of 97%. Tmax threshold decisions were in agreement with the qualitative read of perfusion deficit in 88% (73/83) of the scans with a positive predictive value of 96%. **Conclusion:** TBS, using an ADC value of 615 mm^2/seconds and Tmax value of > 6 seconds, is strongly correlated with qualitative reads of acute stroke MRI scans and demonstrates potential for use in acute intervention decision making. Future studies of this large MRI dataset are planned to further explore TBS decisions.

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Th P85

E-learn CT Angiography: a Virtual Training Ground Prepares for Stroke Imaging

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Introduction: Imaging methods including CT-angiography (CTA) are increasingly available and may support decision-making in acute stroke treatment. We developed a three-step e-learning concept after the principle test-teach-test and tested it in two stroke related subjects, vascular occlusion and spot sign, on two groups of volunteers. We assessed the hypothesis that an e-learning program trains learners with varying experience in basic CTA interpretation skills in a stroke setting. **Methods:** We developed an HTML-based program with a teaching segment and two matching test segments within the two subjects. Tests were taken before and after the teaching segment and tests were 40% of the size of the teaching segment, 15 vs. 40 cases in the vascular occlusion series and 6 vs. 10 cases in the spot sign series. The vascular occlusion series required correct answers for type of pathology (4 choices) and location (5 choices). Spot sign was answered with presence or absence. Learners were also asked how confident they felt about their diagnosis. The number of correct answers and the ratings of self-perceived diagnostic confidence were analyzed to quantify the learning potential of each series. **Results:** Four neurological consultants and four radiological residents completed the program. The vascular occlusion teaching segment increased diagnostic correctness from 42% to 68%, p= 0.005. The neurological consultants showed significant progress with average scores 50% vs. 75%, p= 0.027, and the radiological residents with average scores 33% vs. 60% showed near-significant progress, p= 0.081. Spot sign was detected correctly by 69% before the teaching segment and by 92% afterwards, p=0.009. In the spot sign series the group reported a median self perceived diagnostic certainty in 50% of cases vs. 75% after the teaching segment, p= 0.030. Self perceived diagnostic certainty showed no significant increase in vascular occlusion. **Conclusions:** We show improved diagnostic accuracy and confidence through a teaching segment for both inexperienced and trained personnel in two targeted topics of varying difficulty. Teaching vascular occlusion yielded best results with some prior knowledge, whereas the spot sign recognition required none to achieve diagnostic accuracy above 90% and self perceived diagnostic certainty in 75% of cases through a teaching segment. We conclude that the e-learning tool is a useful educational approach for users of varying experience, e.g. for investigators in clinical trials and for clinicians, and that the teaching course is useful for certification.

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Th P86

MR Perfusion And Reperfusion As Predictors Of Hemorrhagic Transformation In Hyper-Acute Ischemic Stroke: A Voxel-Based Analysis

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Background: Studies examining MRI predictors of hemorrhagic transformation (HT) after ischemic stroke have demonstrated that severely decreased ADC is predictive. In this study, we hypothesized that in addition to severe ischemia, reperfusion may predict HT in ischemic stroke patients. **Methods:** Acute ischemic stroke patients underwent two MR scans: within 4.5 (tp1), at 6 (tp2), and at 24 hrs (tp3) after stroke onset. Susceptibility-weighted imaging (SWI) or gradient-echo (GRE), ADC, mean transit time (MTT), cerebral blood flow (CBF), and cerebral blood volume (CBV) maps were obtained at all time-points. HT was delineated by a neuroradiologist (RP) on SWI or GRE at tp2 or tp3. Blood on tp1 was excluded from the analysis. To assess the effect of radiological variables (ADC, MTT, CBF, and CBV) in predicting HT, voxels from HT patients were pooled in a logistic regression (LR) model predicting the outcome of HT or no HT within the ischemic hemisphere. An equal number of voxels were randomly selected from the HT or non-HT regions to balance the influence of each patient on the final analysis. Each MRI parameter at tp1, tp2, or Δ (tp2-tp1) was individually assessed as an independent predictor of HT. Significant variables ($p<0.05$) were entered (forward selection) until additional variables no longer increased the model's goodness of fit [c-statistic/area under the curve (AUC)]. **Results:** Thirty-two ischemic stroke patients were imaged with MRI at 3.0±.8 hrs, 6.4±.4 hrs, and 24 hr after onset. Six patients with HT > 1 ml were included in the analysis (range 1-50.4 ml); only 1 HT was symptomatic. Cohort characteristics: 63 yrs-old; 1 female; NIHSS 15.3; 3 of 6 received IV tPA. In the pooled LR analysis, the overall model predicted HT ($\chi^2=4188$, df=3, $P<0.01$) with the strongest predictor being MTT tp1 [$\beta=0.145$, B=1.2, $P<0.01$, corresponding to a 20% increased HT risk with each 1 sec increase in MTT (increase=more severe ischemia)], followed by ADC tp1 [â=-0.06, B=0.94, $P<0.01$, 6% increased HT risk for each 1 mm^2/sec decrease in ADC (decrease=more severe ischemia)], followed by ΔMTT [$\beta=-0.02$, B=.98, $P<0.01$, 2% increased HT risk for 1 sec decrease in ΔMTT (decrease=reperfusion)]. While adding ADC tp1 to MTT tp1 in the model increased the AUC from 0.723 to 0.826, adding ΔMTT increased the AUC to 0.827. In individual analyses of the 6 patients, significant predictors of HT were: MTT tp1 (5 pts), ADC tp1 (4 pts), and ΔMTT (2 pts). ΔMTT alone was most predictive in the 2 pts with largest HT volumes: pt with 50 ml HT (AUC=0.80); pt with 9.3 ml HT (AUC=0.76). **Conclusion:** This voxel-based analysis suggests that early MTT, an indicator of severe ischemia, may be as predictive as ADC for HT. While reperfusion was a weak predictor in the overall population, it was a strong predictor in two patients with the largest HTs. Further study is needed to confirm these findings in a larger cohort and determine if asymptomatic HT has a deleterious effect on outcome.

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Th P87

Early Performance of MRI reduces the rate of Stroke Misdiagnosis in Young Adults

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Introduction: The misdiagnosis of acute ischemic stroke in young adults is a significant problem since patients with stroke may have many decades of potential disability. Also, proven therapies for acute stroke may not be administered in misdiagnosed patients. In previous work, we found that stroke misdiagnosis occurs in 14% of young adults and that patients with posterior circulation strokes were more likely to be misdiagnosed (J Stroke Cerebrovasc Dis, in press). Hypothesis: We assessed the hypothesis that early use of MRI, arrival by ambulance, and presentation to a Primary Stroke Center (PSC) would be associated with a reduced rate of misdiagnosis. **Methods:** A prospective database of young adults (ages 16-49 years) with ischemic stroke (final diagnosis provided by vascular neurologists) was reviewed. We collected information on several variables, including age, gender, race, arrival by ambulance, whether brain MRI was performed within 48 hours, and initial presentation to a PSC. Ambulance arrival was determined by retrospective queries to patients. Variables were tested against emergency department (ED) misdiagnosis with chi square testing. Variables with a p value of able model. **Results:** 77 patients with a mean age of 37.9 years were reviewed. Women composed 57% of the group and race included White American (58.4%), African American (37.7%), and other groups (3.9%). 48.3% of patients arrived by ambulance, 53.2% had a brain MRI within 48 hours, and 23.4% initially presented to a PSC. The overall rate of ED misdiagnosis was 14.5%. Univariate testing for key variables and misdiagnosis was as follows:

	Misdiagnosis	Correct diagnosis	P values
age	34.5 ±9.2	38.4 ±7.9	0.15
Sex: (n-77)			0.51
Male (n=33)	6	27	
Female (n= 44)	5	39	
Race: (n=74)			0.51
Black (n=29)	3	26	
White (n=45)	8	37	
Arrived by ambulance (n=60)			0.18
Yes (n=29)	3	26	
No (n=31)	8	23	
MRI within 48 hours (n=62)			0.036*
Yes (n=33)	2	31	
No (n=29)	8	21	
Presentation to a Primary stroke center: (n=77)			0.44
Yes (n=18)	1	17	
No (n=59)	10	49	

In multivariable testing, performance of MRI within 48 hours (p=0.023) was associated with a lower rate of misdiagnosis and age <35 years was linked with greater likelihood of misdiagnosis (p=0.047). There was a trend for arrival by ambulance to be associated with a lower rate of misdiagnosis (p=0.06). **Conclusions:** Early performance of MRI leads to greater accuracy of stroke diagnosis in young adults presenting to the ED. Patients less than age 35 years have a greater risk of misdiagnosis. ED physicians tend to diagnose stroke more accurately in patients arriving via ambulance. This study and recent professional guidelines on acute stroke imaging support greater use of urgent MRI in young adults presenting with stroke-like symptoms.

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Th P88

Diffusion Imaging 24 Hours After Stroke Onset Accurately Represents Final Infarct Volume

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Background and Purpose: Infarct growth is used as a surrogate for clinical outcome in early phase stroke trials. Assessment of infarct growth earlier than the traditional 90 days may be equally accurate and yield practical advantages. We aimed to correlate 24 hour and day 90 infarct volumes. **Methods:** Patients presenting to two institutions with acute ischemic stroke within 6 hours of onset were imaged with a protocol that included MRI at 24hours and 90 days. Infarct volume was assessed on diffusion-weighted-imaging (DWI) at baseline and 24 hours after stroke onset and on FLAIR images at day 90. The DWI and FLAIR lesions were manually outlined to their maximal visual extent by two independent stroke neurologists and the volumes averaged. Inter-rater consistency was assessed using the median difference in lesion volume between raters and Bland-Altman plot. The relationship between 24hr and day 90 infarct volumes was assessed using linear regression, Pearson's correlation and Lin's concordance co-efficient (ñ) as well as a Bland-Altman plot. **Results:** Imaging data were available for 83 patients, mean age 69 years (SD 10), median baseline NIHSS 14 (IQR 10), 77 (93%) treated with tPA. The median time from onset to "24hr" MRI was 25.9hr (IQR 4) and median time to follow-up was 91 days (IQR 8). The DWI infarct volume at 24 hours had strong linear correlation with day 90 FLAIR infarct volume ($r=0.98$, 95%CI 0.97-0.99, Lin's $ñ=0.93$). The 95% limits of agreement of the Bland-Altman plot were -9.1 to 30.5mL. The baseline DWI to day 90 correlation (assessable in 40 patients) was significantly lower ($r=0.92$, 95%CI 0.85-0.96). Infarct growth occurred between baseline and 24hours (mean 15mL absolute, 224% relative). Significant infarct shrinkage occurred from 24 hours to day 90 (mean volume 11mL, st dev 8.3mL, paired Wilcoxon $P<0.001$) and this was reflected in the regression equation: FLAIR lesion volume (mL) = 0.85xDWI lesion volume (mL) - 5.1 mL with $R^2=0.96$. The median ROI volume discrepancy between raters was smaller for DWI than for FLAIR (1.4mL (8%) vs 1.8mL (17%), $p=0.002$) and the Bland-Altman limits of agreement were narrower for DWI (-5.6 to 4.1mL) compared with FLAIR (-10.2 to 6.4mL). Visual review did not identify any patients with expansion of infarction between 24hrs and day 90. **Conclusions:** Infarct growth occurs early such that DWI lesion volume at 24 hours accurately reflects the final infarct volume at day 90. DWI is more reproducible than FLAIR. The use of an earlier assessment has the potential to reduce loss to follow-up and the resultant bias in trials.

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Th P89

Utility of the NIHSS Exam and Cortical Score to Predict New Cortical Stroke on MRI

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Background: The NIHSS exam is routinely used to identify stroke and determine stroke severity. Studies targeting cortical strokes often require advanced neuroimaging, which can delay intervention and limit potential study sites. Our prior exploratory study demonstrated that the cortical score (total points given on NIHSS for findings of gaze palsy, visual field deficit, aphasia, and neglect) of $\geq$2 points yielded a positive predictive value (PPV) for a cortical stroke of 88%. We sought to validate this finding in a second population of patients with acute ischemic stroke (AIS) qualifying for intravenous thrombolysis (IV tPA). **Methods:** All patients admitted to our center from 7/2008 - 12/2009 with a final diagnosis of AIS who were treated with IV tPA within the first 3 hours of stroke onset were identified from our stroke registry. Patients were excluded if they did not have admission NIHSS exam or received intra-arterial therapy. MRI diffusion weighted images (DWI) were reviewed to determine the presence of acute infarction. Patients with DWI lesions were divided into two groups depending on the presence or absence of cortical involvement. Various combinations of NIHSS exam components and the cortical score were evaluated for sensitivity, specificity, and PPV for identifying the presence of an acute cortical stroke. **Results:** 60 patients meeting inclusion criteria had DWI evidence of new infarction. 55 patients (91.7%) had cortical findings on NIHSS and 46 patients (76.7%) had cortical involvement on DWI. The median NIHSS was 12 (1-29). 93% of patients with a cortical stroke had at least one cortical sign or NIHSS $\geq$4 points. The PPV of a cortical stroke was 78% for a cortical score of $\geq$2 and 83% for a cortical score of $\geq$3. Forced gaze, global aphasia, and complete neglect each yielded a PPV $>$88%. When excluding patients with a prior history of stroke (n=15), the PPV for a cortical score $\geq$2 did not improve. **Discussion:** Not all patients who demonstrate cortical findings on the NIHSS exam will complete a cortical infarct. The PPV herein likely underestimates the true value in patients treated with thrombolysis, since the cortex might be saved by recanalization and reperfusion in some patients. Severe deficits in the individual NIHSS exam cortical elements can predict cortical stroke with higher reliability than the cortical score, but the cortical score can be generalized to the entire population of AIS patients. A larger study of patients with AIS should be performed to determine if the cortical score can serve as a surrogate marker for a cortical stroke.

test	sensitivity	specificity	PPV	NPV
any cortical sign	**0.93**	0.14	**0.78**	0.4
cortical score ≥2	0.76	0.29	**0.78**	0.27
cortical score ≥3	0.63	0.57	**0.83**	0.32
cortical score ≥4	0.5	0.57	0.79	0.26
cortical score ≥5	0.37	0.71	0.81	0.26
cortical score ≥6	0.24	0.86	0.85	0.26
cortical score ≥7	0.07	0.93	0.75	0.23
cortical score ≥8	0.02	1	1	0.24
≥2 cortical signs	0.7	0.36	**0.78**	0.26
≥3 cortical signs	0.5	0.57	**0.79**	0.26
4 cortical signs	0.13	0.79	0.67	0.22
abnl gaze	0.61	0.43	0.78	0.25
forced gaze	0.17	0.93	**0.89**	0.25
abnl visual fields	0.61	0.57	0.82	0.31
hemianopsia	0.3	0.71	0.78	0.24
abnl language	0.61	0.29	0.74	0.18
≥2 on language	0.41	0.71	**0.83**	0.27
mute and global	0.2	0.93	**0.90**	0.26
any neglect	0.43	0.57	0.77	0.24
complete neglect	0.15	0.93	**0.88**	0.25
NIHSS ≥4	**0.93**	0	0.75	0
NIHSS ≥6	0.83	0.21	0.78	0.27
NIHSS ≥8	0.72	0.36	0.79	0.28
NIHSS ≥10	0.65	0.5	0.81	0.3
NIHSS ≥12	0.57	0.5	0.79	0.26
NIHSS ≥14	0.46	0.64	0.81	0.26
NIHSS ≥16	0.39	0.71	0.82	0.26
NIHSS ≥18	0.24	0.86	**0.85**	0.26
NIHSS ≥20	0.17	0.86	0.80	0.24
cortical score/NIHSS ≥10%	**0.89**	0.14	0.77	0.29
cortical score/NIHSS ≥20%	0.78	0.29	0.78	0.29
cortical score/NIHSS ≥30%	0.41	0.64	0.79	0.25
cortical score/NIHSS ≥40%	0.15	0.93	**0.88**	0.25
cortical score/NIHSS ≥50%	0.04	0.93	0.67	0.23
NIHSS ≥8 and cortical score ≥2	0.67	0.43	0.79	0.29
NIHSS ≥8 and cortical score/NIHSS ≥20%	0.46	0.71	**0.84**	0.29
NIHSS ≥10 and cortical score ≥2	0.61	0.5	0.80	0.28

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Th P90

Whole Brain CT Perfusion Using Time-to-Peak Maps in Evaluation of Minor Stroke

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Background: The use of thrombolysis in minor stroke is controversial. Treatment decisions may be influenced by identifying patients with large areas of tissue at risk and distinguishing patients with stroke mimics. Whole brain CT perfusion allows for possible assessment of these parameters and is not limited to discrete areas of brain coverage as in previous generations of CT scanners. Whole brain CT perfusion maps can be rapidly generated on the Toshiba 320 Aquilon ® CT without additional contrast or scanning time over standard CT angiogram acquisition, making it an ideal tool in acute stroke settings. Time-to-peak (TTP) maps have been identified as a sensitive parameter for assessment of ischemia. We analyzed the ability of TTP maps to predict eventual infarcts in patients with mild stroke presentations. **Methods:** We retrospectively reviewed the clinical and imaging data of 134 consecutive patients presenting with acute stroke in less than 6 hours from onset of symptoms irrespective of the use of IV thrombolysis. Patients presenting with a NIH Stroke Scale score $<$5 were subjected to subgroup analysis. Whole brain perfusion scans were acquired on the 320 detector CT scanner. TTP perfusion deficit with delays of more than 3 seconds were considered significant for underlying ischemia. The sensitivity, specificity, positive and the negative predictive values were estimated for perfusion parameters in predicting the presence of ischemia based on follow-up imaging and NIHSS at 24 to 48 hours. **Results:** 134 consecutive patients were included in the study. 41 patients were excluded due to inadequate studies (n=14) and no follow up scans (n=27). 38 of remaining 93 patients had minor neurological deficits (NIH $<$ 5) at presentation. 31 of the 38 patients were followed up with MRI and the remaining patients had an unenhanced CT. Seven patients received iv-tPA. The TTP map had the highest level of sensitivity in detecting small infarcts (91%), followed by CBV and CBF (51%, 51%), and MTT

had a lower sensitivity compare to others (49%). Importantly, TTP analysis provided a very high negative predictive value (93%). However, there was a relatively lower specificity (63%) and a tendency to overestimate the size of infarct. **Conclusion:** TTP perfusion is highly sensitive in predicting small regions of ischemic infarct in patients with minor stroke. Just as importantly, the high negative predictive value may be helpful in differentiating between stroke and stroke mimics.

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Th P91

Can We Rely On Negative Diffusion Weighted Imaging?

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Background - Sudden focal neurological deficits call for urgent clinical and radiological evaluation. If acute radiological screening is negative, doubt about the finding's reliability often leads to diagnostic uncertainty. This holds true for CT but also diffusion weighted MRI (DWI), especially when it comes to infratentorial infarction. We hypothesized that patients without neurologic symptoms would not show infarction in a follow up examination. We thought the NIH stroke scale (NIHSS) would be a valid tool to screen and triage those patients. Methods - Adult patients with suspected cerebral ischemia underwent stroke MRI (T2*, high resolution DWI, MRA, FLAIR, perfusion imaging) and NIHSS examinations acutely and on the following day. Patients with negative acute DWI were eligible for this analysis. We calculated odds ratios to assess strength of association between DWI shown ischemia on follow up scans and dichotomized NIHSS (0 vs. >=1), as well as possible confounders. Multivariate analysis was not performed due to sample size. To assure usability as a screening tool we calculated the negative predictive value (NPV) for a dichotomized NIHSS. **Results & Discussion:** Regardless of the final diagnose, 151 patients had negative acute DWI, 63 subjects received a follow up MRI. DWI was positive in 11.1 % of patients on the second day. Median admission NIHSS score was 0. We found a strong association between dichotomized NIHSS and DWI on the second day (OR 17.50 95% CI 2.83-108.12). NPV of dichotomized NIHSS score on the second day for infarction as shown by DWI was 0.96. A borderline association could also be shown for atrial fibrillation (OR 5.14 95% CI 0.95-27.98) and delay between onset of symptoms and imaging (p-value 0.1 for Mann-Whitney-U-test). This study was underpowered to safely exclude those variables as confounders. However, even after Bonferroni adjustment for multiple testing the association of NIHSS score on the second day and the follow up DWI remained significant. **Conclusion:** Based on our data set, we found the NIHSS to be a good screening tool to determine whether or not a second MRI is necessary to establish cerebral infarction via DWI.

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Th P92

Hyperintense ICA Sign: A Marker For Worse Stroke Outcome

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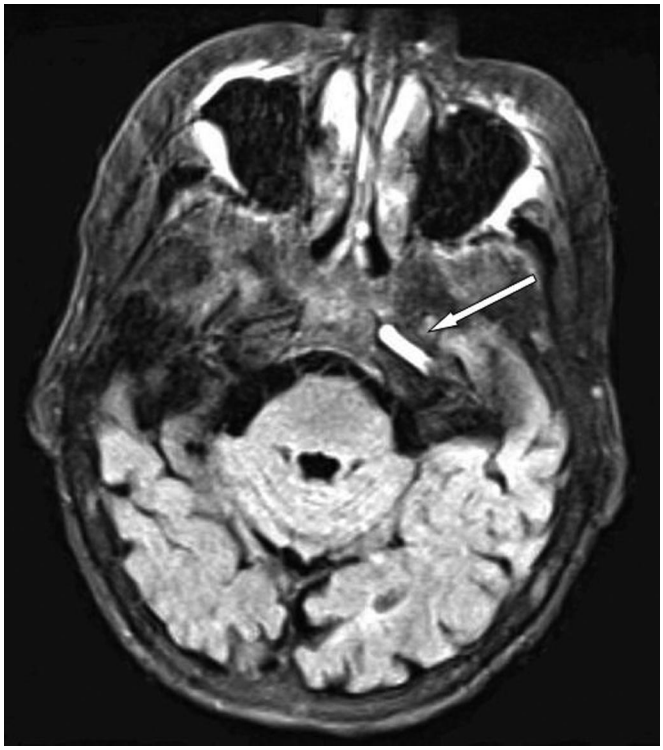
Background: Fluid-attenuated inversion recovery vascular hyperintensities (FVH) on MRI may be seen proximal and distal to occlusions in acute stroke. These findings, suggestive of slow flow, may carry different prognostic information in proximal versus distal vessel segments. We evaluated the presence of proximal FVH in the internal carotid artery (ICA) and hypothesize that this finding may be associated with worse angiographic and clinical outcomes in patients undergoing intervention for acute ischemic stroke. **Methods:** We analyzed consecutive patients between January 1, 2007 and July 31, 2010 who presented with acute strokes from ICA or middle cerebral artery (MCA) occlusions and underwent angiography for any potential endovascular intervention. Patients who received intravenous tPA (IV-tPa) prior to angiography were included. The presence of proximal FVH in the intracranial ICA and the number of segments (petrous, cavernous, clinoid, terminal) based on consensus MRI review by two investigators. These findings were compared to angiographic recanalization scores (AOL and TICI) and functional status at discharge [modified Rankin Scale (mRS)]. **Results:** Among 89 patients, median age was 66 (range 22-95), 63% were female, and occlusion locations were ICA in 32 (36%) and MCA in 57 (64%). Interventions included mechanical thrombectomy in 65 patients, acute angioplasty with stenting in 14, partial aortic occlusion treatment in 8, IA lytics in 7 and IV-tPA in 17. Proximal FVH was noted in 29 (32.6%) cases of which the median number of ICA segments with hyperintense signal was 3 (IQR 2 -4). Frequency of segment involvement was: petrous - 96.6%, cavernous - 86.2%, clinoid - 79.3%, terminal - 34.5%. The presence of proximal FVH was associated with worse discharge functional outcome (mRS median 5 vs 4, P<0.001). Greater number of ICA segments involved similarly correlated with higher discharge mRS scores (r = 0.22, p< 0.05). Among patients who underwent endovascular recanalization, a significant association between proximal FVH was not found with AOL and TICI scores. Proximal FVH did not affect recanalizaton success, with TICI 2b or higher achieved in 50% with FVH vs 51.1% without, p= 0.54. As expected, mRS scores were inversely associated with recanalization AOL scores (r = -0.30, p=0.01) and TICI scores (r = -0.32, P<0.05) in this study. **Conclusions:** The hyperintense ICA sign, a marker of delayed flow below an occlusion, is present in one-third of patients and is a potential prognostic sign for worse functional outcome in patients with MCA and ICA occlusions.



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Th P93

Optical Measurements of Cerebral Hemodynamics in Acute Cortical Stroke

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Background and Purpose: A major goal in the care of acute ischemic stroke (AIS) is optimization of cerebral blood flow (CBF) in order to salvage as much of the ischemic penumbra as possible. CBF becomes dependent on cerebral perfusion pressure due to impaired autoregulation, but clinically there is no realtime bedside method for monitoring CBF available. Current guidelines recommend a flat head-of-bed (HOB) position to maximize CBF following AIS, based on blood velocity data measured by transcranial Doppler (TCD) ultrasonography. Diffuse correlation spectroscopy (DCS) is a novel technology for non-invasive transcranial measurement of CBF. We sought to determine if DCS is sensitive to changes in CBF with manipulation of HOB angle, and if CBF changes are comparable to those in blood velocity measured by TCD. **Methods:** We explored the utility of DCS to measure the effect of HOB positioning at 30°, 15°, 0°, and -5° in patients with AIS. We enrolled patients with unilateral acute middle cerebral artery cortical infarction within 72 hours of onset. Measurements were made simultaneously with TCD and DCS bilaterally, and each contralesional hemisphere served as a control. **Results:** 13 subjects were prospectively enrolled. HOB positioning at 15° resulted in a 9% decrease (95% CI: 5-13%; p=0.0007) in CBF ipsilesionally and 30° resulted in 15% decrease (95% CI: 6-24%; p=0.003) in CBF ipsilesionally, relative to a flat HOB. Similarly, a 30° HOB angle resulted in an a 6% decrease (95% CI: 2-11%; p=0.011) in blood velocity relative to a flat HOB in the ipsilesional hemisphere. Similar directions of relative flow and velocity changes were observed in the contralesional hemisphere, but differences were smaller and non-significant. Linear regression demonstrated that HOB angle is strongly correlated with CBF ipsilesionally (Adj R^2:0.40; coef:-0.52 per degree; P<0.001) and contralesionally (Adj R^2:0.22; coef:-0.33 per degree; P<.001). HOB angle was also correlated with blood velocity both ipsilesionally (Adj R^2:0.40; coef:-0.23; P<0.001) and contralesionally (Adj R^2:0.36; coef:<-0.16; P<0.001). Additionally, CBF and velocity were found to correlate both ipsilesionally (Rho:0.46; p=0.0008) and contralesionally (Rho:0.34; p=0.046). **Conclusions:** Both DCS and TCD demonstrate impairment of cerebrovascular autoregulatory mechanisms in the region of the infarct. Further, a flat or -5° HOB angle maximizes perfusion of the infarcted region for the majority of patients. Blood velocity and CBF strongly correlate across a range of HOB angles, but CBF changes exceed velocity changes, suggesting DCS measurements of CBF may be more sensitive. Real time noninvasive monitoring of CBF may allow for individual optimization of HOB position and other hemodynamic parameters during the acute management of stroke.

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Th P94

Anterior Choroidal Artery Diffusion-Weighted Imaging Patterns at Onset Predict Disability from Carotid Occlusion

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Background: The prognosis of acute internal carotid artery (ICA) occlusion may be difficult to predict. Although extensive baseline diffusion-weighted imaging (DWI) lesions are known to sway outcome, the predictive role of specific DWI patterns in critical regions such as the anterior choroidal artery (AChA) remains unknown. Early AChA infarction may reflect extensive ICA thrombus extending to the AChA origin and/or poor collateral status. We hypothesized that spared or minimal AChA infarction following ICA occlusion predicts fair outcome, defined as modified Rankin Scale (mRS) 0 to 3, at discharge. **Methods:** We studied consecutive acute ICA occlusion patients evaluated between January 2002 through August 2010, who underwent MRI followed by catheter angiography. Pattern of AChA involvment on initial DWI was categorized as spared, partial, and full. Partial involvement of AChA was further categorized into 6 subgroups: mesial temporal (MT), posterior limb of internal capsule (PIC), posterior part of peri-ventricle (PPV), MT+PIC, MT+PPV, and PIC+PPV. Two neurologists independently labeled the AChA infarct pattern. The association of AChA infarct pattern and fair outcome at discharge was calculated by logistic regression with adjustment of age, admit NIHSS scores, time between last known well and MRI, and recanalization status. **Results:** Among the 60 patients meeting study entry criteria, mean age was 68.3 years, mean pretreatment NIHSS was 17.7 and mean time from last known well to MRI was 361 minutes. AchA territory was spared in 19 patients, partially involved in 26, and fully involved in 15. Among patients with spared AchA infarct, 52.6% had fair discharge outcome while 34.6% of AChA partially involved patients and 13.3% of AChA fully involved patients had fair discharge outcome. The infarct pattern of AChA was independently associated with fair discharge outcome after adjustment (P=0.028). Among patients with partial AChA infarct, infarct restricted to MT had 50% fair outcome while infarct beyond MT had 33.3% fair outcome. When we categorized AChA infarct pattern as spared and MT only vs. other partial infarct pattern and full infarct, the former was independently associated with fair discharge outcome after adjustment (51.9% vs. 21.2%, P=0.017). **Conclusion:** In acute ICA occlusion, spared or AChA infarction restricted to the mesial temporal field on baseline DWI independently predicts fair discharge outcome. Analysis of AChA infarct patterns on DWI may improve early prognostication and decision-making.

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Th P95

Thrombus Hounsfield Units on Thin-Section Noncontrast CT Predicts Early Vascular Recanalization and Stroke Subtype After Thrombolysis

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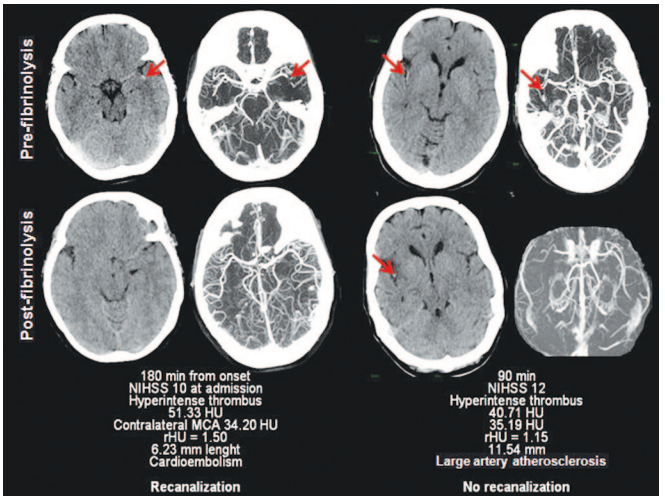
Background and Purpose: Thin-section noncontrast CT (NCT) can detect thrombi in large arteries in acute stroke and provide a measure thrombus composition based on Hounsfield units (HU). Thromboembolic stroke can be caused by white, red, or mixed clots. White (platelet-rich) thrombus is resistant to thrombolytic drugs, but red (erythrocyte-rich) is not. HU are lower in white thrombi than in red. We investigated whether HU in thin-section NCT can differentiate subtypes of acute ischemic stroke and predict the lysability of thrombi. **Methods:** Two readers blinded to clinical data reviewed 1.25mm-section NCT studies obtained immediately before IV thrombolysis of middle cerebral artery (MCA) acute thrombi within 4.5 hours of stroke onset. Stroke subtype was assigned using TOAST criteria. HU values and ratios (rHU) were measured on thrombi and contralateral normal segments. We also evaluated the effected MCA segment, thrombus length, and time from onset. Recanalization was assessed by CT or MR angiography after IV thrombolysis. We found the cut-off value of thrombus HU for lysability by binary logistic regression. We sought associations between recanalization and stroke subtype, affected MCA segment, thrombus length, and time from onset with ANOVA, chi-square, and T-test. **Results:** We evaluated 39 patients (22 men, 17 women; aged 68.74±11.94 years). Breakdown of stroke subtype: 43.5% large artery atherosclerosis (LAA), 43.5% cardioembolism (CE), and 13% unknown/other. CT angiography detected thrombi in all patients. Recanalization occurred in 35.9% of patients. Mean rHU of recanalized and unrecanalized thrombus were 1.57±0.23 and 1.11±0.15, respectively (p<0.001). An rHU > 1.278 best predicted thrombus lysability (sensitivity 96.0%, specificity 92.9%, positive predictive value 96.0%, negative predictive value 92.9%). rHU values were 1.372±0.31 for CE, 1.101±1.17 for LLA, and 1.462±0.26 for unknown/other. rHU in LLA thrombi were lower than in CE and unknown/other stroke thrombi (p=0.004). Length, time from onset, and affected MCA segment did not correlate with early recanalization (p=0.219, p=0.184, and p=0.168, respectively). **Conclusion:** Measuring thrombus HU can help determine stroke subtype and prognosis of IV thrombolytic therapy, enabling the best reperfusion strategy and early secondary prevention measures to be chosen for individual patients.



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Th P96

The Value of CT Perfusion (CTP) Prognostic Maps in Predicting Reversible and Irreversible Neurological Dysfunction Following Reperfusion Therapies

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Background&**Purpose:** We aimed to evaluate the ability of a commercially available CTP prognostic maps software to identify reversibly and irreversibly damaged brain functions in the best case scenario: patients who achieved early and complete tissue reperfusion. Subjects&Methods: Consecutive ischemic stroke patients who received reperfusion therapies, those with early (< 2 hours from treatment initiation) and complete (TIMI III-or equivalent) reperfusion were included in the analysis. CTP prognostic maps (Phillips Brilliance CT) were assigned as "red", or irreversible if CBV fell below 2 ml/100g and "green", or recoverable if the affected/un-affected MTT ratio was >1.4. Only patients with MCA territory affected were included and subcomponents of the NIHSS scale pre- and post-treatment were analyzed based on anatomical correlation of the affected CTP areas and corresponding neurological functions. ASPECT scores and early ischemic changes in the corresponding vascular territories were also obtained from a non-contrast pre-treatment CT scans independent of CTP and clinical findings. **Results:** Among 109 consecutive patients who had intra-arterial reperfusion procedures (age 60±15 years, 55% men, median NIHSS 15, interquartile range 9.5-21), 18 had pre-treatment CTP and had early complete reperfusion. We identified 50 affected areas on CTP [red 13 (26%), green 37 (74%)] with corresponding measurable neurological deficits including aphasia, arm, face weakness, and inattention. The lowest follow-up NIHSS subcomponent scores were obtained after treatment until discharge. Red areas correctly identified 11/13 (85%) of functions that did not recover despite early reperfusion. Red portions >30% of the total affected area correctly predicted 92% of irreversibly lost function, while red portions ≤30% of the total area identified 40% of lost functions (OR 7.2, 95% CI 1.7-30.3, p=.006). "Green" correctly identified 17/37 (46%) of functions that recover after early reperfusion (OR 4.7, 95%CI 1.0-21.3, p=0.095). ASPECTS ≤7 for irreversible loss were correct in 34/44 (77%), while ASPECTS >7 predicted 11/28 (39%) of recoverable functions (OR 2.2, 95% CI 0.8 - 6.1, p=0.184.)**Conclusions:** In patients achieving early and complete reperfusion, pre-treatment CTP prognostic maps had the highest predictive value for irreversibly lost neurologic functions with CBV<2ml/100g particularly when red areas extended to over 30% of the total affected area. Prediction of recoverable functions on CTP had a modest value similar to that of the ASPECT score from a non-contrast CT.

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Th P97

Qualitative Evaluation of Mismatch in Acute Stroke Using CT and MRI Perfusion. Do Readers Agree? Do Modalities Agree?

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Background: Cerebral perfusion imaging in acute stroke could improve patient selection for reperfusion therapies. CT perfusion and MR perfusion are competitively used to image core/penumbra mismatch in acute stroke. We sought to assess the agreement of these two techniques on qualitative assessment of mismatch**Methods:** Patients with acute ischemic stroke from 2 major academic hospitals who had undergone both CT and MRI perfusion at baseline were included in the analysis. All perfusion images were independently interpreted in a blinded fashion and random order by two experienced vascular neurologists who were unaware of the clinical presentation. For each patient, readers scored the presence or absence of a clinically significant CBV/Tmax mismatch on CT, and a DWI/Tmax mismatch on MRI. Interreader and intermodality agreement analysis was then performed using kappa statistics. **Results:** A total of 19 patients were included in the analysis. Time interval between obtaining CT and MR images ranged from 33 to 185 minutes. 12/19 patients were treated with intravenous rt-PA. Interreader agreement on mismatch was perfect with kappa=1.00 for both CBV/Tmax (19/19; mismatch present in 15 cases, absent in 4), and DWI/Tmax (17/17; 12 present, 5 absent, 2 uninterpretable due to poor bolus). Intermodality agreement was present in 13/17 cases (kappa=0.36, p=0.12). Of the remaining four cases, three had a mismatch based on CT perfusion (CBV/Tmax) but not on MRI and one patient had a mismatch on MRI (DWI/Tmax) but not on CT perfusion. All four of these patients were treated with intravenous rt-PA. A review of corresponding CTAs and MRAs revealed no evidence for interval recanalization. **Conclusion:** Our results demonstrate an excellent interreader agreement on mismatch classification for both CTP and MRI. The agreement between two techniques was modest. Potential causes for this difference may include the impact of intravenous thrombolytic therapy, time interval between the two studies, and suboptimal CTP coverage.

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Th P98

Clot Or Not: Using The Sigmoid Plate Sign On Head CT to Differentiate Transverse Sinus Thrombosis from a Congenitally Atretic Cerebral Transverse Sinus

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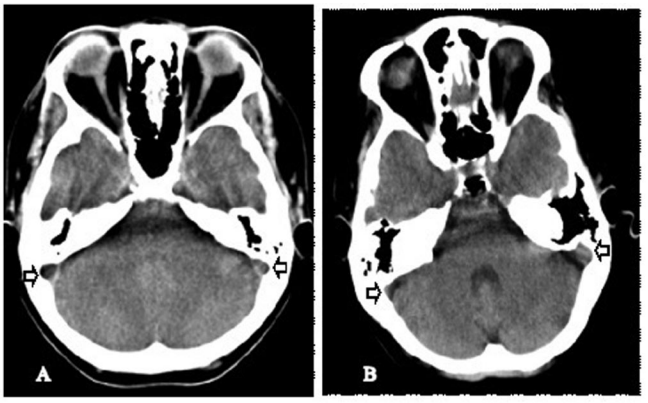
Background: Transverse sinus venous thrombosis can be a difficult diagnosis given its non-specific clinical signs and lack of specificity on MR venograms. We hypothesize that comparison of the sigmoid plates on non-contrast brain CT can differentiate transverse sinus clot from a congenitally atretic sinus when dropout of transverse sinus flow is seen on MRV. **Methods:** We collected 53 subjects with MRV dropout of a transverse sinus. A retrospective review of all available brain imaging and medical records on each subject (our gold standard) determined 11 had thrombosis and 42 had an atretic transverse sinus. De-identified non-contrast brain CTs, marked with side of MRV dropout, were sent to 2 blinded neurologists for adjudication of the presence or absence of the sigmoid plate sign. A positive sigmoid plate sign was defined as an asymmetrically smaller sigmoid plate, hypothesized as consistent with an atretic sinus, in the presence of MRV dropout on that side. A mutual answer was provided by the reviewers when they disagreed. Sensitivity, specificity, a Fisher's exact test, and odds ratio for the distribution of the sign in subjects with clot and subjects with sinus atresia were calculated. **Results:** Each blinded neurologist had a sensitivity of 91% (detecting 10/11 clots based on absence of the sigmoid plate sign) and specificity of 71-81% (detecting atretic sinuses based on presence of the sign), compared to the gold standard diagnosis. Cohen's kappa was 0.60. The composite sensitivity was 91% and specificity was 86%. 9% of individuals (1/11) with clot had a positive sigmoid plate sign, compared with 86% of individuals with an atretic sinus ($p<0.001$). An absent sigmoid plate sign in the presence of MRV dropout was associated with a 60-fold higher odds (95% CI 6.45, 558) of having clot, compared to subjects with a positive sigmoid plate sign. Sensitivity and specificity improved to 100% and 92%, respectively, in the 19 cases where MRV dropout was on the right side. **Conclusion:** Asymmetries of the sigmoid plates on non-contrast brain CT are a very sensitive and specific measure of differentiating transverse sinus thrombosis from an atretic transverse sinus when dropout of MRV flow is visualized.



Both subjects A and B had right MRV dropout. Subject A has absence of the sigmoid plate sign suggesting right transverse sinus clot; Subject B has presence of sigmoid plate sign as the right sinus is smaller than the left suggesting right atretic sinus. Arrows identify the sigmoid plates.

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Th P99

MRI As Witness: Ready For Prime-time?

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Background: Approximately 25% of stroke patients have unwitnessed strokes. These patients are often ineligible for IV thrombolysis because the last known well time (LKW) was >4.5 h before ED arrival, even if their true onset time was within 3 h. Recent studies suggest that negative FLAIR MRI can be used to identify patients with LKW < 3 h. Controversy exists on the reproducibility of this technique in a clinical setting. One study reported mean kappa (κ) agreement values regarding FLAIR negativity to be only 0.29 among 4 readers. It has been suggested that combining qualitative review of DWI and FLAIR MRI with region of interest (ROI) analysis can improve time prediction reliability. We sought to investigate interrater and intersite agreement using this approach. **Methods:** MRI from patients with witnessed left anterior circulation strokes within 24 h of LKW were analyzed. Two readers at 2 sites first qualitatively classified FLAIR lesions as negative or positive based on a brief description and 3 representative FLAIR images: 1 negative, 2 positive (1 subtle, 1 obvious). The signal intensity ratio (SIR) of the mean signal intensity (SI) of an ROI on the lesion to the mean SI of an ROI on the opposite side was measured. For ROI placement, readers were instructed to: (1) choose the slice with the greatest FLAIR SI that corresponds to the acute DWI lesion; (2) select the slice that matches the largest DWI lesion if FLAIR is negative; (3) select the brightest lesion in cases of multiple areas of infarct. A decision tree was created using recursive partitioning with cross-validation where the inputs were the 4 qualitative assessments and 4 SIR reads. **Results:** MRI from 85 patients were analyzed: 56 with LKW < 3.5 h (Early) and 29 with LKW > 3.5 h (Late). The derived tree model resulted in the rules: (1) if SIR≥1.26, the pattern was Late. (2) Otherwise, if the patient was visually deemed FLAIR negative, the pattern was Early. (3) If the patient was visually FLAIR positive but had SIR<1.13, the pattern was Early. (4) Patterns not meeting any of these criteria were Late. For qualitative FLAIR reads, Fleiss' κ=0.36, sensitivity (sens)=41%, specificity (spec)=80%. Intraclass correlation coefficient for SIR was 0.66. Using SIR<1.26 for Early or Late classification resulted in a κ=0.45, sens=87%, and spec=57%. Using the combined visual inspection and SIR, Fleiss' κ=0.47, sens=66%, spec=68% across 4 readers. Site 1 interrater κ=0.50. Site 2 interrater κ=0.55. Comparing the best readers at each site, intersite κ=0.59. **Conclusion:** Combined FLAIR and ROI analysis produced improved agreement in classifications of Early and Late stroke patterns while maintaining good sensitivity and specificity. We obtained moderate interrater and intersite agreement using simple rules that can be easily and rapidly performed at MR consoles. With formal rigorous training on a representative dataset, agreement will likely increase substantially.

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Th P100

Value of Computed Tomography Perfusion Imaging in Evaluation of Patients withTransient Ischemic Attack

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Background: The presence of tissue at risk can be identified on computed tomography perfusion (CT-P) imaging using a combination of increased mean transit time (MTT), decreased

cerebral blood flow (rCBF), and normal or increased cerebral blood volume (rCBV). The value of CT-P abnormalities in identifying patients with transient ischemic attack (TIA) at risk for subsequent ischemic stroke is not known. **Objective:** To determine the role of CT-P imaging in the diagnostic imaging of patients with TIA within 24 hours of symptom onset. **Methods:** A review of 400 consecutive patients with a pre-admission diagnosis of TIA (ICD-9 435.9) admitted to two University affiliated stroke medical centers was performed. The patterns of MTT, rCBF and rCBV on the initial CT-P were categorized as either preserved (no change), increased or decreased. We evaluated the relationship between CT-P abnormalities and infarction on subsequent magnetic resonance imaging (MRI) and new stroke within 48 hours of TIA. **Results:** A total of 83 patients (mean age±standard deviation, 66±15 years, 40(48%) were men) of 400 patients with TIAs underwent CT-P study within 24 hours of symptom onset. The following patterns of the CT-P were observed: The risk of new stroke within 48 hours of

TIA Patients	n=400
CT-P performed	83 (21%)
CT-P patterns	
Preserved MTT, rCBF, rCBV	73(88%)
Increased MTT, preserved rCBF and rCBV	2(2%)
Increased MTT, decreased rCBF, preserved rCBV	4(5%)
Increased MTT, decreased rCBF and rCBV	2(2%)
Relative MTT and rCBF, decreased rCBV	1(1%)
Preserved MTT, decreased rCBF and rCBV	1(1%)

TIA was not different among patients with preserved CT-P parameters (0 of 73) compared with those with abnormalities in one or more of the parameters (0 of 10). Among the 73 patients with preserved CT-P parameters, 63(86%) had a subsequent cranial MRI and 11(15%) were found to have infarctions. A total of 10(12%) patients had changes on the CT-P with 5 of the patients having subsequent cranial MRI that did not show any infarction. **Conclusion:** Abnormalities on CT-P are infrequent among patients with TIAs and were not associated with either MRI demonstrated infarction or new stroke within 48 hours of TIA.

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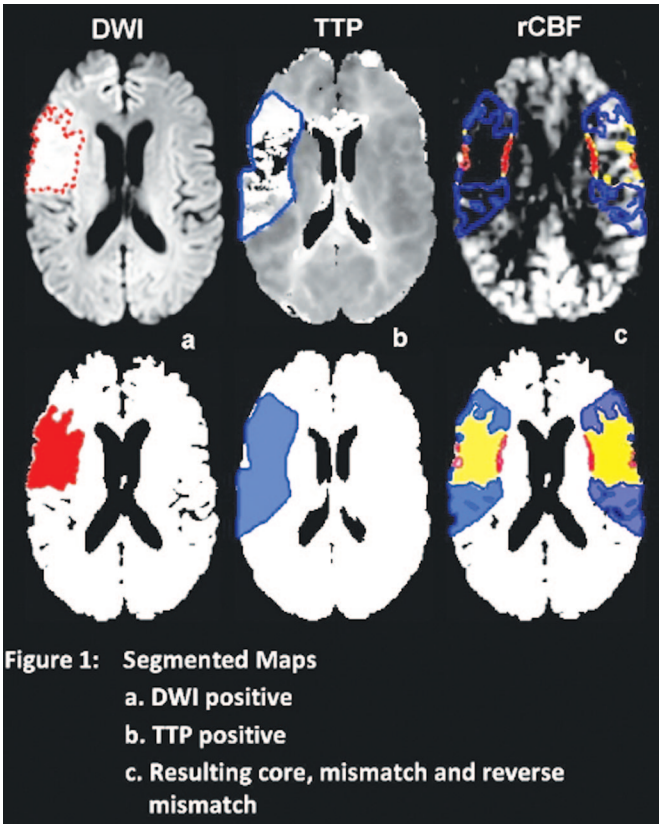

Figure 1: Segmented Maps
a. DWI positive
b. TTP positive
c. Resulting core, mismatch and reverse mismatch

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Th P101

Cerebral Blood Flow Quantification Utilizing Pseudo-Continuous Arterial Spin Labeling in Acute Stroke Patients

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Introduction: In routine clinical practice, relative cerebral blood flow (rCBF) is estimated using gadolinium-based contrast (dynamic susceptibility contrast (DSC)) magnetic resonance imaging (MRI), which is sensitive to arrival and transit delay time. Arterial spin labeling (ASL), a technique that magnetically labels blood flowing to the brain, is a non-invasive alternative that can be used to quantify cerebral blood flow. Our goal was to test whether ASL could be used to quantify rCBF values in the core, mismatch and reverse mismatch in acute ischemic stroke patients. **Methods:** Acute stroke patients were imaged with a 3T-Philips MRI to identify diffusion (DWI) and perfusion (ASL and DSC) deficits. Following DWI, DSC and ASL image coregistration, the acute diffusion and perfusion deficits were segmented on DWI and DSC time to peak (TTP), blinded to ASL (Figure 1a, 1b). TTP was estimated using DSC. Three regions were defined: core (DWI+, TTP+), mismatch (DWI-, TTP+), and reverse mismatch (DWI+, TTP-). Resulting volumes of interest (VOIs) were mirrored across midline into the contralateral hemisphere. All VOIs were copied to the ASL images; and rCBF was calculated as the ratio of the mean signal intensity measured on the side of the lesion to that of the homologous region in the contralateral hemisphere (Figure 1c). Mismatch, reverse mismatch and core VOIs $\geq$ 2cc were used for paired comparison Wilcoxon ranks test between regions. **Results:** Thirty patients (66.4±16.8 years) were included in the study. Patients had a median NIHSS of 9 (IQR 4-19.5). Median time from onset to MRI was 5.8 (IQR 2.6-17.3) hours. Median volumes were: DWI, 11.3 cc; TTP, 53.5 cc; core, 8.1 cc; mismatch, 41.9 cc; and reverse mismatch, 2.8 cc. The average rCBF ratios were significantly higher in the mismatch (0.51±0.23, $p \leq 0.05$) versus the core (0.36±0.33) and reverse mismatch (0.65±0.47, $p \leq 0.01$) versus the core (0.35±0.34). **Conclusion:** We have shown that rCBF calculated using ASL was greater in the mismatch (DWI-, TTP+) versus the core, suggesting relatively higher blood flow in the mismatch and supporting the concept of salvageable tissue. By using DSC for detection (of a perfusion deficit) and ASL for an independent measure of rCBF values, the strengths of each technique can be used synergistically.

Th P102

A Regional Model of Collateral Perfusion Accurately Predicts Tissue Fate in Acute Ischemic Stroke

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Background: A reliable method for prediction of tissue fate during the acute phase of ischemic stroke may be used to tailor therapeutic decisions and prognostication. Predictive models have primarily focused on numerical simulations to improve accuracy without consideration of the underlying pathophysiology of collateral perfusion. As in the pulmonary circulation, regional perfusion in the brain may vary depending on compartmental pressure differentials. We developed a regional model of collateral perfusion that incorporates such cerebrovascular physiology to predict infarct evolution from core to surrounding tissue. **Methods:** Consecutive cases of acute middle cerebral artery occlusion (MCAO) with serial MRI at baseline and day 5 were analyzed. Measures of cerebral perfusion pressure, tissue pressure and venous pressure were extracted from diffusion-weighted and dynamic susceptibility contrast enhanced perfusion imaging. Based on pressure differentials validated in blood flow models, we identified 3 distinct zones corresponding to core, penumbra, and benign hyperemia. Following co-registration with day 5 images, a nonlinear statistical model was used to quantify the predictive capacity of the regional maps and accuracy was compared with Tmax. **Results:** 42 cases (mean age 66.7±18.5 years; 26 women, 16 men) of acute MCAO with serial MRI were analyzed. Distinct zones reflecting pressure differentials between the arterial, tissue and venous compartments were constructed and displayed as parametric images. Regional zones comparable to core, penumbra, and benign hyperemia were identified. The regional model was able to accurately classify voxel outcome defined as infarction on day 5 fluid attenuation inversion recovery sequences across various grades of reperfusion. Voxel classification results revealed accuracies of 93.8±2.05% for the regional model compared with 92.2±3.25% using Tmax. Using two distinct models based on dichotomized reperfusion status, accuracies of the regional model improved to 95.7±1.9% for the regional model versus 94.4±2.5% using Tmax (no reperfusion) and 94.4±2.5% for the regional model versus 93.0±4.3% using Tmax (reperfusion). Unlike Tmax prediction, poor quality images and noise on multiparametric images limited the regional model in isolated cases. **Conclusions:** A regional model of collateral perfusion can reliably predict tissue fate for infarction with accuracy that exceeds Tmax prediction. Incorporation of reperfusion status and other angiographic variables can be used to maximize performance of this novel prediction algorithm derived from underlying vascular pathophysiology.

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Th P103

Optimizing Arterial Input Functions In Acute Stroke MRI - A Comparison With O15-Water-PET

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Background: The arterial input function (AIF) is a precondition for MR perfusion imaging. However so far there is no validation of the optimal localisation of the AIF in acute stroke. We assessed the different AIF's from the M1, M2 and M3 branches of the Middle Cerebral Artery (MCA) to detect the penumbral flow threshold defined by 150-water positron emission tomography (CBF-PET) (<20 ml/100g/min). **Methods:** In acute and subacute stroke patients, the CBF-PWI maps generated with AIF's from the different MCA branches (M1, M2, M3) contralateral to the ischemic hemisphere were compared on a voxel based approach with CBF-PET. In a receiver operating comparison (ROC-analysis), the influence of the AIF on PW derived maps was assessed using quantitative CBF-PET maps as the gold standard with respect to penumbral flow <20ml/100g/min. The performance of the AIF to define the penumbral flow was calculated for each MCA branch. **Results:** In an analysis of 8 stroke patients (median time MRI to PET: 66 minutes; patients imaged within 22 hours after stroke) the best MCA branch for the definition of the AIF with the highest area under the curve (AUC) to identify penumbral flow (<20ml/100g/min on CBF-PET) was the M3 segment. Median AUC was 0.94 (IQR 0.87-0.96), 0.91 (IQR 0.84-0.95), 0.86 (IQR 0.79-0.90) in M3, M2 and M1 respectively. **Discussion:** Quality in terms of AUC was enhanced in more distal MCA branches. In conclusion, our data support that AIF's for the generation of PW-CBF maps in acute stroke should be defined via selection of distal branches of the MCA.

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Th P104

Delayed Perfusion Predicts The Volume Of The Perfusion Lesion

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Intro: There is current speculation over the most accurate method of identifying the ischemic penumbra using imaging. The Perfusion techniques used show a great deal of variability in their definition of the perfusion lesion, both for MRI and CTP. This project aims to add to the body of knowledge attempting to predict the volume of tissue destined for infarction should reperfusion not occur in an ischemic stroke. **Methods:** Acute CTP was coregistrerd and compared to subacute MRI-DWI images in 76 hemispheric ischemic stroke patients without rperfusion. A pixel-based Receiver Operator Characteristic cure analysis was used to determine which CTP threshold would best predict the follow-up MRI-DWI lesion on the CTP map. **Results:** A Tmax (time to peak of the residual function) of + 2 seconds showed the greatest level of accuracy (AUC 0.82, Sensitivity 0.89, Specificity 0.78, Positive Predictive Value 0.79) in predicting the extent of tissue death in a setting of no reperfusion. **Discussion:** Tmax thresholds, particularly a threshold of +2 seconds compared to contralateral hemisphere baseline Tmax is the best predictor of the perfusion lesion.

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Th P105

Oxygen Challenge MRI Provides a Measure of the Underlying Haemodynamic and Metabolic State of the Tissue

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Background We recently presented pilot results for the development of Oxygen Challenge MRI (Santosh et al, JCBFM, 2008; Dani et al Annals of Neurology, 2010). Transient application of hyperoxia during T2*-weighted MRI precipitates signal increases in healthy tissue, exaggerated signal increases in likely 'penumbral' tissue, and attenuated signal increases in infarct core, thus reflecting underlying deoxyhaemoglobin concentration. In this voxel based study we further examined the influences on T2*-weighted signal changes. Methods Data from subjects for whom there was a measurable lesion detectable by imaging and who had PWI and Oxygen Challenge data acquired were analysed (n=12; median NIHSS = 12; median time to imaging = 20h). Two slices which showed the largest lesions were selected from each subject giving 53 955 voxels incorporating unaffected tissue (n=12 subjects), hypoperfused DWI lesion (n=9), reperfused DWI lesion (n=3), and PWI-DWI mismatch tissue (n=6). For each voxel, cerebral blood volume (CBV), perfusion state (TMAX) and apparent diffusion coefficient (ADC) were recorded and if necessary transformed to achieve Gaussian distribution. Data were entered into a multivariate linear regression model to predict the percentage signal change (PSC) after Oxygen Challenge. Results Univariate analyses showed that all 3 predictors were significantly correlated with PSC ('natural log' CBV, Rho=0.3, P<0.0001; reciprocal TMAX, Rho = 0.15, P<0.0001; ADC, Rho=0.19, P<0.0001). When all 3 predictors were entered into a multiple linear regression model only transformed CBV (r=0.2, P<0.0001) and ADC (r=0.1, P<0.0001) were independently predictive of PSC (R^2 =7.2%). A multiple linear regression analysis using only voxels from within the DWI lesion (n=8280) demonstrated that all 3 predictors were statistically significant (transformed CBV, r=0.19, P<0.0001; reciprocal TMAX, r = 0.02, p=0.047; ADC, r=0.12, P<0.0001). **Conclusions:** In addition to CBV, parameters which are likely to be related to tissue metabolic state, such as diffusional state (ADC), and possibly the depth of hypoperfusion (TMAX), are independent predictors of the Oxygen Challenge response. Oxygen extraction fraction is likely to account for much of the unexplained variance. PSC after Oxygen Challenge is dependent on deoxyhaemoglobin concentration and thus provides an integrated measure of the haemodynamic and metabolic state of the tissue and may potentially image the penumbra.

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Th P106

DWI-ASPECTS vs.CT-ASPECTS In Hyper-acute Stroke Patients

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Background and Purpose: There were few reports of the direct comparison of ischemic detection between CT-ASPECTS and DWI-ASPECTS within 3 hours of stroke onset. Our aim is to assess the utility of DWI-ASPECTS against CT-ASEPCTS in hyper-acute stroke patients eligible for thrombolysis. Methods - Consecutive anterior circulation stroke patients underwent DWI and CT within 3 hours of stroke onset. Two observers independently assessed CT and DWI findings blind to backgrounds of patients apart from side of stroke symptoms. Firstly, we examined the presence and absence of ischemic lesion on DWI and CT. Secondly, we assessed the points of DWI-ASPECTS and CT-ASPECTS, and calculated kappa statistics to examine reliability between two scores. In addition, when we set the each DWI-ASPECTS regions (10 points) as a gold standard, sensitivity and specificity of presence of the ischemic lesions at each CT-ASPECTS region were calculated. **Results:** The subjects consisted of 130 consecutive patients with stroke (71 males; median age, 75 years). The mean interval between symptom onset and imaging study was 1.9 hours for CT and 1.6 hours for DWI. DWI more frequently demonstrated the fresh ischemic lesions than CT (76.9% vs. 30.0%, P=0.001). Median CT-ASPECTS score was 10 while median DWI-ASPECTS score was 7 (p<0.001). CT-ASPECTS had poor agreement with DWI-ASPECTS in patients with hyper-acute stroke (0.06 of kappa values). The highest-detectable region on DWI-ASPECTS was insular cortex (77 of 130 cases, 59.2%) and the lowest was internal capsule (9 cases, 6.9%). On the other hand, in CT-ASPECTS, the highest was lentiform nucleus (26 cases, 20%) and the lowest was caudate head (1 case, 0.8%). When DWI-ASPECTS as a gold standard, the sensitivity and specificity of the presence of the ischemic lesions at each CT-ASPECTS region were as follows; insular cortex, 0.25 of sensitivity/0.98 of specificity; caudate head, 0.06/1.00; internal capsule, 0.00/0.98; lentiform nucleus, 0.37/0.93; M1, 0.20/0.99; M2, 0.12/1.00; M3, 0.11/1.00; M4, 0.19/0.99; M5, 0.21/0.99; M6, 0.12/0.99. Overall, sensitivity of CT-ASPECTS was extremely low in comparison with DWI-ASPECTS. **Conclusion:** In hyper-acute stroke, DWI-ASPECTS is a practical scoring method for assessing the presence of fresh ischemic lesions compared with CT-ASPECTS.

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Th P107

Test-Retest Reproducibility of Cerebral Blood Flow Measurements Using Pseudo-continuous Arterial Spin labeling at 1.5T

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Test-Retest Reproducibility of Cerebral Blood Flow Measurements Using Pseudo-continuous ASL at 1.5T introduction non-invasive whole-brain cerebral blood flow (CBF) quantification has become practically feasible. The purpose of this study was to investigate the reproducibility of a pseudo-continuous ASL (PCASL) imaging sequence. Subjects and**Methods:** MRI was performed on a 1.5T whole body scanner (body coil for transmit; 12-channel head coil for receive). Pulsed continuous ASL was performed using a back ground suppressed 3D FSE readout with the following parameters: TR/TE 13250/5 ms; FOV 24 cm; 5mm slice thickness, 1.9 mm in-plane resolution; Label time/post-label delay: 1500/2000 ms; imaging time 5 min. For spatial coregistration and normalization a T1-weighted FSPGR (voxel size 1x1x1 mm^3; 130-160 slices) were acquired in the same session. Calculation of CBF-maps was performed. Resting CBF maps were obtained from 16 subjects (9 female, 27±1.8 y). The study consisted of two scanning sessions per subjects, separated by one week on average. All subjects underwent 4 PCASL scans. Two perfusion measurements were obtained during each session and during the first session, the second scan was repeated without any repositioning of the subject, whereas for session 2 the second scan was acquired after repositioning the volunteer in the scanner. Spatial preprocessing, calculation of CBF-maps and statistical analysis were performed with custom programs written in MATLAB and SPM5 (http://www.fil.ion.ucl.ac.uk/spm). Repeatability was assessed using Bland-Altman methods. Reliability was computed as an intraclass correlation coefficient (ICC). **Results:** ICCs in the global brain, gray matter, and white matter area are 0.8399, 0.8403, and 0.8389 respectively. In Bland-Altam plot tests (± 1.96 SD), there is no bias between PCASL session 1 and 2, and within each sessions. Mean and stdev of CBF(ml/100gm/min) on the whole brain are followed in the 4 sets of PCASL: 1st session 1st t scan 44.75 ± 7.02, 1st session 2nd scan 43.0 ± 7.49, 2nd session 1st scan 44.3± 7.85, 2nd session 2nd scan 43.4 ±7.89. **Conclusion:** Perfusion measurements based on PCASL show good reproducibility.

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Th P108

The Superiority of MRI over CT in the Diagnosis of Acute Ischemic Stroke Increases with Patient Age

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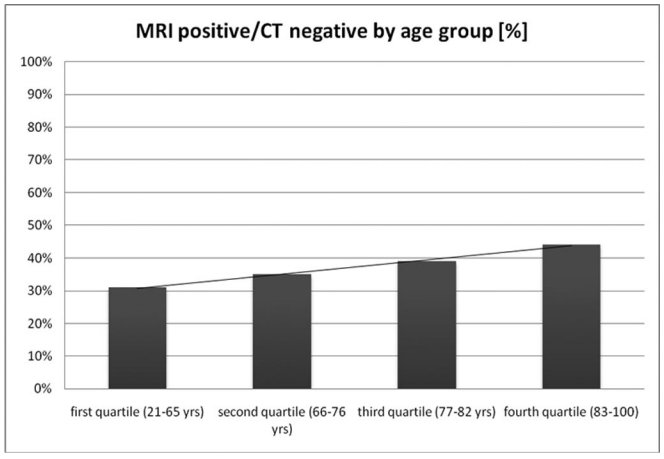
Background: Age related changes in the brain cause hypoattenuation on CT. Chronic as well as acute ischemia also appear as hypoattenuation on CT, whereas on DWI-MRI acute ischemia causes a hyperintense signal and chronic ischemia an iso- or hypointense signal. In a previous study DWI-MRI has been shown to be superior to CT in the diagnosis of acute ischemia unrelated to time from symptom onset to scan or stroke severity. Since chronic changes in the brain increase with age, we investigated whether age is related to the superiority of DWI-MRI over CT in the detection of acute ischemic stroke. **Methods:** Clinical data and imaging reads of a previously conducted single-center, prospective, blind comparison of non-contrast CT and DWI-MRI in a consecutive series of patients with suspected stroke were evaluated. A logistic regression model was used to examine the association of age with DWI-MRI positive/CT negative scans. The scans had been interpreted independently by four experts, who were unaware of clinical information, MRI-CT pairings, and follow-up imaging. **Results:** 356 patients, 190 of whom had a final diagnosis of acute ischemic stroke, were assessed. The median age was 76. DWI-MRI detected acute ischemic stroke in 164 of 356 (46%, 95% CI 41-51%) patients, CT in 35 of 356 (10%, 95% CI 7-14%). DWI-MRI was positive and CT negative for acute ischemic stroke in 132 of 356 (37%, 32-42%). In a logistic regression model age showed a significant association with DWI-MRI positive/CT negative scans (OR 1.019, 95% CI 1.002-1.036, $p=0.03$). The graph shows the distribution by age group of patients who were positive for acute ischemic stroke on DWI-MRI but negative on CT. Interpretation: Age is related to the superiority of DWI-MRI over CT in the diagnosis of acute stroke. We hypothesize that white matter background disease increasing with age and causing hypoattenuation on CT may make the diagnosis of acute ischemic stroke more difficult on CT as compared to DWI-MRI.



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Th P109

Validation of an Automated Perfusion-Diffusion Lesion Assessment Tool

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Background and Purpose: Penumbral imaging with perfusion (PWI) and diffusion-weighted (DWI) MRI volume assessments in the clinical setting are generally qualitative, but previous investigations have shown that these estimates are inaccurate relative to quantitative volume measurements. Manual planimetric measurements are accurate but are time intensive and impractical in the emergent setting. In this validation study, we aimed to test the accuracy of semi-automated PWI-DWI assessment software (Perfscape) against planimetric measurements. **Methods:** Patients presenting with acute ischemic stroke symptoms who were imaged with PWI-DWI were included. Customized software was used to generate Tmax maps thresholded to +4s using a deconvolution algorithm and a manually selected arterial input function. Planimetric measurements of the Tmax+4s maps and DWI lesion volumes were made using the Analyze software package. The Perfscape software package was used to independently generate Tmax+4s maps, using an automated AIF selection algorithm. This software also calculated Tmax+4s deficit, DWI lesion (based on an apparent diffusion coefficient threshold) and penumbral (Tmax+4s-DWI) volumes automatically. Linear regression and Bland-Altman analyses were used to calculate the accuracy of the Perfscape automated measurements. **Results:** A total of 76 patients were included. The median time from onset to MRI was 9.48 hours (IQR= 5.81,17.43). DWI volumes calculated automatically (17.3±41.0 ml) were strongly correlated with manually determined volumes (29.1±57.9 ml); r=0.69 [95% CI, 0.66, 0.73]). Automated DWI lesion volumes were generally smaller than manually measured volumes (mean difference -11.8 ml, 95% limits of agreement -51.6, 28.0 ml). Similarly, automated (31.7±42.8 ml) and manual Tmax+4s perfusion deficit (52.6±68.2 ml) volumes were strongly correlated (r=0.57 [0.52, 0.63]). Automated Tmax+4s PWI deficit volumes were generally smaller than manually measured volumes (mean difference -20.9, 95% limits of agreement -88.7, 46.9 ml). Finally, automated (14.3±26.4 ml) and manual mismatch volumes (23.5±51.3 ml) were correlated (r=0.42 [0.35, 0.49]. Mismatch ratios assessed automatically (7.0±17.1) were also correlated with those derived from manually calculated volumes (6.88±22.6; r=0.38 [0.23, 0.53]). The automated software detected the presence of a mismatch ratio of >1.2 with sensitivity of 81.6% and specificity of 78.9%. Sensitivity and specificity increased to 92.3% and 84.0% respectively for a mismatch ratio of >2.0. **Conclusions:** Automated DWI lesion and PWI deficit volume assessment is feasible. The Perscape tool generally underestimates DWI and PWI volumes, relative to manual planimetric measurements. Despite this, mismatch ratios were quite similar. This automated tool may facilitate treatment decisions based on penumbral imaging patterns.

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Th P110

Secondary Signal Changes And Apparent Diffusion Coefficient Decrease Of The Substantia Nigra Following Striatal Infarction

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Background and Purpose: A secondary signal change of the substantia nigra on diffusion-weighted imaging (DWI) in subacute phase of ipsilateral striatal infarction is known as a pitfall because it may be misdiagnosed as a recurrence of stroke. However, clinical factors related to such a signal change and a decrease of apparent diffusion coefficient (ADC) of the substantia nigra remains unclear. [Methods] We prospectively recruited consecutive stroke patients with acute ischemic lesions in hemilateral caudate nucleus, putamen, globus pallidus, external capsule or internal capsule on MRI on admission. ADC of the bilateral substantia nigra obtained from follow-up MRI were analyzed; ADC ratio (lesion side/contralateral side) ysis of normal control subjects, was regarded as a significant decrease of ADC. We investigated clinical factors related to significantly decreased ADC on the lesion side. [Results] Out of 90 patients, 18 patients who underwent follow-up MRI within 3 days of stroke onset were excluded because none of them revealed significant ADC changes; residual 72 patients (median 79 years, 35 male and 37 female) were analyzed. Twenty-seven (38%) patients demonstrated a significant decrease of ADC. Patients with significant decreased ADC revealed higher NIHSS score on admission than patients without decreased ADC (median 16 vs. 9, $P = 0.008$). Ischemic lesions in globus pallidus (82% vs. 11%, $P P = 0.001$) were more frequent in patents with decreased ADC, whereas lesions in putamen, external capsule, or internal capsule were not different between the two groups. In patients with decreased ADC, dyslipidemia was less frequent (4% vs. 29%, $P = 0.009$), while emboligenic diseases (78% vs. 13%, $P = 0.010$) and recanalization of the occluded middle cerebral artery on follow-up (63% vs. 16%, P ysis, globus pallidus lesions (OR 6.93, 95%CI 1.47-32.55) and emboligenic diseases (OR 5.43, 95%CI 1.14-25.94) were independently related to the ADC decrease of the ipsilateral substantia nigra. There was no significant association between decreased ADC and patients' outcome. **Conclusions:** Ischemic lesions in globus pallidus and embolic mechanism may be related to a secondary signal change of the ipsilateral substantia nigra.

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Th P111

Acute Stroke Core on Perfusion and Diffusion Images

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Purpose: Mismatch between volumes of stroke core and critically underperfused tissue is used to identify patients that could benefit from advanced reperfusion therapies. The core can be identified either on ADC maps from MR-DWI, or it can be outlined in regions where perfusion is lost. However, CBV is not always lowered in regions with low ADC, although CBF seem to be always reduced there. We hypothesized that combining regions with reduced CBF and CBV could improve equivalence between perfusion and diffusion stroke cores and thus could allow more consistent identification of mismatch. **Methods:** 36 acute stroke cases imaged with an optimized MR-DWI/DSC-MR-PWI protocol 0-6 hours after stroke onset were analyzed. Patients were scanned 0.5-3 hours after tPA was administered and before mechanical thrombectomy was executed. rCBV, rCBF and Tmax maps were obtained using delay-independent deconvolution. DWI and PWI were spatially coregistered. Stroke cores were segmented based on

following criteria: 1) ADC $<$ 600 x 10^{-6} mm^2/s, 2) rCBV drop below 33% of the contralateral value and 3) rCBF drop below 40% or rCBV drop below 33% contralateral values combined. (Proving equivalence of ADC, CBV and CBF thresholds used was not subject of this study). Consistence of lesion locations among CBV/CBF/ADC was confirmed visually. Critically underperfused tissue was defined as Tmax $>$ 6s. Volumetric mismatch was defined as (underperfused tissue/core) $>$ 1.8 and simultaneously (underperfused tissue - core) $>$ 20ml. **Results:** Using the ADC-based method as a reference, the CBV-only approach identified mismatch identically in 30 cases (23 TP, 7 TN) and differently in 6 FP cases. The difference between ADC-based and CBV-based core volumes was: median 18.6ml, min -3.8ml, max 105.2ml. In the 6 FP cases the difference of core volumes was: median 77.5ml, min 65.4ml, max 105.2ml. Using the CBF & CBV criteria combined, mismatch was identified identically in 33 cases (23 TP, 10 TN) and differently in 3 FP cases. The difference between ADC-based and CBF/CBV-based core volumes was: median 9.75ml, min -20.8ml, max 96.5ml. In the 3 FP cases the difference of core volumes was: median 77.5ml, min 44.6ml, max 96.5ml. **Conclusions:** : The combined CBF/CBV method improved consistency of stroke core identification between DWI-based and PWI-based methods, compared to the traditional CBV-only method. Nevertheless, the cores identified using CBF+CBV combined were not completely identical to those derived from ADC. This suggests that DWI and PWI do not yield identical clinical information. Various effects, such as tPA-induced or spontaneous reperfusion, presence of large vessels in PWI maps, etc. can lead to inconsistent mismatch classification of the stroke patients.

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Th P112

Simultaneous Multiple Lacunar Infarction: Is it different disease entity from Single Lacunar Infarction ?

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Backgrounds: Stroke mechanism other than small artery disease has been reported in patients with lacunar infarction. We hypothesized that acute simultaneous multiple lacunar infarction (sMLI) may have different clinical characteristics from acute single lacunar infarction (SLI). Methods We retrospectively reviewed stroke patients with acute simultaneous multiple lacunar infarction or acute single lacunar infarction in the prospectively collected stroke registry from March 2008 to February 2010. Clinical characteristics including risk factors, premorbid cognitive and functional state, and outcome were assessed. Imaging characteristics including white matter ischemic changes, previous lacunes, micro or macrohemorrhage, and concomitant intra or extracranial stenosis were assessed. SLI was defined as a solitary hyperintense signal identified in the diffusion weighted MRI, $<$2.5cm in diameter, located in the subcortex and perforating artery territories. sMLI was defined as simultaneously identified two or more acute SLI. Results Of 548 acute ischemic stroke patients, sMLI were 23 (4.1%) and SLI were 148 (27%). Vascular risk factors including hypertension, diabetes mellitus, dyslipidemia, smoking or rheological risk factors including D-dimer, fibrinogen, hs CRP, BUN/Cr ratio showed no difference between two groups. Previous history of stoke was more prevalent in sMLI group (38% vs. 16%, P$<$0.05). In sMLI group, age was older (68.4$\pm$11.2 vs. 63.1$\pm$11.5, P$<$0.05) and premorbid functional state was poorer (mRS 1.3$\pm$1.5 vs. 0.4$\pm$0.9, P$<$0.05). sMLI group showed more white matter ischemic changes (Fazeca scale for periventricular white matter hyperintensities, 1.3$\pm$0.9 vs. 0.9$\pm$0.7, P$<$0.05; deep white matter hyperintensities, 1.4$\pm$0.8 vs. 0.8$\pm$0.8, P$<$0.01), number of microbleeds (6.9$\pm$11.4 vs. 1.0$\pm$2.9, P$<$0.05), number of previous lacunes (2.6$\pm$2.5 vs. 0.8$\pm$1.1, P$<$0.01). Cardioembolic mechanism was rare in both groups. Generalized atherosclerosis such as peripheral artery occlusive disease (17.4% vs. 1.4%, P$<$0.01), symptomatic carotid disease (8.7% vs. 1.4%, P$<$0.05) was more prevalent in patients with sMLI than SLI. Although age variant was adjusted, sMLI had significantly higher deep white matter ischemic score (p$<$0.01), number of microbleeds (p$<$0.001), number of previous lacunes (p$<$0.001) and prevalence of preipheral occlusive disease (p$<$0.01) than SLI. **Conclusions:** Mechanism of sMLI might be a small vessel disease rather than other stroke mechanisms. However, clinical and imaging characteristics suggest that sMLI might be a distinct more severe small vessel disease entity from small vessel disease with SLI.

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Th P113

CT Perfusion Source Images are Superior to CT Angiography for Rapid Evaluation of Collateral Status

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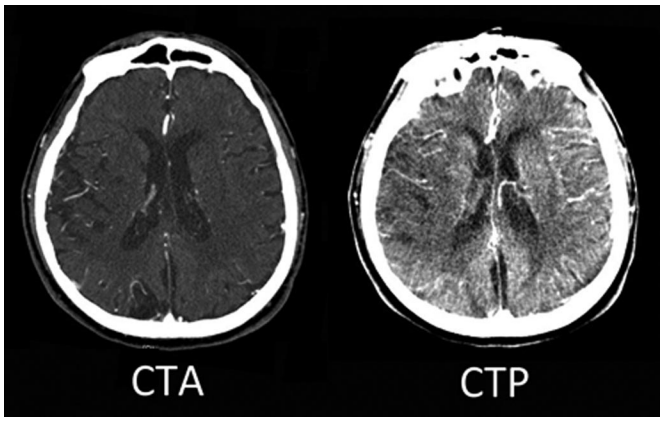
Background: Numerous CT angiography (CTA) scales have been advanced for rapid, noninvasive evaluation of collateral status, yet validation with collateral circulation on digital subtraction angiography (DSA) has not been performed. CT perfusion (CTP) source images offer a potential advantage as they contain temporal, and not just spatial, resolution like CTA. We evaluated the use of previously reported CTA scales separately on source images of CTA (CTA-SI) and CTP (CTP-SI), including validation with contemporaneous DSA in acute ischemic stroke. **Methods:** Consecutive acute MCA ischemic stroke cases with CTA or CTP and DSA. All previously reported CTA collateral scales (including from 3-5 grades) were used to score collateral status separately on CTA-SI and the late phase CTP-SI. DSA collateral grade (ASITN/SIR) was then used to validate all CTA and CTP collateral scores. **Results:** Six distinct CTA collateral scales were identified and evaluated in 36 cases (mean age 69$\pm$19 years; 21 men, 15 women) with acute MCA stroke. DSA collateral grades were evenly distributed from 0-4, median 2. CTA-SI were graded in 33 cases, late phase CTP-SI in 28, with both CTA and CTP in 26. Collateral scores revealed poor discrimination on CTA-SI, with only 3/6 scales demonstrating even binary classification of cases (p$<$0.05) for the presence or absence of any collaterals. Use of all 6 scales on CTP-SI, however, correlated with presence or absence of collaterals (all 6, P$<$0.01). Collateral scores of all 6 scales on CTP-SI exhibited superior discrimination of DSA collateral grade compared with the use of CTA-SI (p$<$0.01). CTA-SI (left) lack temporal



resolution and therefore overestimate collateral status, whereas CTP-SI (right) have both temporal and spatial resolution that better defines the nature of downstream collaterals in this example of right MCA stroke. **Conclusions:** CTA collateral scales principally evaluate the mere presence or absence of collaterals, with poor discrimination of the spatial and temporal extent evident on DSA. Use of the same scales, however, on the late phase CTP-SI may rapidly provide such detailed information.

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Th P114

Delay in Evaluation and Treatment of Posterior Circulation Stroke Compared with Anterior Circulation Stroke

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Background: Lack of recognition of early symptoms of acute posterior circulation cerebral ischemia might delay timely diagnosis and treatment. We investigated whether there were differences in symptom onset to arrival at our emergency department (ED), arrival to Neurology evaluation, and ED arrival to treatment between patients with posterior circulation ischemia (PCI) versus anterior circulation ischemia (ACI). We also assessed if various symptoms were associated with differences in time to evaluation or time to treatment between ACI and PCI. **Methods:** Retrospective chart review of patients was conducted covering the period from January 2008 to May 2010. We evaluated consecutive patients with ACI and PCI, who received standard IV thrombolysis within 4.5 hours from time of onset. We collected demographics, different time intervals in the ED, and symptoms. **Results:** Among 252 patients treated with IV t-PA, 12% had PCI. The demographics and risk factors are shown in Table 1. There were significantly longer intervals in arrival-to-treatment and ED physician evaluation-to-neurology evaluation. There were no statistical differences in symptom onset to ED arrival, time of arrival to CT, or time of neurology evaluation to t-PA administration. There was no statistical significance in outcomes based on neurological worsening, rate of symptomatic intracerebral hemorrhage (sICH), length of stay (LOS), or discharge modified Rankin Scale (mRS). There were significantly higher percentages of nausea, vomiting, and dizziness in the PCI group. The presence of these symptoms was associated with a longer time from ED evaluation to neurology evaluation. The odd ratio for longer time to neurology evaluation was (OR: 3.7, 95%CI: 1.6-8.1, P-value**Conclusions:** Our data indicate that PCI patients had a 15.5 minute delay after initial ED evaluation to neurology evaluation (P-value=0.0084) and a 20 minute delay (P-value=0.0026) in IV t-PA administration compared with ACI patients. There may be difficulties in rapidly recognizing the symptoms of PCI, in contrast to ACI, in the emergency department. However, it may also be that the neurology response time to evaluating patients with PCI was slower than ACI patients. More education may be needed to increase early recognition of posterior circulation and shorten delays to t-PA treatment. Our study is limited by the small sample of PCI patients.

Table 1: Demographics, Risk Factors, Time Points, Clinical Data and Outcomes			
	ACI(n=221)	PCI(31)	P Value
Demographics			
Mean Age (Years) ± SD	67±15	65±14	NS
Male Sex (%)	45	68	0.02
Risk Factors			
Hypertension (%)	71	74	NS
Diabetes (%)	28	32	NS
Smoking (%)	24	23	NS
Hyperlipidemia (%)	26	16	NS
Clinical Time Points			
Onset to Arrival (mins) ± SD	81 ± 39	86 ± 38	NS
Arrival to ER-MD Eval (mins) ± SD	2.3 ± 3.2	2.3 ± 2.9	NS
Onset To tPA (mins) ± SD	155 ± 48	175 ± 39	0.0121
Arrival to Neuro Eval (mins) ± SD	16.5 ± 19	32 ± 30	0.0084
Arrival to CT(mins) ± SD	25 ± 15	31 ± 23	NS
Neurology To tPA(mins) ± SD	57 ± 25	58 ± 28	NS
Arrival to tPA (mins) ± SD	74 ± 30	90 ± 29	0.0026
Clinical Data			
Presenting Symptoms			
Admission NIHSS (Median)	13	6	0.01
Nausea (%)	3	68	<0.0001
Vomiting (%)	3	32	<0.0001
LOC (%)	27	29	NS
Dysarthria (%)	62	61	NS
Diplopia (%)	0.9	3	NS
Dysconjugate Gaze (%)	13	6	NS
Dizziness (%)	3	23	<0.0001
Hemiparesis (%)	88	65	NS
Aphasia (%)	34	6	0.002
Neglect (%)	11	0	0.048
Outcomes			
Neurological worsening (%)	19	19	NS
sICH (%)	7	3	NS
LOS (Median)	5.5	5	NS
Discharge mRs (Median)	4	4	NS
Discharge mRs (≤2)	25%	25%	NS

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Th P115

Does Intracerebral Hemorrhage Mimic Benign Dizziness Presentations? A Population Based Study

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Objective: Uncertainty exists about the use of neuroimaging studies in dizziness presentations. Screening for intracerebral hemorrhage (ICH) with head computerized tomography (CT) is common even when the presentation suggests a benign dizziness disorder. As an early step in informing decisions, we used a population-based stroke database to assess the frequency with which ICH might mimic a benign dizziness presentation. **Methods:** The Brain Attack Surveillance in Corpus Christi (BASIC) project was used to identify cases of ICH from January 1, 2000, to December 26, 2007. The hospital records of ICH cases with a National Institutes of Health Stroke Scale (NIHSS) of < 2 were abstracted for more detailed information. Cases were classified as benign dizziness presentations when isolated dizziness and a normal general neurological examination were documented. Results were summarized using descriptive statistics. **Results:** Of 595 ICH cases, only 2.2% (13 of 595) had dizziness as the primary presenting symptom and an NIHSS < 2. No case mimicked a benign dizziness presentation. Only one case had isolated dizziness symptoms but this patient had dysmetria documented on the exam. All other cases had either focal or global neurological symptoms or exam abnormalities. **Conclusions:** No case of ICH mimicking a benign dizziness presentation was identified in this population-based stroke surveillance study. This finding raises the possibility that screening for ICH may not be necessary when dizziness is an isolated symptom and the exam is normal, but more research is required.

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Th P116

Practice Variation in the Use of Neuroimaging Studies to Evaluate Emergency Department (ED) Patients with a Chief Complaint of Dizziness

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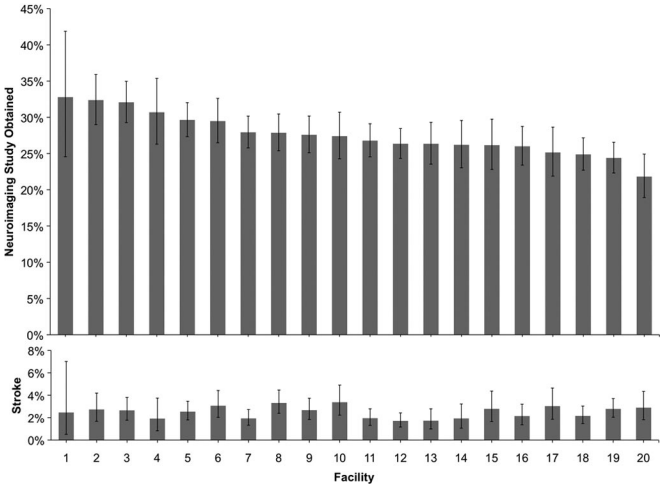
Background: Stroke is an important consideration when evaluating ED patients with dizziness symptoms. However, head CTs are relatively insensitive to posterior circulation stroke and involve radiation exposure, whereas more-sensitive brain MRI studies are costly and must be targeted to the most appropriate patients. Despite these challenges, practice variation in the use of neuroimaging studies the impact of this variation on stroke diagnoses has not been well described. **Methods:** We reviewed comprehensive electronic medical records for all adults with a chief complaint of dizziness who were evaluated at the 20 EDs of a large Northern California integrated health care program in 2008. Patient demographics, vascular risk factors, and subsequent diagnoses of stroke were abstracted from medical records. The primary outcome was a head CT or brain MRI within two days of the initial ED presentation. We used a random-effects logistic model to account for patient-level differences in demographics and vascular risk factors at each facility. **Results:** Of 378,992 adult patients seen in 2008, dizziness was listed as a chief complaint in 20,795 (5.5%) patients, varying from between 3.3% and 8.5% of all patients at each site. Overall, 5,585 (26.9%) patients had a head CT and 652 (3.1%) had a brain MRI. The proportion of patients who had any neuroimaging varied from a low of 21.8% to a high of 32.8%, which represents a 1.5-fold difference in centers with the lowest and highest rates of neuroimaging ($p<0.001$, Figure). Differences in patient-level factors_including age, sex, and vascular risk factors (hypertension, hyperlipidemia, diabetes, and atrial fibrillation) as well as differences in site-level factors such the proportion of patients with dizziness and the proportion of patients with dizziness who were admitted to hospital_did not account for the variation in neuroimaging rates. Higher neuroimaging rates by site was not associated with a greater number of strokes diagnoses (Figure), with an incidence of stroke diagnosis of 2.4% overall and a range of 1.7% to 3.4% by site. **Conclusion:** There is substantial variation in the use of neuroimaging for ED patients with dizziness without an associated improvement in detection of stroke. This suggests that standardized methods for targeting imaging to the most appropriate patients have the potential to reduce low-yield neuroimaging without sacrificing diagnostic accuracy.



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Th P117

Transient Isolated Dysphasia is Associated With a High Rate of Potential Cardiac Sources for Embolism

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Background: A cardiac source is often implicated in strokes in which the deficit includes aphasia. However, much less is known about the etiology of isolated dysphasia after transient ischemic attack (TIA). **Objective:** To determine if patients with transient ischemic attack, presenting with isolated dysphasia are more likely to have a potential cardiac source for embolism than those with other forms of transient ischemic attack. **Methods:** We prospectively identified and followed a cohort of patients receiving a final diagnosis of TIA in eight

tertiary-care emergency departments. Patients with symptom duration greater than 24 hours and individuals and in whom the speech disturbance could not be classified by direct examination by a physician were excluded. Patients with isolated dysphasia were identified if the clinical record revealed an isolated language deficit; expressive or receptive. Potential cardiac sources for embolism were defined as atrial fibrillation identified on history, ECG, holter monitor; or thrombus on echocardiography. Proportions were compared using Fisher's exact test. **Results:** 2574 patients were enrolled in the study; 1369 arrived in the ED with symptoms and were included in the final analysis. Of these patients, 48 were identified as having isolated dysphasia. Both groups had a similar proportion of males (50.1% vs. 60.4%, p=0.187) although those with isolated dysphasia tended to be older (67.1 ± 14.4 vs. 73.0 ± 10.4, p=0.007). There was no difference in the rate of hypertension (60.7% vs. 70.3, p=0.098), coronary artery disease (19.4% vs. 33.3%, p=0.062), history of atrial fibrillation (8.1% vs. 14.6%, p=0.112), diabetes (20.2% vs. 20.8%, p=0.856), or previous stroke (14.5% vs. 16.7%, p=0.676) between the two groups however patients with isolated dysphasia were more likely to have congestive heart failure (2.5% vs. 8.3%, p=0.038). In both groups the symptoms lasted for more than one hour (86.2% and 87.5%, p=0.488). Patients with isolated dysphasia were twice as likely to have a potential cardiac source of embolism (10.0% vs. 20.8%, p=0.026). In contrast, there was no difference between the groups in the rate of any carotid stenosis (41.1% vs 41.7%, p=0.862) or severe (>70%) stenosis (4.3% vs. 8.3%, p=0.259). **Conclusion:** In patients with TIA, isolated dysphasia is associated with a high rate of potential cardiac sources of embolism; the most common being atrial fibrillation. The identification of isolated dysphasia in individuals with speech disturbance is helpful in determining etiology and warrants rapid screening for a cardioembolic source.

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Th P118

Sudden Headache Preceding Cardiac Arrest: Frequency and Underlying Cause Evaluated with Post-Resuscitation CT Scan.

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Background. Headache is one of the most frequent presenting symptoms of non-traumatic intracranial hemorrhage, which is also a common cause of cardiac arrest and/or sudden death in adults. History of sudden headache preceding collapse may be a helpful clue to estimate the cause of out-of-hospital cardiac arrest (OHCA). **Methods:** This is a retrospective study conducted in a single teaching hospital. The witnesses of OHCA patients' collapse were interviewed in the emergency department (ED), and the information of when and how they collapsed was recorded in an institutional database. The database was reviewed to identify those who experienced sudden headache preceding collapse, and their incidence was reported. Brain CT scan is obtained prospectively in our institution, immediately after OHCA patients achieve return of spontaneous circulation (ROSC). CT diagnoses of those who collapsed complaining of sudden headache were also reviewed. **Results:** From April 2007 to March 2009, a total of 179 patients who sustained a witnessed non-traumatic OHCA were treated in our institution. Among them, 103 (58%) collapsed without complaining of any pain, and 8 (4%) complained of sudden headache preceding collapse. Seven of the 8 patients achieved ROSC after cardiopulmonary resuscitation. Post-resuscitation CT scan showed that all of the 7 patients had a fatal intracranial hemorrhage: Five had a severe subarachnoid hemorrhage (SAH), whereas the other two had a massive cerebellar hemorrhage. None of the 7 patients were discharged alive. On the other hand, 52 of the 103 (50%) patients who collapsed without complaining of any pain achieved ROSC and underwent brain CT scan. Among them, another 8 patients were found to harbor a SAH. Thus, a total of 15 among the 179 witnessed non-traumatic OHCA patients (8%) were found to harbor a fatal intracranial hemorrhage. Post-resuscitation brain CT scan was obtained safely in all patients, with an average ED door-to-CT table time of 40 min. **Conclusions:** While OHCA patients who collapse complaining of a sudden headache are rare, with the frequency of 4%, the presence of prodromal headache strongly suggests the diagnosis of fatal intracranial hemorrhage. Their prognosis is extremely poor, although they are easily resuscitated in the ED. In addition, approximately half of patients whose OHCA are caused by an intracranial hemorrhage collapse without preceding headache. Brain CT scan obtained immediately after resuscitation can be performed safely, and it can identify those with "neurogenic" cardiac arrest, in whom aggressive treatment such as therapeutic hypothermia may not be indicated.

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Th P119

Early Clinical Deterioration of Stroke Patients Assessed in the Field within Two Hours of Symptom Onset

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Background: Although studies have described rates of clinical deterioration in hospitalized stroke patients, we know of none which evaluated rates and predictors of clinical deterioration among patients assessed in the field during first two hours after symptom onset. **Objective:** To determine how often stroke patients clinically deteriorate in the first hours after symptom onset. **Methods:** The study population is comprised of subjects enrolled in the NIH-funded FAST-MAG (FM) clinical trial, a randomized placebo-control phase 3 study of paramedic-initiated magnesium sulfate vs. placebo for patients with stroke symptom onset = 2 points on the GCS in between the prehospital and emergency room evaluation. Clinical, demographic, and initial radiographic data were compared in those with and without deterioration. Last known well time (LKWT) was confirmed by FM study nurse in the ED. **Results:** A total of 987 consecutive subjects were administered the GCS in the field a median of 46 minutes after LKWT. Mean age was 69 and 41% were female. The median field GCS score was 15, IQR14-15. Overall 12% of patients (120/987) experienced clinical deterioration by >= 2 points between the prehospital and ED GCS. The second GCS exam was performed a median of 108 minutes following the paramedic evaluation GCS. Intracerebral hemorrhage (ICH) was noted on initial imaging in 23% of subjects (N=229). Age, gender, ethnicity, time from LKWT to paramedic evaluation were not associated with CD. On univariate analysis, predictors of CD were higher initial blood pressure (SBP 171 vs. 159, P<0.001, DBP 95 vs. 90, p=0.004), history of hypertension (87% vs. 74%, p=0.018), history of diabetes (29% vs. 20%, p=0.019), and ICH on initial imaging (40% vs. 7%, P<0.0001). Predictors of non-deterioration were atrial fibrillation and valvular heart disease. In multivariate analysis, independent predictors of clinical deterioration were: ICH on initial imaging (OR = 5.75) and a history of diabetes (OR = 1.89). **Conclusions:** Hemorrhage stroke subtype and history of diabetes predict early clinical deterioration between paramedic arrival on scene and examination in the ED. Among ICH patients, 4 of 10 experience clinical deterioration. The FAST-MAG clinical trial will be able to assess the effects of prehospital neuroprotective therapy upon early CD.

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Th P120

Association between Time Spent in the Emergency Department and Stroke Outcome

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Background: Early initiation of close monitoring of neurological status and of measures such as control of blood pressure, serum glucose levels, and body temperature is considered to be essential to improve outcome in acute stroke patients. Initiation of these measures may be delayed in patients who spend more time in the emergency department (ED). **Objective:** To assess whether the length of time that stroke patients spend in the ED correlates with worse outcome. **Methods:** Data of ischemic and hemorrhagic stroke patients treated at a comprehensive stroke center between January 2009 and May 2010 were abstracted from a prospective registry (Minnesota Stroke Registry). Unfavorable outcome was defined as death or non-ambulatory status at the time of discharge. We analyzed whether demographic factors, stroke risk factors, stroke type (ischemic vs. hemorrhagic), and stroke severity [National Institutes of Health Stroke Scale Score (NIHSSS) for ischemic stroke and Glasgow Coma Scale (GCS) for hemorrhagic stroke] were associated with time spent at ED using logistic regression after adjusting for potential confounders. ED time was expressed in quartiles. **Results:** We analyzed the data of 363 patients, 167 (46%) women. Mean age was 63 ± 15 years and most patients (n=274, 75.5%) had ischemic strokes. Among ischemic stroke patients mean NIHSSS was 6.8 ± 5.4 and among hemorrhagic stroke patients mean GCS was 13 ± 3.4. Median ED time (interquartile range) was 146 minutes (range 76-289 minutes). Time spent at the ED was inversely associated with age (p=0.006) and NIHSSS (p=0.003) and directly associated with GCS (<0.0001). Ischemic stroke patients spent more time in the ED than hemorrhagic stroke patients (p<0.0001). Unfavorable outcome was observed in 135 (37%) patients. Time spent at ED was inversely associated with unfavorable outcome (p=0.002, test for trend). **Conclusion:** Contrary to our hypothesis, longer ED times are associated with favorable outcome from stroke. This is a reflection of the fact that younger patients and patients with less severe strokes tend to spend more time in the ED. Our data suggest that ED time is not useful as a surrogate for quality of care for stroke.

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Th P121

Low dose rFVIIa Could effectively Reverse Elevated INR but Did not Chang The Outcome of Patients on Warfarin who Developed Intracerebral hemorrhages

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Background To quickly and effectively reverse elevated International Normalized Ratio (INR) in patients on warfarin who developed intracerebral hemorrhage (ICH) is urgent but of challenge. Fresh frozen plasma (FFP), intravenous or oral vitamin K are the standard ways of reversing INR. However, both treatments may take hours to reverse coagulopathy. rFVIIa is easy to mix and administer but costly ($1,600-7,800). To reverse INR with rFVIIa has been reported in a small series. The dose range to effectively correct INR has not been well established. We here report so far the largest series of reversing INR with rFVIIA in patients on warfarin and developed ICH's. Knowing rFVIIa was costly and higher doses (80 mcg/kg) would cause thrombotic events, only 1-2 vials were used at our center regardless to how high the INR was elevated. Method This is a retrospective study. Records of all patients with diagnosis of ICH and received rFVIIa were reviewed. Data tabulated include demographics, taking or not taking

warfarin, doses of rFVIIa, length of stay (LOS), mortality and discharge destination. Patients with available INR data and ICH or IVH or SAH on CT findings both pre and post rFVIIa were included. Descriptive statistics were used to analyze the data. Results From 1/2006 to 7/2010, 554 patients had ICH's. Seventy four (13%) patients received rFVIIa. Forty two (57%) were male and 32 female. Average age was 66 (20-91). Forty seven (64%) had ICH's, 23 (31%) had ICH+IVH's and 4 (5%) had IVH+SAH's. The average dose of rFVIIa was 1.4 mg. Forty three had CT scans pre and post rFVIIa. In 26 (35%) patients on warfarin, the average INR on admission was 3.17 and post rFVIIa was 1.18. Only an INR of 20 was not corrected to <1.4. Eight (35%) on warfarin had IVH+ICH's and 5 (19%) died. In 48 (65%) not on warfarin, 13 (27%) had ICH+IVH and 2 (4%) died. The average size of hematoma pre rFVIIa was 4.1x3.5 cm and post rFVIIa 4.4x3.3 cm. Of these, 21 patients were on warfarin with the average initial ICH size of 6.2x3.6 cm compared to 3.8x2.8 cm in 32 patients not on warfarin. The average LOS was 10 days. Including hospice care, 19 (25%) died at discharge and 8 (42%) were on warfarin. Five (6%) patients went home; 33 (45%) to rehabilitation; 17 (24%) to skilled nursing facility. **Conclusion:** In our experience, low dose rFVIIa effectively reversed the elevated INR's induced by warfarin to a normal range. However, the size of hematoma was not reduced and the mortality rate was higher in the warfarin group. Normalized INR would not equate to improved outcome. Our study confirmed the finding that patients on warfarin usually had larger ICH's and higher mortality, especially if ICH patients also had IVH's. If elevated INR needs to be corrected quickly, one vial of rFVIIa (1.2mg) instead of using weight based dosage plan may work for INR level < 20. The significance of these findings and the related medical economics may need to be studied further in a larger prospective trial.

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Th P122

Oral Anticoagulant Use and Decreasing Hematocrit are Significantly Associated with Discrepant ED Point-of-care INR Results in Patients with Acute Cerebrovascular Disease

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Background: Previous studies comparing point-of-care (POC) INR accuracy relative to central laboratory (CL) INR in emergency department (ED) patients with acute ischemic stroke (AIS), transient ischemic attack (TIA) or intracerebral hemorrhage (ICH) suggest that significant discrepancy between the two values can be detected that may confound rapid treatment decision making in patients with acute cerebrovascular disease. **Purpose:** We hypothesized that specific clinical and operational variables were associated with POC INR discrepancy versus CL INR in ED patients with AIS, TIA or ICH and that the incidence of discrepancy decreased over time as a marker of effective quality assurance. **Methods:** A consecutive series of 637 patients with a final diagnosis of AIS (n=427), TIA (n=105) or ICH (n=105) underwent both POC INR and CL INR testing during ED presentation at our institution. All patients were tested by trained technicians using the i-STAT© POC analyzer (Abbott, NJ) with a quality assurance program. Patients with POC INR results more than 0.25 INR units from the CL INR were considered discrepant. We analyzed potential predictors of POC INR discrepancy including demographic (age, gender, race), clinical (NIH stroke scale, smoking status, antiplatelet, oral anticoagulant, hypertensive, cholesterol or diabetic medication use, hematocrit, glucose, aPTT, platelet count, body mass index) and operational (ED patient census on presentation) variables using multivariate logistic regression. We evaluated the change in incidence of POC INR discrepancy over 30 months using $\div^2$ methodology. **Results:** Discrepant POC INR results were found in 21.5% (137/637) of patients and 17.3% (110/637) were taking oral anticoagulants. The mean bias between POC INR and CL INR was 0.02±0.73 (range -11.3 to 10.5) INR units. Significant covariates of POC INR discrepancy were anticoagulant use (OR=3.00, CI 1.34-6.59, p=0.01), hematocrit (OR=0.94, CI 0.89-1.00, p=0.04), and aPTT (OR=1.06, CI 1.01-1.11, p=0.01). Oral anticoagulant use most significantly contributed to POC INR discrepancy [41.8% discrepancy in anticoagulated patients (46/110) versus 17.3% discrepancy non-anticoagulated patients (91/527), *z* statistic=5.5, p<0.001]. The incidence of POC discrepancy decreased over time (39% discrepancy during the first 7.5 months to 14% discrepancy during the last 7.5 months, $\div^2$=29.8, P<0.001). **Conclusion:** Anticoagulant use, decreasing hematocrit and increasing aPTT were significantly associated with ED POC INR discrepancy in patients with AIS, TIA or ICH. The incidence of POC INR discrepancy decreased over time, suggesting quality assurance efficacy.

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Th P123

Multimodal Predictors of Massive Ischemic Stroke.

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Introduction: Severe stroke carries a high short and long term disability and fatality rate. Nevertheless, the profile of these patients in the acute phase is poorly defined. The aims of this study are to determine the characteristics of patients with severe ("massive") ischemic stroke at onset regarding a large range of clinical and paraclinical parameters. **Methodology:** Using a prospectively constructed acute ischemic stroke databank (Acute STroke Registry and Analysis of Lausanne, ASTRAL), we compared all patients with massive stroke defined as a NIHSS ≥ 20 at admission with all other patients. The variables included in a univariate and then in a multivariate analysis included demographic factors, vascular risk factors, clinical presentation, stroke mechanism, previous clinical or silent ischemic events, medication and acute radiological and metabolic findings. **Results:** Among 1915 acute ischemic patients, 243 (12.7%) had massive strokes. On multivariate analysis massive stroke patients had higher prestroke modified Rankin Scale (OR=1.28, 95%CI=1.04/1.56, P<0.019), more unknown onset (>1h but less than 24h) (OR=2.35, 95%CI=1.14/4.83, P<0.02), more early ischemic CT/MRI findings (OR=2.65, 95%CI=1.79/3.92, P<0.000), less chronic radiological infarcts (OR=0.43, 95%CI=0.25/0.71, P<0.001), more arterial occlusions in the ischemic territory on admission vascular imaging (OR=0.03, 95%CI=0.01/0.08, P<0.000), lower Hb concentration (OR=0.97, 95%CI=0.96/0.98, P<0.000), higher WBC (OR=1.05, 95%CI=1.00/1.11, P<0.045), and more cardio-embolic stroke mechanism (OR=1.74, 95%CI=1.19/2.54, P<0.004), With this profile, the area under the ROC curve showed a trade-off between sensitivity and specificity of 86%. **Conclusion:** Stroke severity is predicted by multiple clinical, radiological and laboratory anomalies of which several are modifiable. Interestingly, unlike previous on the topic, age, admission blood pressure and past history are not associated with severe stroke. This study confirms the necessity to consider a broad range of clinical and laboratory values in the acute phase of ischemic stroke, including detailed neuroimaging. The predictors of poor or good outcome in these patients still need to be studied.

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Th P124

Factors Affecting Inequality In Acute Stroke Care In An Urban Hospital

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Objective To investigate trends in racial and socioeconomic disparities in acute stroke care which may affect the decision for intravenous tPA (IV-tPA) use in an inner-city hospital providing care to an underserved population. Background Previous studies suggest that minorities have higher risk of stroke and stroke severity. The acute phase of stroke care is an important period affecting stroke severity. Prompt presentation to emergency rooms affects the decision for treatment with IV-tPA and stroke outcomes. Previous studies have suggested racial and socioeconomical inequalities in health care. We sought to evaluate patients presenting within the expanded acute window for treatment with IV-tPA (i.e. 4.5 hours), and describe the role of socioeconomic status and race in this phase of acute stroke care. Design/Methods We evaluated consecutive patients presenting to our stroke center with an acute stroke alert between January and May of 2010. Symptom onset to ER arrival time, ER arrival to CT scan time, and door to needle time for IV-tPA were studied. These measures were stratified by race and insurance status (used as a proxy for socioeconomic status). Race and insurance status were stratified in 4 groups and descriptive statistics are presented. Results Eighty seven (87) patients presented to the ER with stroke symptoms within 4.5 hours during the study period. The youngest group (mean age) were Hispanics (52yrs, n=5), followed by other ethnic groups (59yrs, n=10), Blacks (61yrs, n=41), and Whites (68yrs, n=31). Mean time from symptom onset to ER arrival was longest for Hispanics (117min) and other ethnic groups (94min) as compared to Whites (71min) and Blacks (71mins). Uninsured patients showed the longest time to arrival to ER from symptom onset (104min, n=10) when compared to patients on Medicaid (75min, n=19), Medicare (80min, n=32), and Private insurance (80min, n=26). In addition, uninsured patients had the longest ER arrival to CT scan times (114min) in comparison with Medicaid (55min), medicare (38min), and patients with private insurance (59min). Only 9% of patients received IV-tPA. **Conclusions:** Our findings suggest race and socioeconomic disparities play a role in the acute phase of stroke care. While our study is limited by its small sample size and study design, our preliminary data warrants further investigation to assess potential reasons for these differences such as cultural factors, language barriers, awareness of stroke symptoms, patient's monetary concerns, and physician biases.

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Th P125

TeleStroke 2010: A Survey of Currently Active Stroke Telemedicine Programs in the US

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Introduction: Little is known about adoption or success of telestroke networks outside of federally funded programs or those reported in the literature. Our objective was to conduct an environmental scan of telemedicine-based (telestroke) stroke programs in the United States. Hypothesis: We hypothesized that US telestroke programs have diverse structures but face similar obstacles. **Methods:** We conducted Google and Pubmed searches to find any potential telestroke programs operating since 2000. A dedicated project analyst contacted all identified programs, interviewed respondents in-depth and collected online survey data using a tool developed to assess various structural and functional aspects of the programs. **Results:** In total, 100 possible programs in 43 states with active telestroke programs were identified and 38 programs agreed to participate. The programs that did not participate were similar to the ones that did, in terms of county level data (total population, % population age ≥25 yr, % of individuals below poverty line), annual hub hospital admissions, number of beds and annual emergency department (ED) visits. The top 3 clinical needs met by the telestroke programs were: ED consultation (100%), patient triage (83.8%), and inpatient teleconsultation (46.0%). The median telestroke program length was 891 days [495.5, 1256]. Most of the programs (94.6 %) used two-way, real-time interactive video plus teleradiology to support the consultation process. Dedicated telemedicine software was used by 44.44% of the programs to document and store consults. The mean number of spokes per hub increased from 2007 to 2009 (3.78 vs. 7.60; P<0.05; range 0-28). In 65.5% of hubs, more than 80% of spoke sites were rural and in 51.7% of hubs, more than 80% of spokes were small hospitals (0-99 beds).

Reimbursement for telestroke was limited: none (43.2 %), private insurance (29.7%), Medicare (27.0%), Medicaid (21.6%), and Tricare (5.4%). The 3 most important factors driving creation of telestroke programs were to provide a community benefit (97.3%), improve clinical outcomes (91.9%) and improve clinical process effectiveness (75.7%). Sites rated inability to obtain physician licensure (27.77 %), lack of funds (27.77 %) and lack of reimbursement (19.44%) as the most important barriers to program growth and development. **Conclusion:** Telestroke is a widespread and growing practice model. Important barriers to expansion relate mostly to organizational, technical and educational domains internal to organizations, and economic and regulatory forces externally. National standards for licensure, credentialing and reimbursement could have substantial impact in access to acute stroke care.

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Th P126

Acute Stroke Patients Benefit from Emergency Transfer within a Telemedicine Stroke Network

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Background&**Purpose:** Telemedicine aids selection of stroke patients who may require an emergency transfer to a comprehensive stroke center to receive additional therapies other than intravenous (IV) thrombolysis. We report our experience on emergency transfers within the telemedicine Stroke East Saxony Network (SOS-NET) of 14 cooperating hospitals covering a population of 1.7 million people in eastern Saxony, Germany. Subjects&Methods: We reviewed consecutive acute stroke patients who were transferred emergently from remote spoke sites to our comprehensive stroke center. Teleconsultations were performed 24-hours/day by certified stroke neurologists with access to high-speed videoconferencing and transfer of neuroimages. Recommendation for emergent transfers was given by the stroke neurologist on service. Clinical data including National Institutes of Health Stroke Scale (NIHSS) score at baseline and the modified Rankin Scale (mRS) score at discharge were prospectively documented in the databank of the telestroke service. Favourable outcome at discharge was defined as mRS scores 0-2. **Results:** In 2009, we conducted 550 teleconsultations and recommended transfer in 139 (25%) patients (mean age 64±14 years, 55% men, median NIHSS score 6 [interquartile range 3-16.5]). The mean time from teleconsultation to arrival at our stroke center was 1.8±0.9 hours. Twenty-nine (21%) emergent transfers had a non-stroke diagnosis (brain tumours, 9 [6%]; seizures, 5 [4%]; other etiologies, 15 [11%]). The remaining 110 tranferred patients had stroke diagnoses (ischemic strokes, 47 [34%]; transient ischemic attacks, 5 [4%]; intracranial hemorrhages [ICH], 58 [42%]). Of the 47 ischemic stroke patients, 12 (26%) received IV tPA at spokes ("drip&ship"). Intra-arterial reperfusion procedures were performed in 6 (13%) and decompressive hemicraniectomy was done in 6 (13%) ischemic stroke patients. In ICH patients, acute interventions were: endovascular procedures, 3 (5%); neurosurgical hematoma evacuation, 19 (33%); aneurysm clipping, 3 (5%); and additional or isolated external ventricular drainage, 13 (22%). At discharge, 37 (34%) stroke patients had a favourable outcome while mortality rate was 9%. **Conclusions:** Telemedicine based selection of candidates for transfer to a comprehensive stroke center can be a beneficial concept for stroke patients by delivering interventional stroke therapies that require advanced multi-specialty experts.

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Th P127

Variability in the Quality of TeleStroke Informed Consent for IV-TPA

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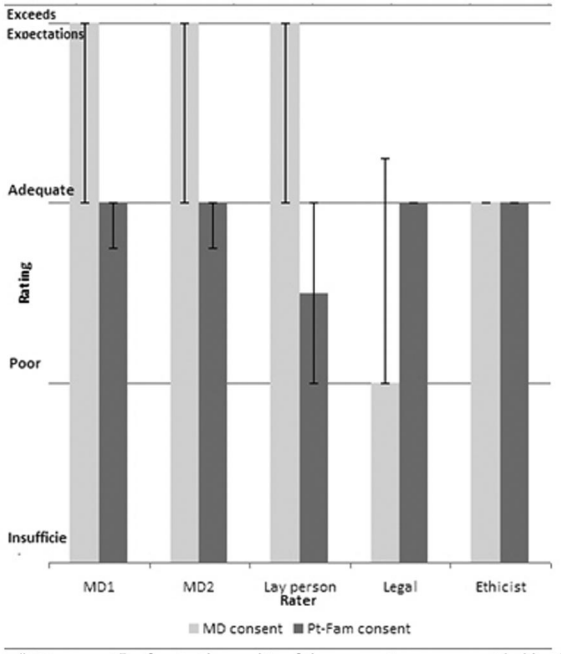
Objective: To study the perceived quality of informed consent for thrombolysis in acute ischemic stroke (AIS) patients receiving IV- tPA. **Methods:** Videotapes of 14 randomly selected telestroke cases with IV tPA administered were independently reviewed for adequacy of informed consent by 5 independent raters: a neurologist and emergency physician who routinely treat stroke, a medical risk management paralegal, a bioethicist, and a lay person. A 4 point Likert scale (insufficient (0), poor (1), adequate (2), exceeds expectations (3)) was used to assess the quality of the informed consent presentation by the treating physician (MD) and the degree of understanding demonstrated by the patient or family (Pt-Fam) authorizing consent. Factors associated with adequacy of consent (age, sex, education level, duration of consent, NIHSS, Pt vs. family) were analyzed by t-test or Wilcoxon, inter-rater reliability by kappa. **Results:** All patients were English speaking with a mean age of 69 ± 15.8 and median NIHSS score 11.5. Family members gave primary consent in 50% of cases after a mean duration of consent lasting 2.7 ± 1.3 min. Consent was rated adequately understood by Pt-Fam in 78.6% cases. There were no significant differences between the two groups (Table). Distribution of scores varied between raters (Figure). The inter-rater reliability between all 5 raters, the 2 MD or the 3 non-MD raters was (k=0.07 vs. 0.24 vs. -0.06) for quality of MD consent and (k= 0.12 vs. -0.06 vs. 0.17) for Pt-Fam understanding, respectively. Median Pt-Fam understanding ratings did not differ from MD consent ratings (Pt-Fam = 2 [IQR 2-2] vs. MD rating = 2 [2-3]). Consent interactions rated unacceptable (insufficient or poor) with regards to Pt-Fam understanding also had (non-significantly) lower ratings for MD consent performance when compared to cases with higher Pt-Fam ratings (1.67 vs 2.45; p=0.21). **Conclusion:** Despite high variability in the perceived quality of informed consent in this time-sensitive clinical situation, almost 80% of patients were rated by all reviewers as having adequate understanding of risks and benefits of tPA. The telestroke consent scenario likely reflects in-person practice. This study suggests the need for a standardized but brief tPA consent process that includes patient/family demonstration of understanding.

Table: Patient Characteristics

	Pt-Fam Acceptable Consent (n=11)	Pt-Fam Unacceptable Consent (n=3)	P
Age (mean yrs ± SD)	68.8 ± 16.4	69.7 ± 16.4	0.94
Female	5 (45.5%)	0 (0%)	0.26
High school graduate (n=10)	4 (50%)	2 (100%)	0.47
History of hypertension	9 (81.8%)	3 (100%)	1.00
History of diabetes mellitus	2 (18.2%)	1 (33.3%)	1.00
History of hyperlipidemia	4 (36.4%)	3 (100%)	0.19
Family present for consent	9 (81.8%)	2 (66.7%)	1.00
Person authorizing consent			
Patient	3 (27.3%)	1 (33.3%)	
Family	6 (54.6%)	1 (33.3%)	
Both	2 (18.2%)	1 (33.3%)	0.78
Duration of consent process (minutes ± SD)	2.8 ± 1.3	1.8 ± 1.3	0.33
NIHSS (median (IQR)	11 (7-17)	12 (11-18)	0.58
NIHSS item 9 Best Language (median (IQR)	0 (0-3)	1 (0-2)	0.92

Figure: Median and Interquartile Range for Individual Raters for Adequacy of MD Performing Consent and Patient/Family Understanding of Consent



"MD consent" refers to the quality of the consent process provided by the treating physician; "Pt-Fam consent" refers to the adequacy of the understanding demonstrated by the patient/family authorizing consent

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Th P128

Organization of a U.S. County System for Acute Stroke Care

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Introduction: Organized systems of acute stroke care improve delivery. The hospitals of Orange County, CA, the 5th most populous US county (3.1 million over 789 sq miles), met over 5 years in a grass roots effort with Emergency Medical Services to establish Stroke Neurology Receiving Centers (SNRC), which would receive patients from 911 calls for suspected stroke $<$5 hr old. The system became policy May, 2009, with 9 hospitals designated as SNRC agreeing to provide acute stroke care compliant with AHA guidelines; note that 8/9 were JCAHO stroke center or AHA-GWTG at system inception. The current report describes the first year experience. **Methods:** Each SNRC completed a form for each patient admitted under this system. Missing data were not imputed. **Results:** From April 2009-April 2010, 1,364 patients with suspected stroke $<$ 5 hr old were evaluated at the 9 SNRCs. Primary discharge diagnosis (n=1,110) included ischemic stroke (49%) and hemorrhagic stroke (19%). Mean age was 74 yrs (range 8-103). Time of arrival was unevenly distributed, e.g., 23% of arrivals were between 11am - 2pm. Median NIHSS score was 7 on admit (n=932) and 3 on discharge (n=683). Gender was 55% F / 45% M, with F having higher baseline NIHSS than M (8 vs 7, $p < 0.04$). Patients were 74% Caucasian, 12% Asian, 9% Hispanic, 1% Black, 4% other; baseline NIHSS differed by ethnicity ($p<0.001$), being higher in Asian and Hispanic patients. Acute therapy was IV tPA in 110 (20.2% of ischemic strokes) and IA procedure in 42 (7.7%); for both, baseline NIHSS was higher ($p<0.0001$) among those so treated, e.g., NIHSS=12 with IV tPA therapy vs. 7 no IV tPA. Change in NIHSS score from admit to discharge was larger among those who did, vs. did not, receive IV tPA (6 vs. 1 point, $p < 0.0001$). Time from door to IV tPA averaged 86 minutes. Death occurred in 11%, and did not vary in relation to IV tPA. There was no significant change over the 12 months in baseline NIHSS, use of IV tPA or IA therapy, death, or time from door to treatment. **Conclusions:** In the first year of this system, we found that women, minorities, and patients receiving acute therapy had more severe strokes. IV tPA, given in $>$20% of ischemic strokes, significantly reduced impairment with no effect on survival. Important aspects of the program include spoke hospital transfer to SNRC without option of diversion; and SNRC requirements for community outreach, neurosurgical capabilities, and stroke specific rehabilitation programs. A countywide stroke response system, organized among hospitals most of which were organized stroke centers at the start, can provide effective stroke care.

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Th P129

Data Sharing to Facilitate the Establishment of Stroke Systems of Care in California

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Background: In 2009, California's Stroke Systems Work Group developed recommendations for acute stroke care. These recommendations include a call for ongoing education for Emergency Medical Services (EMS) personnel to optimize the treatment, transport, and destination of suspected acute stroke patients. Ongoing education is enhanced by linking pre-hospital data with hospital and outcomes data. **Methods:** To provide feedback to local EMS agencies (LEMSAs), the California Stroke Registry (CSR), a registry that contains de-identified acute stroke patient-level hospitalization data, is piloting several data sharing methodologies, based on the experiences of other states. Model 1 (M1):The CSR received de-identified EMS data on suspected stroke transports from the LEMSAs and, using four data fields, matched each EMS record with the corresponding CSR patient record. Model 2 (M2): The CSR sent selected hospital data, including patient identification numbers, to LEMSAs. The LEMSAs received from the hospitals patient-level identifier data (i.e., patient names with corresponding identification numbers - numbers consistent with those in the CSR). Using these patient-level identifier data (or "bridge" data), the LEMSAs linked individual-level EMS and CSR data. Method 3 (M3): For each EMS-transported stroke patient, a unique EMS Run Sheet Number/Incident Number (RSN/IN) was entered into the hospital record. The CSR sent selected data, including the RSN/IN, to the LEMSAs. The LEMSAs merged CSR hospital data with EMS data, based on the RSN/IN, at the individual-level. **Results:** Three different data sharing methodologies have been developed. M1, in three unique attempts, yielded successful match rates of 47%, 50%, and 53%. This method may be inadequate as suggested by the low match rates. The success rate of M2 was close to 100%. This model proved successful from a data perspective but requires considerable human resources. The process for M3 is undergoing refinement and the results will be forthcoming. M3 appears promising and plans are underway to develop a secure web-based portal for use by the LEMSAs and the CSR to facilitate data sharing and report generation. **Discussion:** As Stroke Systems of Care are developed and implemented throughout California, it is imperative that data inform the process. In particular, data should be used to optimize decision-making regarding the treatment, transport, and destination of suspected stroke patients and to support continuous quality improvement efforts. In California, the CSR and the LEMSAs are working to make this happen.

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Th P130

A Systemwide Approach to Decreasing Door-to-Needle Times in Acute Stroke

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Background: Ischemic stroke patients receiving intravenous tissue plasminogen activator (IV-tPA) within 90 minutes of symptom onset have better outcomes than those receiving thrombolytics later.[1] The American Stroke Association's Get With the Guidelines (GWTG) Program now recommends a door-to-needle time $<$60 minutes $\geq$50% of the time. Despite increased awareness of the time-sensitive nature of acute stroke treatment among providers and patients alike, door-to-needle rates $<$60 minutes remain low.[2] **Objective:** We hypothesized that establishing strict parameters would improve compliance with acute stroke triaging. A 90% compliance goal was established for the following parameters in stroke patients presenting within 12 hours of last known well: door-to-CT complete $<$25 minutes, door-to-CT notify $<$45 minutes, door-to-needle $<$60 minutes, and door to lab posting $<$45 minutes. Percentage of patients receiving stand-alone IV-tPA (i.e. no intra-arterial tPA or mechanical clot retrieval) was also monitored. Data from four large Primary Stroke Centers (two community hospitals, one Level 1 Trauma Center, and one academic/university hospital) within the Detroit Medical Center (DMC) were used. Routine monitoring began in September 2009. Compliance was evaluated by use of an acute stroke order set and was initially reviewed weekly with a multidisciplinary team (emergency medicine, neurology, radiology, pharmacy, nursing, laboratory) at each site. In May 2010, changes in the DMC electronic medical record permitted an automated stroke log and daily evaluation of the above parameters, resulting in more timely feedback and improvements. **Results:** (see attached table)**Conclusions:** Use of an electronic medical record and daily automated stroke log resulted in significant improvement in systemwide delivery of timely stroke care and thrombolytic delivery. Over a one-year monitoring period, door-to-needle IV-tPA rates in the first 60 minutes increased from 26.1% to 50% and mean door-to-needle times decreased from 79 to 70 minutes. Slight decrease in standalone IV-tPA rates likely reflects an increased proportion of patients receiving combined IV-tPA/intra-arterial tPA and mechanical revascularization. References: 1. Hacke W, Donnan G, Fieschi C et al. Association of outcome with early stroke treatment: pooled analysis of ATLANTIS, ECASS, and NINDS rt-PA stroke trials. *Lancet* 2004:363(9411);768-74. 2. Saver JL, Smith EE, Fonarow GC et al. Presenting features and lytic therapy in $>$30,000 patients arriving within 60 minutes of stroke onset. *Stroke* 2010;41(7):1431-9. *Data complete through 8/13/2010.

	7/09-12/09	1/10-4/10	5/10-8/10*
Door-to-CT complete <25 minutes	50%	80.4%	71%
Door-to-CT notify <45 minutes	57.9%	75.6%	74.1%
Door-to-lab posting <45 minutes	47.4%	64.4%	66.2%
Door-to-needle <60 minutes	26.1%	27.3%	50%
Mean door-to-needle times (minutes)	79	71	70
% patients receiving standalone IV-tPA	6.6%	6.2%	4.2%

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Th P131

Addressing the Need for Stroke Education Globally: Effectiveness of the Advanced Stroke Life Support Course (ASLS) for Prehospital and Hospital-based Healthcare Providers in Hong Kong.

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Introduction: Comprehensive stroke education is necessary for rapid and effective diagnosis and treatment of stroke victims, especially in the prehospital and emergency department settings. Advanced Stroke Life Support (ASLS®) is a 1-day evidence-based stroke course consisting of 2 hours of lectures and 6 hours of interactive instruction. The participatory sessions include video-based cases where the learners diagnose and develop a management plan for patients with strokes or stroke mimics, skills sessions where learners evaluate standardized patients (portrayed by instructors) who simulate 5 major stroke syndromes (left hemisphere, right hemisphere, brainstem, cerebellum, and subarachnoid hemorrhage), and an interactive game as a course summary. **Purpose:** To assess the efficacy of a one-day interactive stroke course for prehospital and hospital-based providers in Hong Kong. **Methods:** We implemented the Advanced Stroke Life Support curriculum in the Hong Kong Hospital Authority through the Accident & Emergency Training Centre. The course was adapted minimally to ensure consistency with local practice and language variations. The instructors from Hong Kong initially participated in a train-the trainer program in the United States prior to implementing the course. A total of 65 nurses, paramedics and physicians participated in the course between November 23, 2009 and May 9, 2010. Outcomes were measured using

previously validated 20-item written precourse and postcourse assessments. **Results:** The precourse assessment mean score for all participants was 13.88 (69.4%) and the postcourse mean was 17.83 (89.2%) ($p<.001$). The mean improvement was 3.95 [SD 2.84, 95% C.I. 3.25-4.66] or 19.8%. Pretest scores were lowest for prehospital providers (12.78 (64%)), followed by nurses (14.27(71%)), and doctors (15.00 (75%)). Prehospital providers had the greatest improvement in knowledge [5.61 (27.4%)] [Pre 63.89%, Post 91.25%], followed by physicians [3.50 (17.5%)] [Pre75.0%, Post 92.5%], and nurses [3.31 (16.5%)] [Pre 71.5%, Post 88.0%]. **Conclusions:** Prehospital and Hospital-based emergency providers in Hong Kong significantly improved their knowledge of stroke diagnosis and management after participating in a 1-day stroke course.

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Th P132

Access Of Rural Hospitals To Acute Stroke Care Through Telemedicine: The Structure Of The Arkansas Saves (stroke Assistance Through Virtual Emergency Support) Telestroke Program

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Objective: To describe the structure and function of a telestroke program established to offer acute stroke care to patients in rural hospitals across the state of Arkansas. Background: Telestroke programs have emerged as important links in the evaluation and treatment chain of acute stroke, thus filling in a gap created by shortage of stroke neurologists. The number of telestroke networks is on the rise, however establishing and funding such programs is challenging, and self-support is even more difficult. Design/Methods: We describe the establishment, structure, and function of the Arkansas SAVES telestroke program. **Results:** The AR SAVES telestroke program operates under the auspices of the University of Arkansas for Medical Sciences Center for Distance Health. It was created by a grant from the Arkansas Department of Human Services; its goal is to offer evidence-based acute stroke care, ultimately to most rural hospital in the state, thus increasing the rate of intravenous thrombolysis, improving outcome, and cutting direct and indirect costs of stroke care. It was launched in November 2008. It utilizes the TANDBERG®, point-to-point video-conferencing systems connecting through T1 lines across the state. Three stroke neurologists, from both the private and academic sectors participate in the program. They are part of two hub PSC, covering calls 24/7 for which they are remunerated. Spoke hospitals are screened for basic capabilities and are brought on board sequentially following a period of on and off-site training, by dedicated health educators and outreach nurses, and mock telestroke runs that continue later after joining the program; nurses train and certify in administering the NIHSS; furthermore, the program funds different community education activities across the state. Neither spoke hospitals nor patients incur extra costs. Conversely, the program covers part of the salary of a nurse liaison and an information technologist at the spoke hospitals. A call center serves as the link between rural hospitals and hubs and arrange for patient transfers when needed. A central imaging repository allows spoke hospitals to push brain CT for the stroke neurologists to review. To date, 20 rural hospitals in 20 of 73 medically underserved counties in Arkansas have become part of the program. We have completed 276 consults of which 57 patients were treated with IV thrombolysis. We plan to add nine to twelve hospitals every year, while increasing our workforce to match the demand that rises with these additions. **Conclusions:** Telestroke programs have different structures and belong to different models. Government funding could be a viable alternative to the classic business model, especially if overall cost cutting to the system could be achieved. Furthermore, private and academic neurologists could form a pool of physicians to cover calls in a telestroke network.

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Th P133

Prevent Controversial Stroke Trial Results by Better Balancing Baseline Covariates

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It is well known that the primary outcome in stroke trials is highly dependent on baseline conditions, such as baseline NIH Stroke Scale, age and time from stroke onset to treatment. The results of some large trials such as the National Institute of Neurological Disorder and Stroke Recombinant Tissue PlasminogenActivator (NINDS rtPA) trial were controversial due to serious imbalance of important baseline covariates. However, balancing of these covariates was often ignored in the randomization algorithm. This is mainly due to the belief that baseline covariate distributions will tend to be balanced for trials with a large sample size, and a randomization algorithm balancing multiple baseline covariates, both categorical and continuous, is not available in most commercially developed clinical trial management systems. In this presentation, we define two goals for subject randomization in clinical trials: prevention of selection bias and protection of compatibility between study groups. Failure to reach both of these goals seriously impacts trial validity. We propose a randomization strategy that simultaneously controls serious imbalance for multiple baseline covariates of different types, including categorical, ordinal and continuous, while maintaining a high level of randomness for treatment allocation. Performance of this new randomization strategy has been evaluated with computer simulation based on subject randomization sequence and baseline covariate data of the National Institute of NINDS rtPA trial, and are compared with commonly used randomization methods, i.e. permuted block randomization stratified by clinical site. Results show that even with large samples, exclusion of important baseline covariates in the randomization algorithm can lead to serious imbalance of these baseline covariates between treatment arms, and hurt the compatibility of the two treatment groups. Implementation of this new randomization strategy in two large multi-center phase III trials conducted within the Neurological Emergencies Treatment Trials (NETT) network funded by the National Institute of Neurological Disorder and Stroke will be presented.

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Th P135

Recruitment of Ischemic Stroke Patients in Clinical trials in General Practice and Implications for Generalizability of Results

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Background: While results of clinical trials are used to impact practice among patients with ischemic stroke, very little information is available regarding proportion and characteristics of patients recruited in clinical trials in general practice. **Methods:** We performed this analysis to provide an audit of recruitment in clinical trials among patients with acute ischemic stroke using data from University Healthsystems Consortium (UHC) benchmarking project. A review of 40 consecutive ischemic stroke cases meeting inclusion criteria and discharge within a 6 month period was conducted in 32 hospitals. We performed a multivariate analysis to identify demographic and clinical factors associated with recruitment of patients with ischemic stroke into clinical trials. **Results:** A total of 1256 patients (mean age 67 years, range 18-99 years) were included. Most presented through the emergency department ($n=1035$). A total of 77 (6%) patients were recruited in clinical trials; 33 and 14 patients recruited in drug or device trials, respectively. In the multivariate analysis, age under 80 years (odd ratio [OR] 2.3, 95% confidence interval [CI] 1.1 - 5.1), white or African-American race as compared with others (OR 2.6, 95% CI 1.0 - 6.9), evaluation by a neurologist or stroke team (OR 15, 95% CI 2.0 - 108), and the use of intravenous thrombolysis (OR 7.2, 95% CI 4.1 - 13) were associated with recruitment in clinical trials. There was no relationship between patient's gender and recruitment in clinical trials. The rate of intracranial hemorrhage (6% vs 2%, $P<0.05$) and progression of stroke (12% vs 3%, $P<0.05$) were higher among those recruited in clinical trials. **Conclusions:** Only a minority of patients with ischemic stroke in practice are recruited into clinical trials. Patients recruited in clinical trials appear to have different characteristics from those who are not recruited limiting the generalizability of results from current trials.

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Th P136

Un-witnessed Stroke: Impact of Different Onset Times on Eligibility into Stroke Trials

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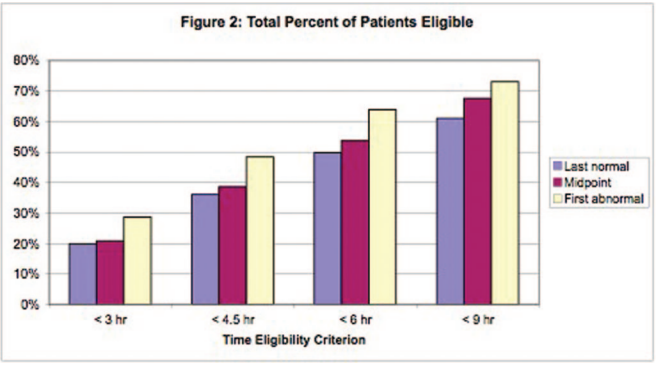
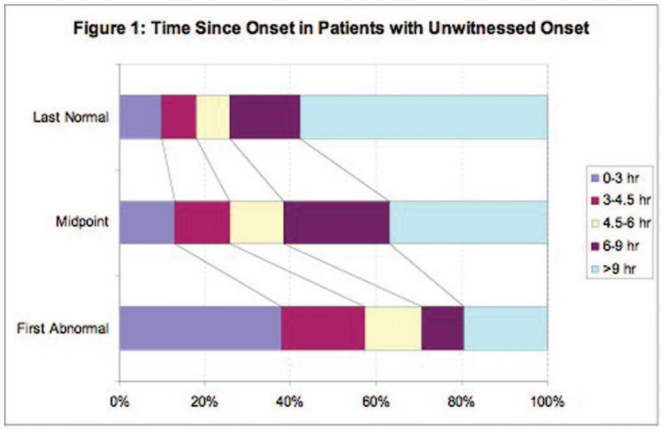
Background: In patients with un-witnessed stroke the actual onset time is variable; e.g. for 'wake-up' strokes the onset may be closer to the time first seen abnormal (FSA). Trials enrolling patients with un-witnessed stroke onset (over 25% of all strokes) have conservatively used 'last seen well' (LSW) as the time of stroke onset, which is appropriate given time-sensitive risks. While this LSW approach is appropriate to minimize risk with thrombolysis, it limits patient recruitment. In a NINDS funded phase II acute stroke trial of normobaric oxygen (NBO) therapy, we used the mid-point between LSW and FSA. The rationale was to assess the safety of hyperoxia at delayed timeframes. Here we explored the impact of alternative methods of determining onset time, on trial eligibility. **Methods:** We analyzed 641 consecutive patients with suspected stroke presenting to our hospital from Jan 2007 to July 2008. Time of onset was calculated by three**Methods:** (1) LSW, (2) FSA, (3) midpoint between LSW and FSA. Subjects with incomplete data or a non-ischemic stroke final diagnosis were excluded. Rates of NBO trial eligibility based on different onset times were compared, with 9 hours being the inclusion time window. **Results:** Onset time was known in 440 subjects (69%). Of the remaining 201 patients with un-witnessed onset, 114 (57%) were 'wake-up' strokes. Among un-witnessed stroke subjects (Figure 1), eligibility increased from 42.2% using LSW, 63.2% using the midpoint, and 80.6% using FSA (Chi square $P<0.001$). The impact on overall enrollment for the full cohort (Figure 2) was still significant with an increase from 61% to 67% to 73% ($p<0.001$). **Conclusion:** Given potential advantages in safety evaluation and inadequate enrollment rates in acute stroke trials, alternative onset time definitions, perhaps in combination with advanced neuroimaging methods of onset time estimation (e.g. FLAIR-DWI mismatch), should be considered for early phase trials.





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Th P137

Challenges in Accessing Medical Records in a Multi-Site Stroke Trial

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Background Federal research guidelines mandate that health researchers obtain accurate, complete, timely data and monitor study subjects for serious adverse events. Barriers to accessing medical records to fulfill these requirements are growing, including misinterpretation of HIPAA regulations and increasing use of electronic medical records (EMRs) that are not readily available to research coordinators and monitors. The NIH Field Administration of Stroke Therapy - Magnesium (FAST-MAG) study is a large stroke trial in Los Angeles. Research staff at a centralized research center coordinates the study at 50 hospitals and multiple other care facilities. This design allows for significant information sharing regarding the process of obtaining data. Purpose To describe the challenges for researchers in accessing study subjects' medical record data, in light of HIPAA and the transition from paper-based medical records to EMRs. Methods A survey and focus group discussion with 8 FAST-MAG research staff was performed for a descriptive analysis of the challenges faced in obtaining study data. Results Among the 50 participating hospitals, 8 now employ solely EMRs, 11 remain completely paper-based, and 31 use a combination of both. We identified 13 reported challenges in the overall process of obtaining research data. The most frequently encountered barriers to obtaining data were 1) limited local nursing staff knowledge regarding how to print EMRs, and 2) delays in obtaining medical records after discharge. Also frequent, and particularly distressing to the research nurses, were: 3) local nursing staffs' ambivalence or lack of knowledge regarding the appropriate use of HIPAA for research, and 4) the burdensome task of becoming familiar with an immense variety of documentation systems. **Conclusions:** Hospital staff and systems need to focus on accuracy of research data and ease of obtaining study pertinent data, all the while increasing the privacy of patients' records. Based on the experiences of study nurses, a number of proactive solutions are available to facilitate obtaining medical records. It is invaluable to develop rapport by having one dedicated research RN assigned to each site to identify key personnel, and maintain successful working relationships. It is beneficial to credential research staff as authorized users of site EMRs and to work with site IT staff to create study-specific printing instructions for the staff nurses to use. Ideally, a study specific print option can and should be generated specifically for the study purposes and be made accessible to staff nurses when presented with a signed research HIPAA. This would minimize staff's time, increase accuracy of data, and assure that only study data is transferred, thereby increasing patient privacy.

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Th P138

P2Y12 Receptors In Ischemic Inflammation: A New Role For Clopidogrel?

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Background: Microglia are among the first immune cells to respond to ischemic insults. Triggering of this inflammatory response is not precisely known, but may involve extracellular release of nucleotides from necrotic cells which bind microglial purinergic receptors. One such receptor, P2Y12, implicated in chemotaxis, is the receptor to which clopidogrel binds and inhibits. **Methods:** Primary murine enriched neuronal cultures were prepared with or without the addition of microglia (BV2 cell line), them subjected to oxygen glucose deprivation. siRNA was used to knockdown P2Y12 or NFkB in BV2 cells. Mice deficient in P2Y12, or wildtype littermates (n=6/group), were subjected to 12 min forebrain ischemia and hippocampal CA1 counts were assessed 72 h later. **Results:** The addition of microglia to enriched-neuron cultures increased neuron damage following OGD (oxygen glucose deprivation). Microglia formed clusters around these neurons following OGD. P2Y12-deficient microglia prevented increased neuron injury ($p<0.05$) and prevented microglial clustering ($p<0.05$). Deficiency of NF-kappaB, a major immune transcription factor in microglia led to similar observations ($p<0.05$). To delineate a link between P2Y12 and NF-kappaB activation, added ATP (P2Y12 agonist) increased NF-kappaB activation at potentially pathologic concentrations. Migration assays showed that OGD-conditioned media from neurons, but not astrocytes, led to microglial migration. P2Y12 deficient mice subjected to forebrain ischemia also suffered little hippocampal injury compared to wildtype mice ($p<0.05$), suggesting a toxic potential of the P2Y12 receptor. **Conclusions:** P2Y12 signaling through NF-kappaB appears to play a role in microglial activation and neurotoxicity under ischemic/ischemia-like conditions. We demonstrate a role of P2Y12 in ischemia in terms of microglia-mediated neurotoxicity, and suggests a potential additional benefit of clopidogrel.

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Th P139

Effect of Normobaric Oxygen Therapy in a Rat Model of Intracerebral Hemorrhage

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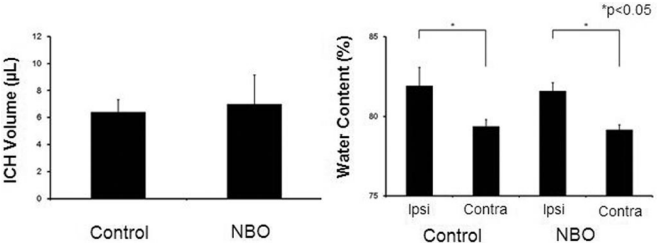
Background: Recent studies suggest that early normobaric oxygen (NBO) therapy is neuroprotective in acute ischemic stroke. Since NBO may be most effective as a pre-hospital therapy (before a definite diagnosis of ischemic versus hemorrhagic stroke can be established), it is important to understand the effects of NBO on intracerebral hemorrhage (ICH). In this study, we tested the effects of NBO in a rat model of striatal ICH. **Methods:** ICH was induced by stereotactic injection of collagenase type VII (0.5U) into the right striatum of anesthetised male Sprague-Dawley rats. One hour later, rats were randomized into Controls (n=13) vs NBO treatment (n=13). NBO was applied for two hours. Hemorrhagic blood volume and brain water content were quantified at 72 hours after injection. Neurological outcomes (forelimb placement test, forelimb asymmetry, neuroscore) were assessed at 72 hours post-ICH. **Results:** NBO did not worsen hemorrhage severity or brain edema (Figure). There were no significant differences in hemorrhagic blood volumes (Control, $6.4\pm0.9\mu l$ versus NBO, $7.0\pm2.1\mu l$, $p=0.18$) or brain water content (Control, $81.9\pm1.1\%$ versus NBO, $81.6\pm0.5\%$, $p=0.58$). NBO did not affect any of the neurological outcome tests. Forelimb placement was significantly affected by ICH (NBO contralateral, $21.5\pm11\%$ vs ipsilateral, $88.5\pm13\%$, $P<0.01$, Controls; contralateral, $14.6\pm9\%$ vs ipsilateral, $86.1\pm10\%$, $P<0.01$), however there was no significant difference between NBO and Controls. NBO also had no significant effect on the forelimb asymmetry test (NBO, $26.0\pm39\%$ vs Controls, $31.1\pm33\%$). Finally, according to the 5-point neuroscore scale, NBO did not affect mortality and neurologic outcomes. **Conclusion:** NBO therapy may not worsen outcomes in ICH. These experimental results require clinical confirmation.



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Th P140

BNIP3 Mediates Autophagic Neuronal Death in Stroke Through a Mechanism Involving Beclin 1

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Excessive autophagy has been implicated in delayed neuronal death in stroke. The aim of the present study is to determine the role of BNIP3 in autophagic neuronal death. We performed immunohistochemistry, quantitative western blot, immunoprecipitation, cell transfection, RNA interference and electron microscopy to analyze the expression and localization of BNIP3 and autophagy markers in degenerating primary neurons in an oxygen and glucose deprivation (OGD) model of stroke, and in a neonatal cerebral ischemia/hypoxia (I/H) animal model. In primary neuronal cultures exposed to OGD for 6 hours followed by reperfusion (RP) for 24, 48 and 72 hours, respectively, an increase of autophagy was observed as determined by the ratio of LC3-II to LC3-I, an autophagy marker protein. Using Fluoro-Jade C and MDC double-staining, and electron microscopy we found that the increment in autophagy after OGD and RP injury was accompanied by increased autophagic cell death rates, while this increase could be attenuated by the specific autophagy inhibitor, 3-Methyladenine (3-MA). The death-inducing gene BNIP3 was highly expressed in neurons exposed to OGD. We proved that the time course and expression levels of Beclin 1 (BECN1), an autophagy-regulating protein, correlated with the expression of BNIP3. Knockdown of BNIP3 by miRNA reduced OGD-induced Beclin 1 expression

in neurons and autophagic cell death. Also, we examined the ischemic brain tissue from rats exposed to transient focal cerebral ischemia/hypoxia on postnatal day 7. Brain tissues were examined histologically, biochemically, and ultrastructurally for autophagic markers. We found that autophagic activities were increased in the ischemic brains from 3 to 7 days post-injury, as shown by increased expression of Beclin 1 and punctate LC3 staining. Electron microscopy confirmed the presence of large autolysosomes and numerous autophagosomes in neurons. Postischemic intracerebroventricular injections of 3-MA markedly reduced the lesion volume after I/H injury. In conclusion, our results indicate that the BNIP3 death gene regulates the autophagic neuronal death in stroke, through a mechanism involving Beclin 1.

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Th P141

Selective Inhibition of NR2B-Containing N-methyl D-aspartate Receptors Attenuates Neuronal Injury after Oxygen-Glucose Deprivation in Cultured Cortical Neuron and Permanent Middle Cerebral Artery Occlusion in Rats

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Introduction: Glutamate is a major excitatory transmitter and plays an essential role in brain insults such as stroke. Clinically, the global antagonist of N-methyl D-aspartate (NMDA) glutamate receptor such as MK-801 proved ineffective. Among NMDA receptor subfamilies, NR2A and NR2B subunits are considered as the main types of functional NMDA receptor. While activation of NR2A receptors is involved in synaptic plasticity and cell survival, activation of NR2B is shown to promote neuronal death. The present study is aimed to investigate whether the selective inhibition of NR2B is neuroprotective in *in vitro* oxygen glucose deprivation (OGD) model and *in vivo* permanent MCA occlusion (MCAO) model. **Methods:** Primary cortical neuronal cultures were prepared from 16-day-old Wistar rat embryos and used 10 to 12 days *in vitro*. As *in vitro* ischemia, neurons were exposed to 210-minute OGD or 15-minute 100 μM glutamate. Cells were treated after OGD with one of the following chemicals: global NMDA receptor antagonist MK-801 (10 μM), non NMDA receptor antagonist CNQX (10 μM), L-type calcium channel blocker nifedipine (5 μM), NR2A-specific antagonist NVP-AAM077 (200 nM), and NR2B-specific antagonist Ro25-6981 (100 nM). Neuronal death was quantified 24 hours later by measurement of lactate dehydrogenase released by dead neurons into the bathing medium. For *in vivo* ischemia model, adult male Wistar rats were anesthetized with halothane, and right MCA was occluded permanently by introducing a 4-0 nylon monofilament suture. Animals were divided into Ro and Vehicle group. Ro group rats were given Ro25-6981 (6mg/kg) intraperitoneally 3 hours after MCAO. Vehicle group rats were given vehicle in a same way. Those rats were sacrificed 12 hours after MCAO, and cerebral cortex was dissected into the core of MCA, the peripheral area of MCA and the ACA area. The level of fodrin proteolysis was analyzed by Western blotting. The other rats were sacrificed 24 hours later, and infarct size was measured with 2,3,5-triphenyltetrazolium chloride staining. **Results:** Treatment with Ro25-6981 was protective *in vitro* as well as MK-801 compared with vehicle treatment in both lethal OGD ($p=0.004$) and glutamate toxicities ($p<0.001$). In contrast, other antagonists such as CNQX, nifedipine, and NVP-AAM077 did not influence the cell injury after OGD and glutamate exposure. Treatment with Ro25-6981 resulted in a significant reduction in infarct volume compared with vehicle treatment in permanent MCAO model (250 ± 101 vs. 354 ± 50 mm^3, mean$\pm$s.d, $p=0.008$). In Ro group rats, the proteolysis of fodrin was significantly attenuated compared with vehicle group in the penumbra area 12 hours after MCAO. **Conclusions:** In conclusion, NR2B inhibition shows a marked reduction of neuronal injury both *in vitro* OGD and glutamate exposure and *in vivo* MCAO model.

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Th P142

White Matter Damage After Stroke And The Effect Of Matrix Metalloproteinases In Type-two Diabetic Mice

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Objective: Diabetes mellitus (DM) is a major health problem, leads to higher risk of ischemic stroke, and increases the extent of the cerebral injured area and results in worse outcome after stroke compared to the general population. Diabetic subjects are more prone to develop more and earlier white matter high-intensity lesions. Understanding the changes and mechanisms underlying the adverse effects of diabetes on the impaired white matter after stroke is important in developing new treatments for stroke in diabetic patients. We therefore, investigated white matter damage and associated molecular events after stroke in type-two DM mice. **Methods:** BKS.Cg-*m* +/+ *Lepr^{db}*/J (db/db) type-two DM mice and m+/+ db non-DM mice were subjected to middle cerebral artery occlusion (MCAo). Mice were sacrificed at 24h after MCAo. A battery of functional outcome tests, immunostaining, zymography, Western blot and real time PCR were employed. **Results:** DM mice exhibited significantly increased lesion volume, brain hemorrhagic transformation and neurological deficit compared to non-DM mice ($n=12$/group, $P<0.05$). To test whether DM enhances white matter impairment, SMI-31 (a Pan-axonal neurofilament marker), Bielshowsky silver (a marker for axons), Luxol fast blue (myelin marker) and NG2 (oligodendrocyte progenitor cell marker) immunostaining were performed. SMI-31, Bielshowsky silver, Luxol fast blue and NG2 expression were significantly decreased, indicating white matter damage, and matrix metalloproteinase 9 (MMP9) expression and activity were significantly increased in the ischemic brain of DM mice compared to non-DM mice ($p<0.05$). To investigate the mechanism underlying DM induced white matter damage, oxygen-glucose deprivation (OGD)-stressed premature oligodendrocyte and primary cortical neuron (PCN) cultures were employed. Lactate dehydrogenase (LDH) and 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium (MTS) assays were performed. High glucose (HG) increased MMP2, MMP9, cleaved-Caspase-3 levels and apoptotic cell number as well as decreased cell survival and dendrite outgrowth in cultured PCN ($n=6$/group, $P<0.05$) were measured. HG increased MMP9 gene and protein expression, increased cell death and cleaved-Caspase-3 level and decreased cell proliferation in cultured oligodendrocytes ($p<0.05$). Inhibition of MMPs by GM6001 treatment significantly decreased HG-induced cell death and apoptotic cell number in cultured PCN and oligodendrocytes ($n=6$/group, $P<0.05$), but did not regulate dendrite outgrowth in cultured PCN ($p>0.05$). Interpretation: DM mice exhibit increased lesion volume, brain hemorrhagic transformation and injured white matter compared to non-DM mice after stroke. MMPs upregulated in DM mice may at least partially exacerbate white matter cerebral damage after stroke in DM mice.

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An experimental Model of Stroke under Oral Anticoagulant Treatment

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Introduction: The prevalence of oral anticoagulant therapy (OAT) for stroke prevention in patients with atrial fibrillation is rising and 30% of all cardioembolic ischemic strokes occur in anticoagulated patients. We therefore aimed to establish a mouse model of ischemic stroke occurring under OAT to assess the frequency and characteristics of hemorrhagic transformation (HT) and the effects of a reversal of anticoagulation with prothrombin complex concentrate (PCC). **Methods:** C57BL/6 mice ($n = 21$) were treated with warfarin (2 mg/kg for 24 h) to achieve an INR value of 2.9 ± 0.9 SD. Untreated mice ($n = 20$) served as controls. Middle cerebral artery occlusion (MCAO) was induced by filament occlusion of the right MCA for 3 h and infarct size and HT were evaluated macroscopically at 24 h. Hemorrhagic blood volume was quantitatively assessed in additional 6 vs. 6 mice with a photometric hemoglobin assay. In a second experiment, we tested whether the rapid reversal of anticoagulation in warfarin mice 1 h after MCAO reduces the risk of HT compared to mice whose coagulation cascade was not restored (6 vs. 6 mice). **Results:** OAT at the onset of ischemia led to HT in all anticoagulated animals while only 14.3 % of the control animals showed HT. The mean hemorrhagic blood volume was 20-fold higher in the brains of warfarin mice after MCAO (5.9 ± 3.6 μl SD) compared to controls (0.3 μl $\pm$ 0.4 SD; $p < 0,01$). Reversal of OAT with PCC reduced hemorrhagic blood volume by 75 % compared to warfarinized mice without substitution ($1,1$ μl $\pm$ 0,6 SD vs. $4,5$ μl $\pm$ 1,4 SD, $p < 0,001$). **Conclusion:** We present a mouse model of ischemic stroke under OAT. Warfarin pretreatment dramatically increased the risk of HT 24 h after MCAO. Reversal of anticoagulation with PCC 1 h after stroke onset was able to prevent excessive hematoma formation.

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Downregulation Of Endothelial Nitric Oxide Synthase Phosphorylation Contributes To Infarct Expansion After Focal Cerebral Ischemia

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Background and Purpose: Endothelial nitric oxide synthase (eNOS) exerts a brain protective effect against brain ischemia. Suppression of eNOS expression or activity exacerbates ischemic brain injury. It was reported that ischemic insult itself increased eNOS expression. However, profile of eNOS phosphorylation in the ischemic brain is not fully elucidated. Because eNOS function is regulated by some phosphorylation sites, such as Ser1177, it is important to investigate eNOS phosphorylation profile after cerebral ischemia. The objectives of this study are; 1) to investigate the expression and phosphorylation profiles of eNOS after transient focal cerebral ischemia, 2) to evaluate the effect of pharmacological modulation of eNOS phosphorylation on infarct size after transient focal cerebral ischemia. Methods - Male Wistar rats were subjected to middle cerebral artery occlusion (MCAO) with the use of a 4-0 nylon monofilament and reperfusion 80 min after induction of ischemia. Tissue damage and localization of eNOS protein were evaluated by immunohistochemistry. Western blot (WB) was performed using phospho-specific antibody of eNOS (Ser1177), eNOS and β-actin. Brain tissue samples for WB were taken from the distinct MCA perfusion area in the ischemic hemisphere, as "MCA core", "MCA peripheral area" and "ACA area" at 6 hours, 24 hours and 48 hours after MCAO. Previously, we reported that Rho-kinase inhibitor can increase eNOS phosphorylation. Thus, Rho-kinase inhibitor, fasudil (2 or 10mg/kgBW) was administered after MCAO to increase eNOS phosphorylation. Infarct size was evaluated by using 2,3,5-triphenyltetrazolium chloride staining 2 days later. **Results:** After cerebral ischemia, eNOS immunoreactivity was preserved even in the MCA core area. Almost all eNOS signals were localized in vascular endothelial cells. WB analysis revealed upregulation of eNOS expression in the whole ischemic hemisphere. In contrast, phospho-eNOS signals were clearly decreased in the MCA core and peripheral area. Inhibition of Rho-kinase activity can acutely enhance eNOS phosphorylation in the brain. Fasudil treatment can suppress infarct expansion after transient focal ischemia (infarct volume: Vehicle 198.2 ± 20.7mm3, fasudil-2mg/kgBW 108.1 ± 15.3mm3, fasudil-10mg/kgBW 133.4 ± 16.8mm3; $n=9$ in each group). **Conclusions:** Although protein expression of eNOS was increased, phospho-eNOS was decreased in the ischemic hemisphere after transient focal cerebral ischemia. Enhancement of eNOS phosphorylation by fasudil leads to suppression of infarct expansion. These findings suggest eNOS function is impaired in the ischemic brain and pharmacological modulation of eNOS phosphorylation may be effective to prevent infarct expansion.

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Th P145

High Resolution Rapid Scanning X-ray Fluorescence Imaging To Track SPIO Labeled Neural Stem Cells In An Experimental Stroke Model

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Introduction: Magnetic resonance imaging (MRI) of superparamagnetic iron oxide nanoparticles (SPIO) labeled stem cells has become a widely used technique for in vivo cell imaging. The MRI signal obtained is however not specific for the SPIO labeled stem cells and experimental paradigms rely on histological verification using Prussian Blue staining. Here we explored synchrotron X-ray fluorescence imaging using a hard X-ray microprobe in continous rapid scanning mode to detect iron in SPIO labeled stem cells after intravascular transplantation in an experimental stroke model. XRF allows element-specific quantitative mapping of metals both in an entire brain section and of individual cells at 3 micron resolution with greater speed than traditional microprobes. **Methods:** Stroke was induced in NodScid mice using a hypoxia-ischemia model. Animals underwent unilateral temporary common carotid artery (CCA) occlusion followed by exposure to 8% O2 for 20 minutes and subsequent reperfusion. On day 3 after stroke 5x105 SPIO labeled human derived embryonic neural progenitor cells (hNPC) expressing a luciferase reporter gene were injected into the ipsilateral CCA. Control animals received either stereotactic intraparenchymal injection of 5x105 SPIO labeled hNPC or saline. Bioluminescence imaging and MRI using a FIESTA sequence were performed 24 hours after cell injection. After transcardial perfusion and slicing at 30μm, whole brain sections were scanned at the Stanford Synchrotron Radiation Lightsource on beamline 2-3 with specific subregions imaged with 3μm spot size and at 200 ms per point. Sections were then stained with Prussian Blue and human specific antibodies. **Results:** Bioluminescence imaging and MRI demonstrated significant homing of hNPC to the ischemic hemisphere but not to the contralateral hemisphere ($p<0.01$). Typical areas of susceptibility artifact were seen in the cortex, the hippocampus and to a lesser extent in the striatum. RS-XRF depicted distinct areas of Fe signal distributed in the ischemic hemisphere correlating with MRI findings. High-resolution scans depicted single cells in clusters with an average iron content of 7.0632pg. Intraparenchymal cell grafts appeared as focal signal on MRI and RS-XRF. Saline controls produced a needle shaped artifact on MRI, which correlated to a Fe signal on RS-XRF very distinct from the cellular morphology of SPIO labeled hNPC. Prussian blue staining correlated with RS-XRF imaging. **Conclusions:** The synchrotron X-ray microprobe in rapid-scanning mode allows high-resolution quantitative Fe specific imaging of single cells. Here we demonstrate its application in a multimodality imaging paradigm to track SPIO labeled hNPC in a stroke model. We found excellent correlation between Bioluminescence imaging, MRI, RS-XRF and histology.

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Th P146

Tissue Plasminogen Activator Induces Vasoconstriction in Acute Ischemic Stroke Rat Model

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Introduction: Tissue plasminogen activator (tPA) is the only FDA-approved drug for the treatment of acute ischemic stroke. Emerging data suggest that exogenous tPA may have pleiotropic actions in the brain: a number of studies have shown that exogenous tPA may have cerebral vasoactivity. For the first time, we performed a dynamic MRI study to investigate cerebral vasoreactivity in response to intravenously administered tPA in a permanent focal stroke model of rats. **Methods:** To characterize cerebral vascular reactivity, 7 Wistar male rats (~270 g) underwent MRI scans (Bruker 9.4T) 2 hours after permanent suture occlusion of middle cerebral artery. T2- and T2*-weighted images were acquired before and after administering blood pool superparamagnetic iron oxide nanoparticles (SPION: 36 mg/kg). For continuous monitoring of cerebrovascular parameters, we alternated gradient (GE) and spin echo (SE) echo planar imaging acquisitions (TR/TE = 3000/12 for GE and 3000/25 ms for SE). Time courses of äR2*(t) (= 1/T2*(t) (post-SPION) - 1/T2*(pre-SPION)) and äR2(t) (= 1/T2(t) (post-SPION) - 1/ T2 (pre-SPION)) maps were created. Then, cerebral blood volume (CBV(t) ~ äR2*(t)) and microvascular volume (MVV(t) ~ äR2(t)) were calculated, from which vessel size index (VSI(t)) maps (~äR2*(t) / äR2(t)) were quantified assuming one GE SE epoch as one time point. CBV, MVV and VSI responses were measured during intravenous tPA injection for 30 min (10mg/kg in 3 rats and 1mg/kg in 4 rats) and hypercapnia (5% CO2, 47.5% air, 47.5% oxygen for 5 min) before and after the tPA administration. Linear mixed model was used to assess temporal changes of cerebrovascular parameters. **Results:** Every rat showed significantly increased CBV, MVV and VSI responses during the first hypercapnia before tPA injection, although response magnitudes were smaller in ipsi-lesional hemisphere than in contralateral side. On the contrary, CBV, MVV and VSI continuously decreased after tPA injection in all rats ($p<0.0001$). The decremental response was more prominent in higher dose (10mg/kg) tPA group than in lower dose (1mg/kg) group ($p<0.0001$). CBV, MVV, and VSI still showed incremental response to the second hypercapnia after tPA injection, but the response magnitudes were significantly lower than those measured in the first hypercapnia. **Conclusions:**These data showed that tPA may cause cerebral vasoconstriction and impair vasodilation, even at the low dose. The findings suggest that cerebral vasoactivity might be one of important pleiotropic actions of tPA in the ischemic brain, especially to those with poor reperfusion efficacy. Development of neuroprotective strategies in targeting tPA cerebral vasoactivity may improve outcomes of tPA thrombolytic therapy.

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Th P147

Elevated Serum Levels of S-100B Reflect Brain Damage and Successful Treatment Effects in a Rabbit Model of Acute Ischemic Stroke

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Background: The astroglial protein S-100B has been implicated as a potential biomarker for the diagnosis of ischemic stroke. Elevated concentrations of S-100B have been reported in patients and some animal models, but studies are limited that evaluate S-100B as a marker of cerebral tissue damage and treatment effects in a rabbit embolic stroke model. **Objective:** To investigate the relationship between S-100B and percent stroke volume in a rabbit model of acute ischemic stroke, and determine if these measurements reflect a benefit from therapeutic intervention. **Methods:** New Zealand White Rabbits (n=31; 5.2±0.04 kg) were embolized with one blood clot (4.0x0.6 mm) injected into the internal carotid artery following a subselective angiographic procedure. Clot was produced in glass tubing at 37°C for 6-hr followed by incubation at 4°C for 72-hr. Follow-up angiography confirmed the occlusion of branches of the internal carotid artery, and treatment was initiated 1-hr post-embolization. Rabbits were randomly assigned to one of three groups: Control (n=8, embolization only), tissue plasminogen activator (tPA) (n=12), and Perflutren Lipid Microbubbles (MB)+Ultrasound (US) (n=11). MB were administered IV (0.6 mg/kg) over 30 minutes; ultrasound was applied transcranially for 1-hr (1-MHz pulsed-wave, 0.8 W/cm^2); tPA (0.9 mg/kg) was administered IV over 1-hr. Blood samples were collected before embolization (baseline) and at 3- and 24-hr post-embolization to determine concentrations of S-100B. Serum concentration of S-100B was determined by enzyme-linked immunosorbent assay. Rabbits were euthanized following the final blood sample (24-hr) and infarct volume was measured by vital stains on 4-mm coronal brain sections. **Results:** The S-100B fold increase over baseline was influenced by time (P=0.0002) and treatment (P=0.04). Control rabbits had a 3.1-fold increase in S-100B at 24-hr, and this increase differed from baseline (P=0.001). Similarly, rabbits treated with tPA had a 3.0-fold increase in S-100B at 24-hr which differed from baseline (P=0.0002). Treatment with MB+US, however, resulted in only a 1.6-fold increase in S-100B at 24-hr which did not differ from baseline (P=0.221). Infarct volume averaged 4.76% for control rabbits, 2.25% for rabbits treated with tPA, and 0.79% for rabbits treated with MB+US (P=0.015 compared to control). Concentrations of S-100B at 24-hr were positively correlated with percent infarct volume (r=0.59, P=0.0004). **Conclusions:** Serum levels of S-100B at 24-hr following embolization were greater than baseline values. 24-hr levels were positively correlated with percent infarct volume, and reflected the reduced stroke volume with microbubble therapy. S-100B can be measured in rabbits and correlates with damage from stroke and successful response to treatment.

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Th P148

Neuroprotective Effect of TAK-937, a Novel Cannabinoid Receptor Agonist, in a Nonhuman Primate Thromboembolic Stroke Model

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Introduction: TAK-937 is a novel, highly potent and selective cannabinoid (CB1/CB2) receptor agonist. In the previous studies, TAK-937 has demonstrated neuroprotective effects in rat transient and permanent middle cerebral artery (MCA) occlusion models. In this study, the effect of TAK-937 was examined in a non-human primate (cynomolgus monkey) thromboembolic stroke model to determine if these effects translate phylogenetically across species. **Methods:** Thromboembolic stroke in male cynomolgus monkeys was induced by injection of an autologous blood clot into the left internal carotid artery to occlude the MCA. Intravenous

administration of TAK-937 at 2 μg/kg/hr plus 0.8 μg/kg loading (n=7) or vehicle (n=7) was started 30 min after clot injection and continued for 24 hr. Cerebral infarct size was determined by 2, 3, 5-triphenyltetrazolium chloride staining method and concentration of S-100β in cerebrospinal fluid (CSF) was measured with ELISA kit 24 hr after MCA occlusion. Physiological parameters including body temperature, blood pressure and heart rate were continuously measured using a telemetry system throughout the experiment. **Results:** TAK-937 showed trend to reduce the infarct volume by 40% and S-100β levels in CSF by 40% compared with vehicle-treatment. S-100β levels in the CSF were positively correlated with infarct volume (r = 0.81). TAK-937 lowered body temperature by about 1.5 °C, but did not change blood pressure or heart rate. **Conclusion:** TAK-937 exerts a neuroprotective effect in a non-human primate stroke model without effects on vital signs. That S-100β levels in the CSF were reduced by TAK-937 in correlation with infarct volume suggests that this may be a good biomarker for the neuroprotective effects of TAK-937.

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Th P149

Granulocyte Colony-Stimulating Factor Enhances Arteriogenesis and Ameliorates Cerebral Damage in a Mouse Model of Ischemic Stroke

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Table of Contents ● Abstract Abstract Background and Purpose: Enhancing collateral artery growth is a potent therapeutic approach to treat ischemic cerebrovascular disease. Granulocyte-macrophage colony-stimulating factor (GM-CSF) has gained attention for its ability to promote arteriogenesis, ameliorating brain damage, by the mechanisms involving monocyte up-regulation. However, the recent clinical study testing its efficacy in myocardial ischemia has raised the question about its safety. It may increase vulnerability of atherosclerotic plaque to rupture. Here we tested alternative colony stimulating factors for their effects on collateral artery growth and brain protection. **Methods:** Brain hypoperfusion was produced by occluding left common carotid artery (CCA) in C57/BL6 mice. Following the surgery, G(granulocyte)-CSF, M(macrophage)-CSF, GM-CSF (100 μg/kg/day), or vehicle (normal saline) was administered subcutaneously for 5 consecutive days. The angio-architecture for leptomeningeal anastomoses was visualized by latex perfusion 2 days after the CSF treatment (n=5, each group). A set of animals underwent subsequent permanent ipsilateral middle cerebral artery (MCA) occlusion and infarct volume was assessed by 2,3,5-triphenyltetrazolium chloride (TTC) staining (n=6, each group). Circulating blood monocytes were counted by the hematology analyzer and blood smear examination (n=5, each group). Mac-2 positive cells in the dorsal surface of the brain were determined by immunohistochemistry (n=7, each group). **Results:** G-CSF as well as GM-CSF promoted leptomeningeal collateral growth after CCA occlusion (G-CSF, 27.5±1.3 μm, 61 vessels, GM-CSF, 28.0±1.8 μm, 59 vessels vs vehicle, 22.5±0.9 μm, 60 vessels, P<0.01, respectively). Infarct volume following MCA occlusion was reduced by G-CSF, similarly to GM-CSF (G-CSF, 35.4±4.7 mm^3, GM-CSF, 38.0±4.1 mm^3 vs vehicle, 53.1±5.2 mm^3, P<0.05, respectively). Both G-CSF and GM-CSF increased circulating blood monocytes (G-CSF, 547.8±/114.1μl, GM-CSF, 536.8±138.0/μl vs vehicle, 101.0±34.4/μl, P<0.01, respectively) and Mac-2 positive cells in the brain dorsal surface (G-CSF, 107.4±14.6, GM-CSF, 104.6±10.1 vs vehicle, 51.4±4.9, P<0.01, respectively), suggesting the mechanisms coupled to monocyte up-regulation might be shared. M-CSF showed none of theses effects. **Conclusion:** G-CSF enhances collateral artery growth and reduces infarct volume in a mouse model of brain ischemia, similarly to GM-CSF.

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Th P150

AMPK Regulates Ischemic Cell Death through GSK3-Beta

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Introduction: Cerebral ischemia can lead to energy failure and thus cell death. AMP-activated protein kinase (AMPK) is involved in an array of cellular cascades activated to deal with changing cellular energy status during cerebral ischemia. Acute activation of AMPK via phosphorylation occurs after stroke and leads to an exacerbation of ischemic injury. Metformin is an AMP-activated protein kinase (AMPK) activator. Although acute AMPK activation is detrimental in stroke, chronic metformin treatment improves stroke outcome by down-regulating AMPK. Glycogen synthase kinase 3-β (GSK3β) is a downstream effecter of AMPK. It has been reported that GSK3β inhibition in stroke is protective by preserving a cellular survival factor β-catenin. In this study, we evaluated the hypothesis that inhibition of AMPK by chronic metformin is neuroprotective by inhibiting GSK3β. **Methods:** Focal stroke was induced by reversible middle cerebral artery occlusion (MCAO-90 minutes) in male wild-type (WT) mice treated with vehicle or 50 mg kg^{-1} (i.p.) Metformin for 3 weeks prior to MCAO. Stroke outcome was determined with CV staining at 24 hrs following MCAO. Phosphorylated GSK 3β (inactivated form), β-catenin and AMPK phosphorylation were determined by Western blot at 4 hours following MCAO. Protein levels were normalized to total GSK3β. *Data were presented as mean±sem P<0.05.* **Results:** Chronic treatment with Metformin reduced infarct size 24 hours after stroke both in the striatum and total hemisphere (Cortex: 48.3±2.1% vs. 32.1±6.6%; Striatum: 53.6±4.0% vs. 45.3±2.9% P<0.05, Total: 45.3±2.9% vs. 29.3±4.9%, P<0.05). Western blots demonstrated chronic metformin reduced pAMPK levels. Stroke induced an increase in pGSK3β 4 hours after stroke (0.4±0.4 Vehicle Sham vs 2.1± 0.4 Vehicle Stroke). Chronic metformin treatment further enhanced the stroke-induced increase in pGSK3β (1.9± 0.1 Sham vs 7.4± 3.6 Stroke). In addition stroke induced a decrease in β-catenin 4 hours after stroke and this decrease was eliminated by chronic metformin treatment. **Conclusion:** Chronic metformin treatment increased pGSK3β (inactivated form) that in turn ameliorated the decrease of β-catenin seen in vehicle treated animals. Our data demonstrated that in the ischemic brain, inhibition of AMPK inactivates pGSK3β and increases β-catenin activity. Our study suggested that GSK3β may contribute to the effect of AMPK in stroke by regulating beta-catenin.

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Th P151

Vagus Nerve Stimulation Through the External Ear in Rat Cerebral Ischemia

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Introduction: Electrical stimulation of the vagus nerve in the neck reduces infarct volume by approximately 50% after transient middle cerebral artery occlusion in rats. VNS, however, is not a feasible intervention in setting of acute ischemic stroke because it requires positioning of an electrode after surgical exposure of the nerve in the neck. In the present study, we explored whether stimulation of vagus nerve dermatome in the external ear reduced infarct size in rats. **Methods:** Stimulating electrodes were implanted on the left auricular concha (cymba concha or cavum concha) to stimulate the auricular branch of the vagus nerve (ear stimulation or ES) in adult male Wistar rats. CBF was measured by laser Doppler flowmeter. Ischemia was produced by filament occlusion of the right middle cerebral artery for 2 hours, followed by reperfusion. In the stimulation group, square pulses were delivered for 30 sec at every 5 minutes for 1 hour starting 30 minutes after the induction of ischemia. In the control group, all the procedures were duplicated but no stimulus was delivered. Animals were euthanized and cerebral infarct volume was determined 24 hours after the onset of ischemia. **Results:** ES did not change the heart rate, arterial blood pressure, blood gases and pH, and temperature. There was an increase in CBF with each stimulation pulse which gradually decreased by the end of the 30 seconds stimulation period and completely returned back to baseline following the cessation of stimulation. The mean maximum increase in CBF was 134.02% ± 43.87% baseline. CBF elevated 20% from baseline in 5 of the 6 ES-treated animals. The mean infarct volume and SEM was 37.97 ± 2.43 % of the contralateral hemispheric volume in control (n=6) and 32.31 ± 3.93 % (n=6) in ES-treated animals (p=0.258). There was a correlation between the magnitude of CBF response to ES and infarct volume (R^2=0.745); as the CBF response increased, the infarct size decreased. Infarct size was smaller in ES-treated animals with positive CBF response as compared with the controls (28.99 ± 2.59 % of the controlateral hemisphere, n=5; p=0.037). **Conclusion:** Electrical stimulation of the vagus nerve dermatome in the external ear causes a specific response characterized by variable increase in CBF. Reduced infarct volume in ES-responders suggests that ES promises to be a practical novel treatment for cerebral ischemia. Further refinement of the technique and validation are needed.

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Th P152

Demonstration of Ischemic Preconditioning in White Matter: Critical Role for Toll-like Receptor-4

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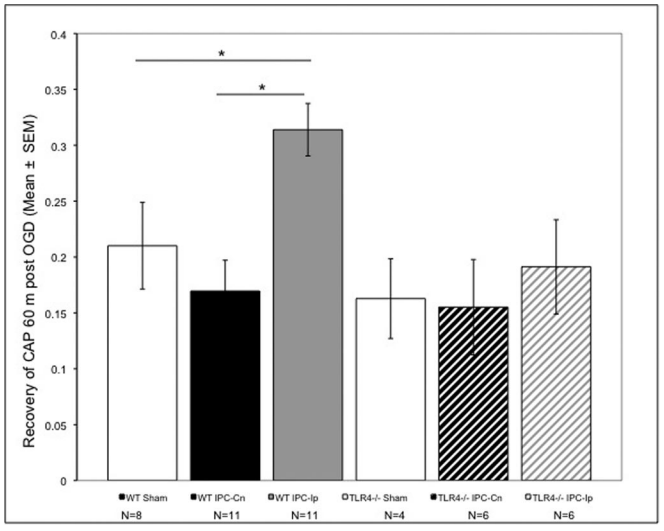
Background: Ischemic preconditioning (IPC) is a robust protective phenomenon in which a brief period of ischemia confers transient tolerance to subsequent ischemic challenge. White matter (WM) injury is critical in the pathophysiology of human stroke. The effect of IPC in experimental models of ischemic injury in WM is unknown. Toll-like receptor-4 (TLR4), a key receptor in innate immunity, mediates robust pro-inflammatory responses and has been mechanistically implicated in IPC. TLR4 is expressed in WM by microglia and astrocytes. TLR4 is activated by endogenous "danger associated molecular patterns" such as heat shock proteins that are released in ischemic brain. We hypothesize that: (i) IPC induces functional protection in WM ischemic injury and (ii) TLR4 signaling is required for this protection. **Methods:** We performed 15 m common carotid artery ligation or sham surgery on 3 mo old male WT and TLR4-/- mice to induce IPC in the ipsilateral (Ip) optic nerve (ON). After 72 h, we sacrificed the mice. Ip and contralateral (Cn) ONs were removed, equilibrated in normoxic/normoglycemic (N/N) artificial cerebral spinal fluid (aCSF), and exposed to 45 m of oxygen-glucose deprivation (OGD) in aglycemic/anoxic aCSF followed by 5 h in N/N aCSF. Compound action potentials (CAP) were evoked and ON function was monitored and quantified. **Results:** In WT, preconditioned (IPC-Ip) ON recovered significantly better (31±3 % baseline) than either sham (21±4, *p<0.05) or IPC-Cn (17±3, *p<0.05) controls. In TLR4-/- mice, recovery in the preconditioned ON (19±4 % baseline) was not significantly different from that in either the sham (16±4, NS) or IPC-Cn (15±5, NS) control ON (Fig). Relative protective effect

of IPC was 2.1-fold greater in WT than in TLR4-/- ON. **Conclusions:** These findings demonstrate that: (i) IPC induces a robust protective effect in WM and (ii) this effect is at least partially dependent on functional TLR4 signaling. This novel experimental paradigm will improve our mechanistic understanding of IPC and WM injury.



Author Disclosures: M.A. Hamner: None. A. Savos: None. J. Colman: None. B.R. Ransom: None. J.R. Weinstein: None.

Th P153

Akt Activation Mediates Human Umbilical Cord Blood Cell Protection

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Background: Systemic administration of human umbilical cord blood (HUCB) cells reduces infarct volume and behavioral deficits in rats following ischemic injury. In previous studies, we reported that HUCB cells release soluble factors that protect oligodendrocytes (OL)s subjected to oxygen glucose deprivation (OGD) by increasing survival associated gene expression. Administration of HUCB cells following permanent middle cerebral artery occlusion (MCAO) elevated the protein products of these genes in OLs. Many of these factors activate gene expression via Akt kinase, which is linked to cell survival. **Purpose:** In the present study, we investigated the role of phosphorylated Akt (P-Akt) in HUCB cell mediated oligoprotection. Methods and**Results:** OL cultures were subjected to 24 hrs OGD or normoxia while coincubated with HUCB cells, HUCB cells+Akt inhibitor IV, or vehicle. OL viability was assessed using lactase dehydrogenase assay. As previously reported, HUCB cell coincubation rescued OLs subjected to 24 hrs OGD ($n=6$, $P<0.05$); this protection was completely blocked by the presence of Akt inhibitor IV ($n=6$, $P<0.05$). Immunohistochemistry showed that the presence of HUCB cells increased P-Akt in OLs exposed to OGD ($n=3$, $P<0.05$), whereas Akt inhibitor IV reduced this phosphorylation. P-Akt was not altered under normoxic conditions. Next, we evaluated P-Akt in the white matter of rats subjected to MCAO. HUCB cells ($1x10^6$) or vehicle were administered systemically 48 hrs post MCAO. Animals were sacrificed 6, 24, or 48 hrs following HUCB cell treatment. Immunohistochemical analysis showed a gradual increase in P-Akt in the white matter ipsilateral to the infarct which peaked at 48 hrs following HUCB cell treatment ($n=3$, $P<0.05$). P-Akt in sham and MCAO vehicle rats was unchanged ($n=3$, $p>0.05$). Because P-Akt inhibits apoptosis, we also examined activated caspase 3 in the white matter following MCAO. Caspase 3 activation was elevated at 54 and 74 hrs following MCAO ($n=3$ $P<0.05$, $P<0.01$) and returned to basal levels 96 hrs post surgery ($n=3$, $p>0.05$). HUCB cell treatment blocked caspase 3 cleavage, where levels remained comparable to sham ($n=3$, $p>0.05$). **Conclusion:** The present results demonstrate that Akt activation is an integral and necessary component of HUCB cell mediated white matter protection. Our data suggest HUCB cell induced P-Akt protect OLs following MCAO by reducing caspase 3 activation.

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Th P154

Trichostatin A Impact Upon Post-stroke Neurogenesis In The Immature Brain Is Dependent Upon The Time-point After Injury Being Assessed

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Background: Stroke in the immature brain usually presents 12-24 hours after the insult with seizures. Post-stroke neurogenesis in the SGZ of the immature brain is decreased and may contribute to the long-term cognitive impairments seen. **Objective:** To determine if chronic histone deacetylase inhibition after stroke in an immature brain enhances post-stroke neurogenesis. **Methods:** Two drug administration protocols were used. In the first (Protocol 1), unilateral carotid ligation of P12 CD1 mice was followed by trichostatin A (TSA, 5 mg/kg i.p.) or DMSO injections twice a day for 2 weeks from P17-P29, BrdU was administered from P18-P20, and animals perfused at P42. In the second (Protocol 2), TSA (2.5 mg/kg) or vehicle was given from P16-P28, BrdU administered from P24-P26, and perfusions at P42. Immunohistochemistry was performed and total counts of BrdU-labeled cells in the dentate gyrus of the hippocampus done. **Results:** Pilot data from protocol 1 did not indicate any significant change in DG neurogenesis in either injured or uninjured animals. Protocol 2 resulted in significant increases in DG neurogenesis (total counts) in both injured (mean ipsilateral counts: TSA ($n=9$) $=$ 85.6 $\pm$19.3 versus DMSO ($n=4$) $=$ 40.2 $\pm$ 4.9, $p=$ 0.049; mean contralateral counts: TSA$=$ 99.6 $\pm$ 15.2 versus DMSO$=$ 49.9 $\pm$ 3.4, $p=$ 0.011) and uninjured animals (mean ipsilateral counts: TSA ($n=5$)$=$86.6 $\pm$ 3.4 versus DMSO ($n=5$) $=$ 43.7 $\pm$ 2.2, $p=0.000$; mean contralateral counts: TSA$=$ 97.6 $\pm$ 6.1 versus DMSO$=$ 45.8 $\pm$ 4.2, $p=0.000$). **Conclusions:** The impact of TSA in this model is likely to depend on the age of the animal, duration of TSA treatment before BrdU labeling, and/or the stage in the evolution of the injury. Further work is being done to determine the extent of histone deacetylation and to determine the long-term impact of TSA-enhanced neurogenesis upon long-term functional outcomes. Improving recovery from neonatal stroke is an important long-term goal.

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Th P155

Systemic Treatment With Direct Angiotensin Ii Type 2 Receptor Agonist, Compound 21, Improved Cognitive Function Via Increase In Cerebral Blood Flow And Enhancement Of Excitatory Post-synaptic Potential With Neurite Elongation

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Background: Our previous studies indicate that relative stimulation of angiotensin (Ang) II type 2 (AT_2) receptor signaling using Ang II and Ang II receptor blockers enhances neurite outgrowth and neural differentiation, resulting in the prevention of cognitive impairment. Recently, a newly developed direct AT_2 receptor agonist, compound 21 (C21), has been reported to improve cardiac function after myocardial infarction in mice, and expected to be effective to other pathological conditions. Here we assessed the possible effects of C21 on cognitive function. **Methods:** Male 8 week-old C57BL6 and AT_2 receptor-null (*Agtr2*$^-$) mice were treated with C21 (0.001, 0.003, 0.01 mg/kg/day) intraperitoneal injection once a day once a day for 2 weeks. Then, mice were subjected to the Morris water maze test for 5 days to evaluate spatial memory. Cerebral blood flow was measured by 2 dimensional laser-Doppler. Excitatory post-synaptic potential (EPSP) was assessed by electrophysiological techniques. Neurite elongation was assessed using hippocampal neurons from GFP-transgenic mouse. **Results:** Blood pressure and mRNA expression of AT_1 and AT_2 receptors were not significantly changed between mice with or without C21 treatment. Interestingly, treatment with C21 significantly improved spatial learning in C57BL6 mice, but this effect was not observed in *Agtr2*$^-$ mice. C21-mediated cognitive improvement in C57BL6 mice was attenuated by co-administration of bradykinin B2 receptor antagonist, icatibant. Cerebral blood flow was significantly increased in C57BL6 mice with C21 treatment. Furthermore, administration with C21 dose-dependently enhanced hippocampal EPSP in C57BL6 mice but not in *Agtr2*$^-$ mice. C21 treatment also promoted neurite elongation. **Conclusion:** These results suggest that a direct AT_2 receptor agonist, C21, is expected to improve cognitive function at least in part via an increase in cerebral blood flow and an enhancement of EPSP with neurite elongation involving bradykinin 2 receptor activation.

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Th P156

Pharmacologic Hsp70 Induction Confers An Anti-inflammatory Response And Protects Brain-derived Endothelial Cells From Microglial Activation

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HSP70 has been shown to improve outcome from experimental stroke. We previously showed that one mechanism of its protective effect is through the inhibition of the inflammatory response accompanying ischemic stroke. In order to explore the translational relevance of HSP70 induction, we tested whether its pharmacological induction by geldanamycin (GA) or its analogues, 17AAG and radicicol might be anti-inflammatory and protective. These compounds all induce HSP70 by its inhibitory effects on HSP90. Since GA has some toxicity in humans, we also studied 17AAG and radicicol, analogues having already been studied at the clinical level in cancer patients and found to have better tolerability. Microglial BV2 cells were activated with lipopolysaccharide (LPS) plus treatment with the various HSP70 inducing compounds. Treatment was begun an hour prior to LPS application to allow for sufficient HSP70 induction. 24hr later, media and cell extracts were assayed for NO and iNOS protein; injury was examined by viability assays. Treatment of BV2 cells with GA or any of its analogs induced HSP70 in a dose dependent manner. Treatment also markedly prevented microglial activation as assayed by iNOS/NO accumulation. LPS-stimulated BV2 cells induced injury to brain derived endothelial cells (EC), and this was prevented by GA treatment ($p<0.01$). A similar protective effect was observed with both17AAG and radicicol. Our data together, showed that GA and its analogs induce HSP70 and inhibit immune responses in microglia. HSP70 induction protects endothelial

cells from microglial toxicity. We suggest that pharmacological induction of HSP70 in microglia might be a useful approach to the treatment of neurovascular pathologies.

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Th P157

The Ratio of Bcl2 and Beclin-1 are Critical in Mediating ROS Neuronal Injury towards Cytoprotective Autophagy or Programed Cell Death

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Introduction: Under stroke-induced conditions of hypoxia/ischemia and nutrient deprivation, autophagy supports neuronal survival by recycling cytoplasmic proteins and organelles to regenerate amino acids and ATP. Autophagy-modulating pre-clinical in vivo studies have produced intuitively contradictory**Results:** stroke lesion size is decreased when autophagy is induced or it is inhibited. **Methods:** To determine a mechanism for autophagy-mediated neuroprotection, PC12 cells were neuronally-induced with nerve growth factor (NGF) and transfected with siRNA against key autophagy regulatory proteins: mTOR, Beclin-1, and Bcl-2. Following siRNA transfection, the cells were treated with either the autophagic inducer rapamycin or the autophagic inhibitor chloroquine, or in combination. We hypothesized that Bcl-2 and Beclin-1 were keys to neuroprotective autophagy and that rapamycin's observed neuroprotection was a result of an increase in Bcl-2. Autophagy was induced with 1mM H2O2, simulating reperfusion injury ROS production. Samples were then used for western immunoblot to determine autophagic induction based on levels of p62 and LC3. **Results:** H2O2 increases LC3II and p62; treatment with rapamycin further increases these autophagy markers. Chloroquine reduces LC3II but allows the accumulation of p62, suggesting proteosomal and chaperone-mediated autophagy clearance of ROS damaged proteins has increased, whereas Macroautophagy is blocked. Rapamycin decreases the apoptosis marker cleaved LaminA. siRNA knockdown of Beclin-1 increases autophagy markers and decreases the apoptosis markers. In contrast siRNA knockdown of Bcl2 increases apoptosis (LaminA cleavage) and decreases autophagy. The levels of Bcl-2 and Beclin-1 and the ratio of these two interacting proteins may be the key to cell survival and the determinant of cytoprotective vs cytodestructive autophagy and apoptotic induction. We further postulate that the previously-observed neuroprotective effects of rapamycin may act through modulation of the levels of Bcl-2, increasing the ratio of Bcl-2:Beclin-1 during rapamycin-induced autophagy. This suggest the enhancement of cytoprotective autophagy as a potential neuroprotective therapeutic approach.

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Th P158

Acute Rosiglitazone Treatment during Reperfusion is Neuroprotective of Hyperglycemic Stroke but Does Not Limit Edema

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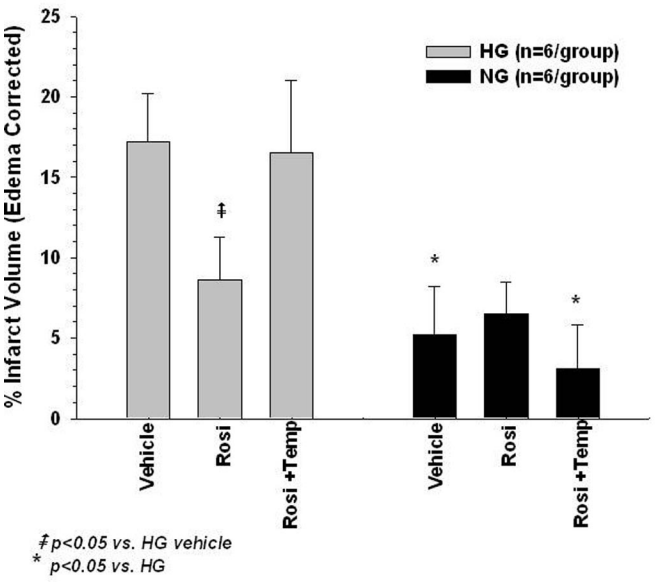
Objectives: Hyperglycemic (HG) stroke is thought to worsen outcome through enhanced oxidative and inflammatory processes. We tested the hypothesis that acute rosiglitazone (Rosi) treatment, a PPAR gamma agonist with anti-inflammatory and anti-oxidant properties, during reperfusion would limit stroke damage. **Methods:** Male Wistar rats (350-380g) that were normoglycemic (NG, n=36) or HG (blood glucose 280-350 mg/dL) for 5-6 days by STZ injection (n=36) underwent 2 hours of MCA occlusion followed by 2 hours of reperfusion. Animals were treated IV with either Rosi (1 mg/kg), Rosi + Tempol (50 mg/kg) or vehicle (saline) 10 minutes prior to reperfusion. Infarct and edema were measured using TTC and wet:dry weights, respectively. CBF was measured using laser Doppler. Blood gases were maintained within normal physiological ranges. **Results:** In vehicle treated animals, HG stroke increased infarction vs. NG (corrected for edema: 17.2±3.2% vs. 5.2±3.1%; P<0.01). Acute Rosi treatment decreased infarction in HG animals to 8.5±2.5% (p<0.05 vs. HG vehicle) but had no effect on NG animals (6.5±2.7%; p>0.05 vs. NG vehicle). The combined treatment of Rosi+Tempol eliminated the protection as this group had similar infarct as vehicle treatment (16.5±4.5%; p>0.05 vs. HG; Figure 1). All groups had increased water content in the ipsilateral vs. contralateral hemisphere, but neither treatment had any effect of edema as the percent water content of the ipsilateral hemispheres were similar between vehicle, Rosi and Rosi+Tempol groups (81.4±0.03%, 81.7±0.3% and 80.6±.9%; P<0.01 vs. Ipsi; p>0.05 vs. vehicle). The lack of protection with the combined Rosi + Tempol treatment was associated with limited reperfusion suggesting an effect on CBF that caused greater ischemia. **Conclusions:** These results suggest that acute Rosi treatment during reperfusion is neuroprotective, but not vascular protective, during HG stroke as infarction decreased but edema was not affected. The combination of Tempol + Rosi increased infarction, possibly due to an effect on CBF that increased the perfusion deficit. The damaging effect of Rosi+Tempol under these conditions may be due to a more pro-oxidative state that altered the effectiveness of these compounds.

Figure 1. Effect of Rosiglitazone and Tempol on Infarction in Normoglycemic and Hyperglyemic MCAO



Author Disclosures: M.J. Cipolla: Research Grant; Significant; NIH. J.G. Sweet: None.

Th P159

Mineralocorticoid Receptor Activation Is Involved In Middle Cerebral Artery Remodeling In Life-long Obesity In Sprague-dawley Rats

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Obesity is a risk factor for the development of hypertension, and chronic hypertension leads to middle cerebral artery (MCA) remodeling and increased damage after cerebral ischemia. The mineralocorticoid receptor (MR) is linked to MCA remodeling, and we have previously shown that plasma levels of the mineralocorticoid aldosterone are increased 4-fold in our model of obesity. Hence, we hypothesized that MR antagonism would reduce MCA remodeling and damage after cerebral ischemia in rats fed a diet rich in fat and carbohydrates. Three week-old male Sprague-Dawley rats were fed a high-fat (HF) diet containing 36% fat and 36% carbohydrate (n=7), or HF plus the MR antagonist canrenoic acid (the active metabolite of spironolactone, HF+Canr, n=8) or regular chow (RC, n= 7) for 18 weeks. MCA tone generation and passive structure were analyzed by pressure myography over a range of intralumenal pressures. Pial blood flow pre-ischemia, post-ischemia and 24 hour post-ischemia was measured by scanning laser Doppler and is expressed as percentage of the contralateral hemisphere blood flow (%CBF). Permanent cerebral ischemia was performed by MCA occlusion (pMCAO) for 24 hours and infarct size was measured as % of the infarcted hemisphere (%IH). Data were analyzed by Two Way Repeated Measures ANOVA (MCA structure) or by One Way ANOVA (pMCAO), and are presented as mean±SEM. At 80 mmHg, HF treatment promoted an increase in MCA wall thickness (RC, 15.1±0.6; HF, 21.8±1.3; HF+Canr, 15.3±0.9μm, P<0.001), wall cross-sectional area (RC, 12654±470; HF, 17238±943; HF+Canr, 12630±652μm2, P<0.05) and wall-to-lumen ratio (RC, 0.06±0.002; HF, 0.10±0.007; HF+Canr, 0.06±0.005, P<0.001). MR antagonism prevented these alterations. HF caused a trend towards a decrease in lumen diameter and Canr prevented this (RC, 251±7; HF, 231±5; HF+Canr, 248±9μm). Tone generation was not different between experimental groups (RC, 39.3±8; HF, 49.1±9; HF+Canr, 47.7±8, %tone). Pial blood flow 24 hours post-ischemia was significantly decreased in HF, and there was a trend towards improvement in HF+Canr (RC, 71±3; HF, 55±4; HF+Canr, 64±3; %CBF, p=0.007 RC vs HF). Similarly, there was a trend towards an increase in infarct size after pMCAO in HF, and canrenoic acid prevented it (RC, 32.0±4; HF, 46.1±8; HF+Canr, 32.7±5, %IH, p=0.09). These results suggest that the elevated aldosterone plasma observed in obese rats is a major contributor for MCA wall hypertrophy. The increase in wall hypertrophy, even without reducing lumen diameter, was sufficient to reduce pial blood flow 24 hours post-ischemia in HF and promote an increase in infarct size. Importantly, MR antagonism attenuated these trends, suggesting a potential protective role against damage after permanent cerebral ischemia. Therefore, MR antagonism might be a valuable therapy for primary prevention of ischemic stroke.

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Th P160

The Role of Mammalian Target of Rapamycin in Focal Cerebral Ischemia: The Link between TSC2 and mTOR Signaling Pathway

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Background: Mammalian target of rapamycin (mTOR) mediates various functions such as cell survival, obesity, and cellular responses to injury including the pathologenic response to ischemic stroke. However, the signaling mechanism linking mTOR inhibition to focal cerebral ischemia is unknown. We postulate that the activation of mTOR may induce neuroprotective effects *via* TSC2/mTOR/S6 pathway. **Methods:** To investigate whether activation of mTOR is neuroprotective, we used a transient focal cerebral ischemia model. Wild-type and TSC2+/- mice (20-22g) were administered either vehicle or rapamycin (5 mg/kg, i.p., 1d and 5d), before MCAo. After 2 hrs of MCAo followed by 22 hrs of reperfusion, infarct size was determined with TTC staining and protein levels of TSC2, mTOR, and S6 were assessed in the ischemic core and contralateral (non-ischemic core) hemisphere region. **Results:** Compared to vehicle, mTOR/S6 level was decreased in ischemic regions during ischemia (0.5, 1, 2h MCAo). After reperfusion (after 2h MCAo), phospho-S6 was rapidly upregulated. Acute administration of rapamycin had no effect on cerebral infarct size in WT mice but chronic administration of rapamycin exhibited significantly increased infarct size and higher NDS following MCAo. Compared to vehicle, TSC2+/- mice showed increased mTOR/S6 levels in the brain and reduced cerebral infarct size (64.2 $\pm$ 5.96; $n=7$ *vs* 92.6 $\pm$ 6.08, $n=7$, $P<0.01$). **Conclusions:** These findings indicate that the inhibition of mTOR worsens cerebral infarct size while the activation of mTOR in TSC2+/- mice reduces cerebral infarction. Therefore, TSC2 provides an important link between neuroprotection and the mTOR signaling pathway in focal cerebral ischemia.

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Th P161

Apyrase, APT102, Improves the Beneficial Effect of rt-PA In Experimental Thromboembolic Stroke

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Background: Inhibition of platelets after ischemic stroke could help to maintain vascular patency and assist rt-PA in recanalization. However, use of available platelet inhibitors may be associated with the increased risk of intracerebral hemorrhage (ICH). **Objective:** To demonstrate in a clinically relevant model of thromboembolic stroke whether novel genetically engineered soluble human apyrase APT102, which has improved enzymatic activity and more potent platelet inhibition capacity than the wild-type form, has therapeutic effect without increased risk for ICH, and also whether APT102 has a synergistic effect with rt-PA without increased risk for ICH. Method: Long Evans rats subjected to thromboembolic stroke were randomly divided into 4 treatment groups: (1) control (saline treated); (2) APT102 at 2.25 mg/kg, (3) rt-PA (at 10 mg/kg) and (4) APT102 at 2.25 mg/kg plus rt-PA. All treatments were initiated at 2 hours following thrombus injection into the internal carotid artery. Infarct volume, incidence of ICH and behavioral deficit were assessed at day 3 after the stroke. **Results:** While APT102 alone did not produce significant effect on stroke outcome as compared to saline control (123.1+/-19.9 vs. 119.9+/-26.4mm^3). APT102 combined with rt-PA significantly reduced infarct volume (71.2+/-16.1) compared to rt-PA alone and saline treated rats ($p<0.05$). Analysis of behavioral deficit was performed on the same groups and APT102 combined with rt-PA reduced behavioral deficit as compared to rt-PA alone and saline treated rats ($p< 0.05$). Visual analysis of brains demonstrated that 2 out of 11 rats with saline and 5 out of 11 animals treated with rt-PA alone demonstrated petechial hemorrhages within the ischemia-affected aspects of the brain. In contrast, no hemorrhage was observed in any of 10 rats treated with APT102 with or without rt-PA. **Conclusions:** This study provides the first evidence that synthetic apyrase used to inhibit platelets after ischemic stroke may be useful in improving the effect of rt-PA without increasing the risk of ICH.

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Th P162

Synergistic Memory Impairment Through The Interaction Of Chronic Cerebral Hypoperfusion And Amlyloid Toxicity In A Rat Model Of Combined Injury

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Background Clinical studies have demonstrated that Alzheimer's disease (AD) and vascular dementia share common cardiovascular risk factors. Further, vascular and AD-related pathology have been shown to coexist in the brain of dementia patients. We investigated how cognitive impairment could be exacerbated in a rat model of combined injury through chronic cerebral hypoperfusion and amyloid β (Aβ) toxicity. Methods Wistar rats received permanent ligation of bilateral common carotid arteries (BCCAo), modeling chronic cerebral hypoperufison at 12 weeks. Additional bilateral intracerebroventricular Aβ used to model Aβ toxicity was injected at 15 weeks in the combined injury group. The experimental animals were divided into four groups using a two-by-two table of BCCAo or Aβ toxicity, including a sham group, as well as BCCAo, Aβ toxicity and BCCAo-Aβ toxicity groups (n=7 per group). Four weeks after sham operation or BCCAo, a Morris water maze task was performed to evaluate spatial memory. Six weeks after sham operation or BCCAo, histologic study including thionin staining, neuroinflammatory markers (OX-6, GFAP), and AD-related pathology (Aβ, amyloid precursor protein, tau-2) was performed. Results Spatial memory impairment was synergistically exacerbated in BCCAo-Aβ toxicity group compared to BCCAo or Aβ toxicity group ($p<0.001$). Neuroinflammation with astroglial and microglial activation was observed in multiple white matter lesions and the hippocampus in BCCAo and BCCAo-Aβ toxicity groups. In rats with BCCAo and BCCAo-A toxicity group, APP and tau-2 staining showed relatively enhanced immuno-reactivity with sporadic cellular or clustered patterns in the cortical or deep gray matter and sporadic cellular patterns in the cortical gray matter, respectively. **Conclusions:** Our experiment supported experimental evidence for the clinical hypothesis of the deleterious interaction between chronic cerebral hypoperfusion and Aβ toxicity. Chronic cerebral hypoperfusion-induced impaired clearance of endogenous or exogenous Aβ may exacerbate cognitive impairment through the pertubated equilibrium between the brain and blood compartments in AD-related pathology.

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Th P163

Reperfusion rather than Ischemia drives the Formation of Ubiquitin Aggregates in the Mouse Neocortex after Middle Cerebral Artery Occlusion

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Background: The ubiquitin-proteasome system (UPS) is the main cellular pathway for degradation of short-lived and misfolded proteins. Thus, target proteins are constantly tagged for selective destruction in proteolytic complexes called proteasomes by covalent attachment of ubiquitin molecules. In brain as in other organs the UPS is fundamental for normal cellular function. In the brain, disruption in the UPS resulting in protein aggregation has mostly been associated with neurodegenerative diseases, but some reports have shown that cerebral ischemia-reperfusion leads to accumulation of ubiquitinated protein aggregates as well (Stroke 38:3230, 2007). However, the factors triggering ubiquitination and their relationship to the outcome of cerebral ischemia remain poorly understood. Here we used a mouse model of middle cerebral artery occlusion (MCAO) to investigate the relationship between ubiquitination and duration of the ischemic insult, presence or absence of reperfusion and tissue damage. **Methods:** The MCA was occluded for 15 min, 30 min or permanently in male C57BL6 mice (n=3-5/group) using an intravascular filament. Ubiquitination in ipsilateral neocortex and striatum was assessed by western blotting at different time points after ischemia. **Results:** Mice sacrificed immediately after 30 min of MCAO (with no reperfusion) had no detectable ubiquitin aggregates, like the sham-operated group. However, 30 min of MCAO followed by reperfusion led to substantial ubiquitinated protein aggregates, which were stably elevated at 1, 3, 6, 9 and 12 hours, and declined at 24 and 72 hours. Ubiquitin-aggregate formation was restricted to the cortex and to a lesser extent the striatum. 15 min of MCAO with reperfusion, which produces only minimal tissue damage, resulted in levels of ubiquitination indistinguishable from those produced by 30 min MCAO, which results in substantial damage (infarct volume at 72 hours: 57$\pm$8mm3; JCBFM 29:66, 2009). In contrast, in permanent MCAO no ubiquitin aggregates were observed after 1, 3, 6 and 24 hours, despite the development of massive tissue damage (infarct volume at 24 hours: 72$\pm$6mm3; JCBFM 29:66, 2009). **Conclusions:** Reperfusion rather than ischemia leads to the appearance of ubiquitinated proteins. The molecular mechanism by which the re-establishment of blood flow triggers ubiquitination remains to be elucidated, but they may include formation of free radicals. Presence of ubiquitinated proteins may be a marker of reperfusion and may identify potentially salvageable tissue.

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Th P164

Moderate Hypothermia Attenuates Peripheral Immunodepression Caused by Stroke in Rats

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Background and Purpose: Stroke results in peripheral (extracerebral) immunodepression occurs with a corresponding reduction in spleen size, while robust inflammation appears in the injured brain. We used a focal ischemic rat model to investigate the protective effects of moderate hypothermia (30^{o}C), a robust inhibitor of ischemic infarction, on the inflammatory response in the brain and peripheral immune suppression. **Methods:** Focal ischemia in the cerebral cortex was induced by permanent occlusion of the left distal MCA and 60 min occlusion of the bilateral CCA under intra-ischemic normothermia (37^{o}C) and moderate hypothermia (30^{o}C) in SD rats. We used quantitative RT-PCR to quantify mRNA expression levels of various cytokines and chemokines in the brain, spleen, liver, and lung at 5, 24, 72h after stoke, and flow cytometry to characterize lymphocyte subpopulations and macrophages at 72h after stroke. We then detected the proliferative response of splenocytes in vitro with a [^{3}H] thymidine incorporation assay. At last, subcutaneous injection of Ovalbumin (OVA) was used to measure a delayed-type hypersensitivity (DTH) reaction in the ears, which represents immune function in vivo. **Results:** In the ischemic brain, stroke increased genes expression of IL-1β, TNF-α, IL-2, INF-γ, IL-10, MIP-2, iNOS ($P<0.05$), and tended to increase IL-4 and COX-2. Hypothermia inhibited expression of the former group, but had no significant effects on the latter two genes. No significant changes in gene expression were seen in the spleen, liver and lung, except for IL-4 in the spleen, which significantly decreased 72h after stroke, and

TNF-α in the lung, which increased 24h after stroke. Hypothermia had no effect on these changes. Total PBMCs and splenocytes numbers were reduced ($P<0.05$) by stroke, but this reduction was attenuated by hypothermia; no changes occurred in the lung. In the blood, the absolute number of B cells, $CD4^+$ and $CD8^+$ T cells, Treg cells, and macrophages decreased after stroke, and hypothermia attenuated this effect. Similar effects of stroke and hypothermia were observed in the spleen after stroke, but not in the lung. In addition, stroke inhibited splenocytes proliferation in vitro, which was reversed by hypothermia. Finally, the DTH reaction was inhibited by normothermic stroke and hypothermia attenuated the inhibition. **Conclusions:** Stroke caused acute significant changes in many cytokines and chemokines gene expression in the brain, and also resulted in peripheral immunodepression. We found that hypothermia both protected against acute inflammation in the ischemic brain and attenuated peripheral immune depression. **Key Words:** focal cerebral ischemia, normothermia, hypothermia, inflammation, immunodepression, delayed-type hypersensitivity

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Th P165

Gender Differences In Brain Atrophy And Neurological Deficits After Intracerebral Hemorrhage

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Purpose: Intracerebral hemorrhage (ICH) results in brain edema, brain tissue loss and neurological deficits in rats. Our previous studies have found that ICH-induced brain edema is less in female rats compared with that in male rats, and that estrogen can reduce perihematomal brain edema in male rats. This study examined whether brain atrophy and long-term neurological deficits are reduced in female rats after ICH. **Methods:** Male and female Sprague-Dawley rats received 100-μl autogolous blood injection into the right caudate. Behavioural tests, including forelimb placing test, forelimb use asymmetry test and corner turn test, were carried out at days 1, 3, 7, 14, 21 and 28. Serial magnetic resonance imaging (MRI) was performed at day 28 after ICH. T2-weighted imaging and T2* gradient-echo imaging (GRE) were used to measure brain atrophy and iron accumulation. Rats were killed at day 28 and the brains were used for histological examination. **Results:** We found that there were no differences in physiological parameters between male and female rats. All three behavioural tests showed that female rats had less ICH-induced neurological deficits ($p<0.05$) than males. Hematoxylin and eosin staining was used to assess caudate atrophy ([ipsilateral-contralateral]/contralateral caudate x100). There was less caudate tissue loss in females (15.9 $\pm$ 8.3% vs. 25.1 $\pm$ 4.1% in males, $P<0.05$) at day 28 after ICH. T2 imaging showed that female rats had less ipsilateral ventricle enlargement (3.4$\pm$ 2.0 mm3 vs. 5.6 $\pm$ 1.7 mm3 in males, $P<0.05$). In addition, T2* demarcated lesions were smaller in females (15.9 $\pm$ 5.2 mm3 vs. 28.3 $\pm$7.4 mm3 in males, $P<0.01$). **Conclusions:** Female rats have less iron accumulation, neurological deficits and brain atrophy after ICH.

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Th P166

Should Statins Be Avoided After Intracerebral Hemorrhage?

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Background: Statins are widely prescribed for primary and secondary prevention of ischemic cardiac and cerebrovascular disease. Although serious adverse effects are uncommon, results from a recent clinical trial suggested increased risk of intracerebral hemorrhage (ICH) associated with statin use. For patients with baseline elevated risk of ICH, it is not known whether this potential adverse effect offsets the cardiovascular and cerebrovascular benefits. **Methods:** We used Markov decision modeling to address the following clinical question: Given a history of prior ICH, should statin therapy be avoided? We investigated how a range of clinical parameters affects this decision, including hemorrhage location (deep vs lobar), ischemic cardiac and cerebrovascular risks, and magnitude of ICH risk associated with statins. Findings: Avoiding statins was favored over a wide range of values for many clinical parameters, particularly in survivors of lobar ICH who are at highest risk of ICH recurrence. In survivors of lobar ICH without prior cardiovascular events, avoiding statins yielded a life expectancy gain of 2.2 quality-adjusted life years compared with statin use. This net benefit persisted even at the lower 95% confidence interval of the relative risk of statin-associated ICH. In lobar ICH patients with prior cardiovascular events, the annual recurrence risk of myocardial infarction would have to exceed 90% to favor statin therapy. Avoiding statin therapy was also favored, although by a smaller margin, in both primary and secondary prevention settings for survivors of deep ICH. Interpretation: Avoiding statins should be considered for patients with a history of ICH, particularly those of lobar location.

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Th P167

Influence Of Statin Pre-treatment On Mortality In Intracerebral Hemorrhage: A Meta-analysis.

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Introduction: The effect of the statin pre-treatment (SP) on the outcome of patients with intracerebral hemorrhage (ICH) is inconsistent across published studies. We evaluated whether an association exists between prior treatment with statins and mortality. Moreover, we included our results in a meta-analysis with other reported studies. METHODS We prospectively studied consecutive patients with spontaneous supratentorial ICH within the first 24 hours after stroke onset. As prognostic predictors we analyzed age, volume of the hemorrhage, Glasgow coma scale (GCS) score, and current treatment with any statin. We performed bivariate analyses and a logistic regression analysis, the dependent variable being death at 3-months follow-up. We also performed a meta-analysis by adding our results to five previously published studies providing data on SP and mortality after ICH. RESULTS We studied 109 patients, with a mean age of 74.6$\pm$10.6 years, 51% of them were men. Mortality at 3 months was 30%, and 21% were currently receiving statins at the time of stroke. In bivariate analysis, increasing age ($p<0.0001$), higher hematoma volume ($p=0.001$) and lower GCS ($p<0.0001$) were associated with increased mortality. Mortality was non-significantly increased in the SP group compared to the non-SP group (43.5% vs 27%, $p=0.13$). Independent predictors of mortality in the logistic regression analysis were: Age (OR 1.099 per year, $p=0.023$), Volume (OR 1.022 per ml, $p=0.015$) and GCS (OR 0.694 per point, $P<0.0001$). Prior treatment with statins was not an independent risk factor for death (OR 2.11, 95%CI 0.81-5.46, $p=0.32$). The meta-analysis of 5 studies included 1843 patients, 428 of them (23%) were pre-treated with statins. Mortality at 3 months (1 study reported death at 1 month and was also included) was 37% in the SP group and 40.5% in the non-SP group (OR 0.84, 95%CI 0.67-1.06, $p=0.13$). **Conclusions:** In conclusion, prior treatment with statins was not associated with mortality neither in our study nor in a meta-analysis of reported studies.

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Th P168

Nationwide Survey of Expert Opinions about Resuming Anticoagulant Therapy After Intracerebral Hemorrhage for Patients with Nonvalvular Atrial Fibrillation

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Background and Purpose: Warfarin-related intrecerebral hemorrhage (ICH) in patients with atrial fibrillation (AF) is associated with high incidence of subsequential hematoma enlargement and high mortality. Conversely, withholding of warfarin has a potential risk to develop thromboembolic complications such as embolic stroke. There is a considerable dilemma concerning when to resume anticoagulant therapy following ICH, because there is no established guideline for appropriate antithrombotic therapy in acute ICH patients with AF. We conducted a nationwide survey regarding resumption of anticoagulant therapy in patients with acute ICH on warfarin with nonvalvular AF. [Methods] A questionnaire on standard therapeutic strategy for warfarin-related ICH in patients with nonvalvular AF was mailed to physicians responsible for ICH management at 416 hospitals in October 2009. [Results] Of those mailed, 329 physicians (79%) responded with a filled-in questionnaire. On admission, all respondents stopped oral warfarin intake and 94% of them normalized prothrombin time (PT-INR) mainly by Vitamin K (63%), followed by fresh frozen plasma (20%), and prothrombin complex concentrations (10%). Regarding the further prevention of thromboembolism, 91% resumed anticoagulant, 3% used antiplatelets instead of warfarin, and 6% disagreed with resuming any antithrombotic therapy. Of those who agreed to resume anticoagulation, the timing was within 4 days in 7%, 5 to 7 days in 21%, 8 to 14 days in 25%, 15 to 28 days in 28% and 29 days or later in 18%. The key findings on follow-up CT to restart anticoagulation were absorption tendency of hematoma in 47%, followed by discontinuation of hematoma growth in 28%, and complete absorption of hematoma in 17%. To resume anticoagulation, warfarin alone was used in 76% and unfractionated heparin alone or combined with warfarin in 20%. Major contraindications for resuming anticoagulation were recurrent ICH and poor functional status corresponding to the modified Rankin Scale score of 4 or 5 (170 respondents, 59.4% for each), followed by dementia or frequent falls (139, 48.6%), suspected cerebral amyloid angiopathy (107, 37.4%), multiple brain microbleeds on T2*-weighted MRI (85, 29.7%), advanced age (80 years old, 71, 24.8%), and so on. **Conclusions:** For acute ICH patients with nonvalvular AF, a large majority of Japanese physicians stopped oral warfarin intake and normalized PT-INR on admission, but resumed anticoagulation several days to months later. However the strategies to normalize PT-INR and to resume anticoagulant therapy enormously varied and depended on physicians decisions.

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Th P169

Tamoxifen Treatment For Intracerebral Hemorrhage

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Introduction: Tamoxifen is a selective estrogen receptor modulator. In this study we investigated whether or not tamoxifen reduces intracerebral hemorrhage (ICH)-induced brain injury in rats. **Methods:** In all experiments, adult male Sprague-Dawley rats received an injection of 100 μl autologous whole blood into the right basal ganglia. In the first set of experiments, rats were treated with tamoxifen (2.5 mg/kg or 5 mg/kg, i.p.) or vehicle 2 and 24 hours after ICH and were killed at day 3 for brain edema measurement. In the second set of experiments, rats were treated with tamoxifen (5 mg/kg) or vehicle and magnetic resonance imaging (MRI) and behavior tests were performed at days 1, 7, 14 and 28. Rats were killed at day 28 for brain histology. **Results:** ICH causes brain edema in rats. Tamoxifen treatment at the dose 5 mg/kg significantly reduced brain water content (82.2 $\pm$ 0.7% vs. 83.4 $\pm$ 1.1% in vehicle treated group, p0.05). Brain histology showed that tamoxifen reduces caudate atrophy at day 28. The brain tissue loss in ipsilateral caudate at day 28 was significantly less in tamoxifen-treated rats (21.9 $\pm$ 4.3% vs. 30.3 $\pm$ 1.8% in vehicle-treated group, $P<0.05$). Tamoxifen also improved functional outcome ($p<0.05$). MRI demonstrated a tendency of smaller T2* lesions in tamoxifen-treated rats (28.5 $\pm$ 4.7 vs. 34.3 $\pm$ 6.1 mm3 in the vehicle-treated group, $p=0.14$). However, 2 out of 5 rats treated with tamoxifen developed hydrocephalus. **Conclusions:** These results suggest that tamoxifen has neuroprotective effects in ICH, but the cause of hydrocephalus development following tamoxifen treatment needs to be examined further.

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Th P170

Prior Antiplatelet Use is Associated With Hematoma Growth in Patients With Spontaneous Intracerebral Hemorrhage

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Objective: Patients presenting with intracerebral hemorrhage (ICH) often report use of antiplatelet medications, even more common than anticoagulants. Recent studies have yielded conflicting results regarding the effects of antiplatelet usage on ICH course. In this study, our aim was to determine the effect of prior antiplatelet medication use on admission hematoma volume and hematoma growth in patients with spontaneous ICH. **Methods:** A consecutive series of patients with cranial computed tomography (CT) within 12 hours of symptom onset and a follow-up imaging within 72 hours were included into the study. Patients using anticoagulants at the time of stroke onset were excluded. Hematoma volume on admission and follow-up CT images were calculated by using the ABC/2 method. In addition to hematoma volume, clinical (age, gender, stroke risk factors, admission stroke severity, admission blood pressure, admission glucose level, antiplatelet usage) and imaging (time of imaging, hematoma location, intraventricular hemorrhage) data were collected in all patients. Univariate and multivariate analyses were performed to determine variables associated with admission hematoma volume and hematoma growth. **Results:** A total of 153 patients (59 female, 94 male) were included into the study. The mean ($\pm$standard deviation) age of the study population was 66$\pm$12 years. Fifty-two (34%) patients were on antiplatelet medication. The median (interquartile range) admission hematoma volume was 23.7 (9.3-71.3) mL. Overall, 64.1% of the patients exhibited some degree of hematoma growth and 27.2% of the patients had significant hematoma growth (defined as an increase of $\geq$33% or 12.5 mL expansion from baseline). Patients on antiplatelet medications tended to have larger admission hematoma volumes [35.0 (11.5-82.3) mL vs. 20.8 (8.0-64.3) mL; $p=0.17$]. Anti-platelet usage was associated with significant hematoma growth in both univariate ($p=0.008$) and multivariate ($p=0.029$) analyses. **Conclusion:** Antiplatelet medication usage at the time of stroke is an independent predictor of hematoma growth. These findings, together with reports on prior literature, suggest a promising role for therapies aiming restoration of thrombocyte function in preventing hematoma expansion during the acute stages of ICH.

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Th P171

The Rate of Contrast Extravasation in Patients with Intracerebral Hemorrhage

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Objective: CT perfusion (CTP)-derived permeability surface area product (PS) is a novel method of measuring the rate of contrast extravasation from the intra- to extravascular compartment. Knowing the rate of contrast extravasation may provide insight into the pathophysiology of hematoma expansion by identifying the target abnormality most likely to contribute to hematoma growth. This study assessed whether CTP derived permeability (PS) measures can distinguish between different rates of contrast extravasation for patients with and without CTA Spot Sign or post contrast CT contrast leakage (PCL). **Methods:** We report CT perfusion (CTP)-derived blood brain barrier (BBB) permeability findings of 16 consecutively screened ICH patients with and without confirmed contrast extravasation within 3 hours of symptom onset. CTP-derived parametric maps of permeability surface area product (PS) were analyzed using custom software (IDL v6.1,RSI Inc, Boulder, Colo. USA). Three regions of interest were placed on perfusion weighted average images: 1) Extravasation positive regions (CT angiographic Spot Sign and post contrast leakage (PCL)), 2) mirrored contralateral hematoma volumes and 3) background hematoma remote from ROI 1. Baseline and follow up hemorrhage volumes were measured. **Results:** Mean PS was 3.8 $\pm$ 2.9 ml-1x min-1x(100g)-1, 0.12 $\pm$ 0.39 ml(min-1)(100g-1) and 0.10 $\pm$ 0.26 ml(min-1)(100g-1), in the extravasation positive, background hematoma and contralateral mirror regions respectively ($p < 0.05$ each). Within the extravasation positive group, mean PS of CTA Spot sign and PCL was 6.5 $\pm$ 1.6 ml(min-1)(100g-1) and 0.95 $\pm$ 0.39 ml(min-1)(100g-1) respectively ($p < 0.05$). Mean hematoma volume increased from 34.1 $\pm$ 41.0 ml to 40.2 $\pm$ 46.1 ml in extravasation positive patients and decreased from 19.8 $\pm$ 31.8 ml to 17.4 $\pm$ 27.3 ml in the absence of extravasation ($p < 0.05$). **Conclusion:** A clinical technique that quantifies the rate of extravasation provides objective assessment of hematoma expansion risk rather than the qualitative approach currently used. Such information may become increasingly important as novel ICH treatments are developed that will target specific lesions. We report a gradation of PS values in CTA and post contrast CT detected lesions and patients without extravasation.

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Th P172

Contrast Extravasation is a More Sensitive Predictor of Intraparenchymal Hemorrhage Growth than Spot Sign

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Background and Objective: Intraparenchymal hemorrhage (IPH) growth is associated with poor outcome. Our objective was to describe the prevalence of a spot sign(SpS), contrast extravasation (CEx) and IPH growth in patients presenting to hospital at various times after symptom onset and to evaluate the performance of SpS and CEx in predicting IPH growth.Methods: We abstracted demographics, clinical data and radiological findings of 284 IPH patients admitted to a tertiary hospital from 2005 to 2008 who had CT angiography (CTA) and follow-up imaging (closest to 24 hours after first scan). We calculated IPH volumes from first and follow up scans using the ABC/2 method; SpS from CTA source images; and CEx from post-contrast images. The proportion of patients with SpS or CEx, and those showing significant IPH growth (>30% or >6cc) are presented for 5 time epochs based on the interval between symptom onset and 1st CT scan (0-6, 6-12, 12-24, >24 hrs and unknown). **Results:** Mean age was 64 years (SD 15), 44% were females, and 72% had hypertension. Mean GCS = 9.8 (SD 4.6) and CT IPH volume = 34cc (SD 35) at presentation. Median time (interquartile range) from onset to first CT = 6.5 hrs (3.2-23), between CT and CTA = 2.9 hrs (0-5.3), and between first and follow-up CT = 12 hrs (5.3-19). Of the 284 patients, 9% had SpS, 23% had CEx and IPH growth was present in 29%. Almost half of the 284 patients (46%) had their first CT from 0-6 hrs from onset, 21% 6-12 hrs, 9% 12-24 hrs, 18% >24 hrs and 6% an unknown time of onset. Ignoring the unknown times, significant decreases over the 4 known time epochs were observed for SpS (13%, 8%, 0%, 2%, $P=0.006$), CEx (36%, 15%, 4%, 6%, $P<0.001$) and IPH growth (39%, 20%, 12%, 18%, $P=0.001$). For unknown time cases, SpS=11%, CEx=22% and IPH growth=33%. IPH growth was significantly associated with SpS (RR 2.3, 95% CI 1.6-3.4) and CEx (RR 2.9, 2.1-4.0). SpS sensitivity for detecting IPH growth was 19% (95% CI 11-29), specificity=95% (91-98) and area under the ROC curve (C) = .57; for CEx sensitivity=46% (35-57), specificity=87% (81-91) and C=.66 (C for CEx > C for SpS, P=.0005). **Conclusions:** Consistent with the literature, SpS, CEx and IPH growth are more common in patients seen earlier after symptom onset. Confirming results of smaller studies, CEx is a more sensitive screening tool than SpS for identifying patients who go on to have IPH growth. All CTA protocols should include post-contrast CT, and CEx should be used for clinical decision making once an effective treatment becomes available. Many IPH patients present without known timing of symptom onset and still have significant rates of CEx and IPH growth. IPH trials focused on reducing IPH growth may benefit from greater patient eligibility and statistical power if inclusion criteria focus on presence of CEx rather than time since onset.

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Th P173

Validation Of A Computerized Planimetric Tool For Quantifying Intraventricular Hemorrhage Volumes.

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Background: Intracerebral hemorrhage (ICH) volume and intraventricular hemorrhage (IVH) extension are independent predictors of outcome following hemorrhagic stroke. Early ventricular rupture and subsequent auto-decompression of parenchymal hematoma is common in ICH. Ventricular decompression decreases ICH volumes, but also results in IVH expansion and increased IVH volume, both of which are associated with poor outcome. Given volume and expansion are common surrogate outcomes for ICH studies, easy and accurate measurement of IVH and volume dynamics following ventricular rupture is relevant to hemostatic trials.

Objective: To develop and validate a computer-assisted planimetric tool to reliably quantify IVH volumes. **Methods:** Quantomo was developed for use in the multi-centre PREDICT study using 3D threshold-based region growing segmentation, but has only been validated for parenchymal hematoma analysis. CT scans containing both ICH and IVH were selected from the PREDICT study. Five raters (2 neurologists, 1 radiologist, 1 neuroradiologist, and 1 radiology trainee) measured IVH volumes, total (ICH+IVH) volumes, and Graeb scores from 20 randomly selected CT scans twice, presented in a blinded, random fashion over 2 reading sessions, separated by a minimum of 7 days. Estimates of inter-rater and intra-rater reliability were calculated using a two way random-effects ANOVA, and expressed as an intra-rater correlation coefficient (ICC). The minimum detectable difference (MDD) was also determined. **Results:** Median total hematoma volume was 43.8ml (inter-quartile range 50.8). Quantomo IVH volume analysis had excellent intra- and inter-rater agreement for (ICC 0.96 and 0.92, respectively), which was superior to the Graeb score (ICC 0.88 and 0.83 respectively). MDDs for intra- and inter-rater volumes were 12.1ml and 17.3ml respectively, and were dependent on the total size of the hematoma: hematomas smaller than the median 43.8ml had lower MDDs (7.7ml and 10ml), whereas those larger than the median had higher MDDs (15.3ml and 22.3ml). Larger hematomas had more distortion of anatomical landmarks. **Conclusion:** We developed a computer-assisted technique that reliably quantified IVH volumes, and we present its ICC and MDD estimates.

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Th P174

Prospective Validation of the IVH Score as a Useful Bedside Tool for Estimating Intraventricular Hemorrhage Volume

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Background and Purpose: Intraventricular extension of intracerebral hemorrhage (IVH) is a critical disease severity factor and an independent predictor of poor outcome. Surgical Trial in ICH (STICH) and NovoSeven trial have recently underscored the impact of IVH volume and its alteration on recovery and survival after ICH. Routine measurement of IVH volume, however, has been impeded by difficult characterization of clots and requirement for time consuming computer-based planimetric analysis. The IVH Score (IVHS) was developed by Hallevi et al (2009) to assess severity of IVH and to rapidly estimate IVH volume at bedside. The aim of this study was to prospectively evaluate the external validity of the IVHS as a useful tool for assessing IVH volume in the setting of ICH. **Methods:** Spontaneous ICH patients with IVH on admission computed tomography (CT) scan were prospectively enrolled into the study between February 2009 and May 2010. All CT scans performed within 6 days of onset were evaluated for IVHS according to the methods described by Hallevi et al (1). IVH volumes were estimated based on IVHS and compared to IVH volumes measured with computer-assisted planimetric analysis. **Results:** A total of 126 CT scans were performed on 51 patients during the study period. The mean estimated IVH volume was not significantly different from the mean measured IVH volume (15.45 $\pm$ 18.57 ml versus 14.88 $\pm$ 15.55 ml, respectively; $p = 0.499$). Regression analysis revealed a strong exponential relationship between IVHS and measured volumes ($R2 = 0.795$, $p < 0.001$) and a strong linear relationship between estimated and measured IVH volumes ($R2 = 0.743$, $p < 0.001$). Furthermore, they were comparable to those reported by Hallevi ($R2 = 0.75$, $P<0.001$ and $R2 = 0.8$, $P<0.001$, respectively). **Conclusions:** To our knowledge, this is the first study to validate the performance of the IVHS as a tool for rapid approximation of IVH volume in the setting of spontaneous ICH. The strengths of association between IVH scores and estimated volumes, and between estimated and measured volumes are similar to those of Hallevi et al, suggesting that the IVHS can be used with reasonable reliability among different centers. (1) Hallevi H, Dar NS, Barreto AD, Morales MM, Martin-Schild S, Abraham AT, Walker KC, Gonzales NR, Illoh K, Grotta JC, Savitz SI. The IVH score: a novel tool for estimating intraventricular hemorrhage volume: Clinical and research implications. Crit Care Med. 2009; 37: 969-e1.

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Th P175

Perihematoma Cerebral Perfusion Pressure is Maintained in Acute Intracerebral Hemorrhage: a CT Perfusion Study

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Background: Although global cerebral perfusion pressure (CPP) can be estimated by the difference between mean arterial pressure (MAP) and intracranial pressure, local CPP is more predictive of regional tissue fate. Hypothetical decreases in CPP in the perihematoma region have been cited as a rationale for a conservative approach to acute blood pressure (BP) control as aggressive antihypertensive use may further reduce CPP resulting in ischemia in this region. Local CPP has been shown to be proportional to the ratio of cerebral blood flow (CBF) to cerebral blood volume (CBV). We assessed local CPP in acute intracerebral hemorrhage (ICH) patients, using CT perfusion (CTP) source data. Given that cerebral blood flow decreases in the perihematomal region, we hypothesized that cerebral perfusion pressure would concomitantly decrease. **Methods:** CTP imaging was performed in acute ICH patients. All patients were acutely hypertensive and systolic blood pressure was treated to a target of mmHg or mmHg prior to the CTP scan. Maps of CBF and CBV were generated using a singular value deconvolution algorithm. In addition, maps of CPP were calculated as CBF/CBV. Region of interest analysis was completed in a 1 cm perihematoma region, contralateral homologous regions and both hemispheres. **Results:** 22 patients were imaged with a median time from onset to CTP of 15.2 (IQR 8.6-21.8) hrs. The mean ($\pm$SD) hematoma volume was 16.8$\pm$20.2 mls. The mean systolic and diastolic BP at the time of the CTP scan were 155$\pm$14 and 80$\pm$13 mmHg respectively. Perihematoma CBF (31.5$\pm$5.5 ml/100g/min) was lower than that in contralateral regions (34.1$\pm$6.1 ml/100g/min, $P<0.001$). Similarly, there was a reduction in perihematoma CBV (2.83$\pm$0.56 ml/100g) compared to contralateral regions (3.08$\pm$0.55 ml/100g, $P<0.001$). Perihematoma CPP (13.9$\pm$2.3 min^{-1}) was not significantly different than that in the contralateral homologous regions (13.8$\pm$2.5 min^{-1}; $p=0.73$). Ipsilateral hemispheric CPP (14.0$\pm$2.6 min^{-1}) was also comparable to the contralateral hemispheric CPP (13.8$\pm$2.1 min^{-1}, $p=0.28$). There was no relationship between perihematoma CPP and hematoma volume ($r=0.02$, [-0.70,0.10]) or BP at the time of the CTP scan (systolic BP, $r=0.02$, [-0.06,0.10]; diastolic BP, $r=0.03$, [-0.05,0.11]); or MAP, $r=0.03$, [-0.06,0.13]). In addition, treatment of blood pressure did not appear to affect CPP as perihematoma CPP was not related to changes in systolic ($r=-0.01$, [-0.07,0.05]), diastolic ($r=0.04$, [-0.03,0.12]) or mean arterial pressure ($r=0.03$, [-0.06,0.11]) between initial presentation and the time of the CTP scan. **Conclusions:** Perfusion pressure of tissue surrounding the hematoma is maintained in acute ICH patients. Hematoma volume and blood pressure management do not affect perihematoma CPP. These results provide further support for the safety of early blood pressure treatment in ICH.

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Th P176

Characteristics Of Non-traumatic Intracerebral Hemorrhages In Relation To Their Cause.

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Introduction and hypothesis: Currently it is unclear which patients with an intracerebral hemorrhage (ICH) may benefit from intracranial vascular imaging. We hypothesized that characteristics of the appearance of the ICH on non contrast CT (NCCT) may help in discriminating between patients with and without a identifiable vascular malformation. **Methods:** We selected patients with primary ICH (PICH, ICH without a macroscopic vascular lesion detected, n=30) and secondary ICH (SICH) caused by rupture of an AVM (n=25) or an aneurysm (n=30). ICH location and relation to the ventricles, subarachnoid space, subdural space, frontal operculum, Sylvian fissure or interhemispheric fissure were assessed, as were features of the ICH itself: volume, shape, density, regularity of the border, and presence of mass effect and edema. Each admission NCCT was assessed independently by two observers who were blinded for demographics and underlying etiology. Subsequently they were asked to list the most likely cause of the ICH. We investigated differences in characteristics between SICH and PICH by calculating relative risks (RR) with 95% confidence intervals (CI). **Results:** A deep location was not observed in aneurysmal ICH and less frequent in AVM ICH (24%) than in primary ICH (60%;RR 0.4, 95% CI 0.2-0.8). Extension to the Sylvian fissure was observed more often in secondary ICH than in PICH (RR 3.8, 95% CI 1.7-8.5). Extension to the frontal operculum was exclusively seen in SICH (67% of aneurysmal ICH and 16% of AVM ICH). No differences in shape (RR 1.0, 95% CU 0.95-1.02), density (RR 1.2 (95% CI 0.7-1.8), regularity of the border (RR 1.0, 95% CI 0.7-1.5) and presence of edema (RR 1.1, 95% CI 0.9-1.5) were found between SICH and PICH. The majority of aneurysmal ICH (97%) and PICH (93%) was diagnosed correctly on NCCT, whereas sixteen AVM-ICH were not identified (64%). **Conclusions:** SICH and PICH do not differ regarding hematoma characteristics, but do differ in location and extension of the hematoma. AVM as underlying cause of the hematoma goes often undetected on NCCT.

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Th P177

Impact of Interhospital Transfer on Complications and Outcome after Intracranial Hemorrhage

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Introduction: Interhospital transfer of patients with intracranial hemorrhage to tertiary centers can offer improved care, but comes at the cost of potential morbidity and mortality related to transfer. Prolonged time of transfer may further worsen outcome. In this study, we assess the effect of transfer and transfer time on admission clinical status, hospital complications, length of stay (LOS) and 3-month neurological outcome. **Methods:** A prospective study was conducted between 2/2008-6/2010 of patients with subarachnoid hemorrhage (SAH), intracerebral hemorrhage (ICH) and subdural hemorrhage (SDH), admitted to the neuro-ICU at a tertiary-care academic hospital. Demographic data, clinical history, ICU admission clinical status (assessed by NIHSS, GCS and APACHE-2), transfer hospital distance, time to transfer, medical complications and LOS were recorded. Functional outcome was assessed at 3-months using the Barthel Index, Modified Rankin Scale (mRS), Lawton Instrumental Activities of Daily Living Scale and the Telephone Interview of Cognitive Status (TICS). **Results:** Of 257 total patients, 120 (47%) were transferred and 137 (53%) were admitted directly from our ED. Eighty-six (34%) had SAH, 80 (31%) had ICH and 91 (35%) had SDH. The median age was 62 (22-94), 37% were white, 38% employed and 86% insured. The median transfer hospital distance was 7.4 miles (1.4-159). The median transfer time was 190 minutes (46-1,446). Initiation of transfer during business hours predicted a shorter time to bed assignment ($P=0.048$), but hospital distance and weekend/holiday transfers did not impact transfer time. Transferred

patients were significantly less educated, less likely to be insured, and more frequently had SAH as a diagnosis than directly admitted patients (all P<0.05). Admission GCS, NIHSS and APACHE-2 scores did not differ between transfers and direct admits and were not significantly related to transfer time. Complications did not differ between transferred and directly admitted patients, however, longer transfer time was associated with aneurysm rebleed (OR 1.0, 95%CI 1.0-1.1, P=0.030), hydrocephalus requiring drainage (OR 1.0, 95%CI 1.0-1.1, P=0.041), tracheostomy (OR 1.0, 95%CI 1.0-1.1, P=0.039) and peg placement (OR 1.0, 95%CI 1.0-1.1, P=0.004). Overall, transferred patients had worse cognitive outcome at 3 months (OR 4.1, 95% CI 1.2-14.0, P=0.025) and longer ICU LOS (8 versus 5 days; P=0.003) compared to direct admits. Longer transfer time was not associated with neurological outcome or LOS. **Conclusions:** Despite similar admission clinical status, transferred patients had worse 3-month cognitive outcomes and longer ICU LOS compared to directly admitted patients. Prolonged time to interhospital transfer was associated with a small, but significant risk of aneurysm rebleed, hydrocephalus requiring treatment, tracheostomy and peg placement.

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Th P178

DVT Prophylaxis after ICH in China: Results from China National Stroke Registry (CNSR)

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Background and Purpose: Non-ambulatory patients with acute intracerebral hemorrhage (ICH) are at high risk of developing deep venous thrombosis (DVT). DVT prophylaxis in these patients is a core measure for the Joint Commission (TJC) certified Primary Stroke Centers in the U.S.. Little is known about DVT prophylaxis after ICH in China. We sought to assess the use of DVT prophylaxis after ICH in Chinese urban hospitals, and to explore the potential reasons associated with non-compliance with this measure. **Methods:** China National Stroke Registry (CNSR) was nationwide stroke registry funded by the Chinese government that included a representative sample of 132 urban hospitals across China. From June 1, 2007, through May 31, 2008, we abstracted data from CNSR prospectively to determine DVT prophylaxis status in consecutive ICH patients, including any reasons for non-compliance with DVT prophylaxis. Compliance was defined as pharmacological prophylaxis such as unfractioned heparin, low molecular weight heparin and heparin analog, or physical prophylaxis such as intermittent pneumatic compression, compression stockings and early mobilization. The reasons for failing to perform DVT Prophylaxis consisted of contraindication for anticoagulation, contraindication for intermittent pneumatic compression and patient or relative refusal. **Results:** A total of 5136 patients with a diagnosis of ICH were included, of which 39.3% were female. The average age was 65.0 $\pm$ 12.6 years. Among these, 3655 (71.2%) were non-ambulatory, of whom 685 (18.7%) received DVT prophylaxis, including 7(1.0%) with unfractioned heparin, 7(1.0%) with low molecular weight heparin, 1(0.1%) with heparin analog, 86 (12.4%) with intermittent pneumatic compression, 21 (3.1%) with compression stockings, 540 (78.8%) with early mobilization. Among the 2651(72.5%) who were not placed on DVT prophylaxis, the vast majority (n=2556, 96.4%) was due to physicians' opinion that ICH was a contraindication for anticoagulation or concerns of hemorrhage extension and extracranial hemorrhage after anticoagulation. Only 21 (0.8%) patients had documented real contraindication for anticoagulation. Other reasons for non-use of DVT prophylaxis included patient or relative refusal (n=13, 0.5%), and contraindication for intermittent pneumatic compression (n=61, 2.3%). **Conclusions:** In China, the proportion of patients with ICH receiving DVT prophylaxis was extremely low, especially pharmacological prophylaxis. Concern of hemorrhage extension after anticoagulation by physicians and failing to adherence to the guidelines in China for the management of ICH was main reason of non-use of DVT prophylaxis. Further studies are needed to elucidate specific barriers to DVT prophylaxis and to develop targeted quality improvement strategies that may target physicians as well as Chinese healthcare system.

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Th P179

Cerebral Microbleeds in Patients With Infective Endocarditis are Associated With Impending Intracerebral Hemorrhage

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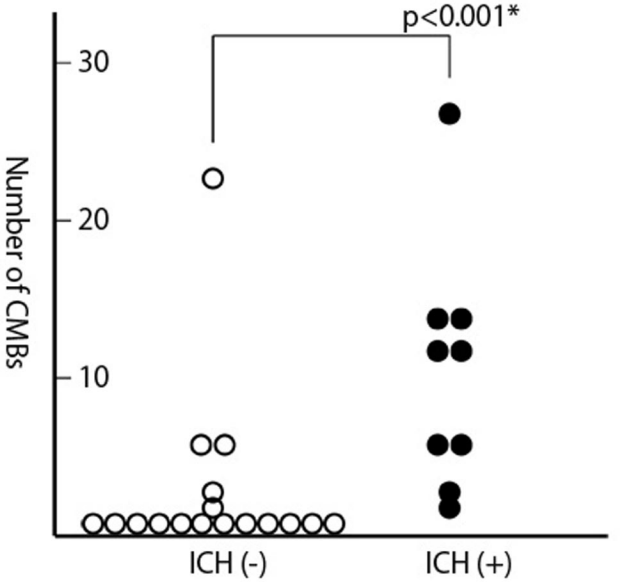
Background: Cerebral microbleeds (CMBs) detected by T2*-weighted MRI have been described as an indicator of hypertension, hemorrhagic stroke, and small vessel diseases. The association between infective endocarditis and CMBs has been reported recently, but the clinical significance of CMBs in patients with infective endocarditis has not been clarified. **Methods:** Among 53 patients with definite infective endocarditis admitted to two medical centers in Osaka, Japan, between January 2006 and June 2010, 26 consecutive patients who underwent brain MRI including T2*-weighted sequences were enrolled. We hypothesized that CMBs in patients with infective endocarditis would associate with vascular vulnerability such as mycotic aneurysm or infectious angitis. We therefore examined incidence of intracerebral hemorrhage (ICH) after the MRI examination and investigated the association between ICH and CMBs or other clinical characteristics. **Results:** ICH was observed in 9 patients (35%) within 30 days after the MRI examination. CMBs were identified in 14 patients (54%) and 66% of CMBs existed in cortical region. There were more CMBs observed in patients who developed ICH than those without ICH (p<0.001) (Figure). In univariate analyses, the presence of preceding ICH (odds ratio, 9.4; 95% confidence interval, 1.3-67.6) and the number of CMBs $\geq$3 (16.3; 2.2-121.4) were significantly associated with the incidence of ICH. In multivariate logistic regression model, adjusted odds ratio of CMBs per unit was 1.15 (1.01-1.40; p=0.035). **Conclusions:** In addition to preceding ICH, the presence of CMBs was a strong predictor of impending intracerebral hemorrhage in patients with infective endocarditis. CMBs might represent vascular vulnerability attributed to infective endocarditis.



Number of cerebral microbleeds in infective endocarditis patients with and without the development of intracerebral hemorrhage. * Mann-Whitney U test.

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Th P180

Glomerular Filtration Rate Is Not Associated With Hematoma Volume Or In-Hospital Mortality In Spontaneous Intracerebral Hemorrhage

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Objective: To determine if intracerebral hemorrhage (ICH) patients with kidney dysfunction (as evidenced by low glomerular filtration rate, GFR) have increased hematoma volume or in-hospital mortality compared to those with normal kidney function. **Introduction:** There is growing interest in the association between abnormal kidney function and spontaneous ICH. Patients with low GFR are known to have endothelial and platelet dysfunction. Those with low GFR are at greater risk for hemorrhagic than ischemic stroke and experience worse long-term outcomes following stroke. It is unclear if patients with a low GFR have larger volume hemorrhages or worse short-term outcome than those with normal kidney function. Design/ Methods: We retrospectively reviewed the charts of 617 consecutive patients diagnosed with spontaneous ICH at our institution between 2006 and 2010. We collected data on patient demographics, admission creatinine, size and location of bleed, and disposition at discharge. Patients with end-stage renal disease (ESRD) and acute kidney injury (defined as rise in creatinine of 0.3 over baseline) were excluded from our analysis. GFR was calculated using the MDRD equation, and patients were divided into two groups based on GFR ($\geq$ 60 vs. $<$ 60). **Results:** Of 617 patients, 143 with acute kidney injury or ESRD were excluded, leaving 474 patients for analysis (mean age 61 years; 51% female; 55% black; mean GFR 74.3; 24.3% had GFR $<$ 60). The median volume of hemorrhage was 11.4 (IQR 3.4-35.0) mL. Two hundred and twenty eight (48.1%) hemorrhages were in the basal ganglia; 71 (15.0%) were infratentorial; and 175 (36.7%) were lobar. There was no correlation between admission GFR and volume of hemorrhage (r_s = 0.016, p = 0.737), irrespective of hemorrhage location and those with GFR $<$ 60 vs. $\geq$ 60 had similar ICH volumes (p = 0.825). Mean GFR was similar in those with survived or died (74.3 vs. 74.3, p = 0.981) and there was no significant association between GFR and discharge disposition. **Conclusions:** Although some studies have suggested that low GFR is associated with poor outcome following hemorrhagic stroke, we were unable to substantiate this relationship in a large cohort of ICH patients. Furthermore, hematoma volume was not correlated with GFR. Future studies should explore whether there is a relationship between GFR and acute hematoma expansion.

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Th P181

Sex-Specific Trends in Mortality amongst Hospitalized Stroke Patients in the United States

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Background: Recent nationwide prevalence studies in the United States (US) demonstrated an increasing prevalence of self-reported stroke in middle-aged women compared to similarly aged men, particularly amongst those aged 45-54 years. It is unclear, however, whether this trend is due to an actual rise in stroke incidence or improved stroke survival amongst young/middle-aged women. Studies of sex differences in stroke case fatality have had variable results and few have focused specifically on individuals younger than age 65 years. We therefore assessed temporal trends in sex-specific mortality amongst US adults aged 35 to 64 years hospitalized with stroke. **Methods:** Data were obtained from all US states that contributed to the Nationwide Inpatient Sample. All individuals aged 35-64 years hospitalized between 1997 and 2006 with a primary discharge diagnosis of stroke (n=2,537,097) were identified using International Classification of Diseases, Ninth Revision procedure codes. We determined temporal trends in sex-specific hospital mortality after stroke. Both unadjusted and adjusted mortality rates were analyzed for men and women between the ages of 35-44, 45-54, and 55-64 years (controlling for sociodemographic factors, comorbidities, stroke type, tissue plasminogen activator, in-hospital complications, and length of stay). **Results:** From 1997 to 2006, mortality after stroke amongst individuals aged 35-64 years decreased in both men (6.06% to 5.15%) and women (6.02% to 4.88%). In the 35-44 year age group, mortality after stroke was lower in 2005-2006 compared to 1997-1998 (OR 0.59, 95% CI 0.51-0.69 in men and OR 0.60, 95% CI 0.51-0.71 in women). Mortality after stroke also decreased amongst those aged 45-54 years and 54-64 years, but to a lesser extent. While unadjusted analysis revealed that women aged 35-44 years had lower mortality after stroke compared to men (OR 0.89, 95% CI 0.83-0.95), this difference became insignificant after controlling for stroke type. On the other hand, comparison of mortality after stroke between men and women aged 45-64 years revealed that mortality was lower for women than men in both the 45-54 year age group (OR 0.94, 95% CI 0.90-0.98) and 55-64 year age group (OR 0.96, 95% CI 0.93-1.00) after controlling for confounders. **Conclusion:** : This study of sex-specific stroke mortality rates amongst individuals aged 35-64 years revealed a decline in mortality rates from 1997 to 2006 amongst both men and women. The most prominent decline in mortality rates has been amongst those aged 35-44 years. The slightly lower mortality in women vs. men aged 45-54 years may in part be contributing to the recently reported rising stroke prevalence observed in midlife women; however, prospective studies are warranted.

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Th P182

Primary Stroke Centers Achieve High Compliance with Disease Performance Measures

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Background: Primary Stroke Centers (PSCs) can achieve improved patient outcomes using a variety of processes. We analyzed standardized stroke disease performance measure data (DPMs) for PSCs to determine if duration of certification correlated with improved compliance with various DPMs. Our hypothesis was that institutions that achieved repeated certification as a PSC would also realize higher rates of compliance with the DPMs. **Methods:** We analyzed data on PSCs certified by The Joint Commission from 2008 through 2010. Characteristics of the PSC and compliance with the eight DPMs were analyzed as a function of the number of certification cycles and teaching status**Results:** Data were available from 745 PSCs (428 teaching, 317 non-teaching) and 361,512 eligible patients. The number of PSCs going through 1, 2, and 3 cycles of certification was 253, 255, and 243 respectively. When comparing PSCs after 1 and 3 cycles of certification, significant improvements were seen in the following DPMs: IV-TPA administration to eligible patients within 3 hours of stroke onset (73.7% vs 84.0%, p = 0.004); anticoagulation for atrial fibrillation (93.3% vs 97.1%, p = 0.03); stroke education (74.6% vs 82.8%, p = 0.02); discharge on statin therapy (86.1% vs 91.0%, p = 0.05); DVT prophylaxis (90.6% vs 95.2%, p = 0.06). Other measures such as antithrombotics by day 2 (96% vs 97%, p = 0.15), consideration for rehabilitation (96% vs 97.3%, p = 0.36), and discharge on antithrombotics (98% vs 99%, p=0.28) were at high levels after one cycle with little room for improvement in compliance by cycle 3. Hospital teaching status did not correlate with compliance for any DPM. **Conclusions:** PSCs that complete multiple certification cycles are more likely to be compliant with several DPMs, especially IV-TPA administration. Teaching and non-teaching institutions achieve equal rates of compliance with all current DPMs.

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Th P183

University of Colorado Hospital In-Hospital Stroke Alert Improvement Project

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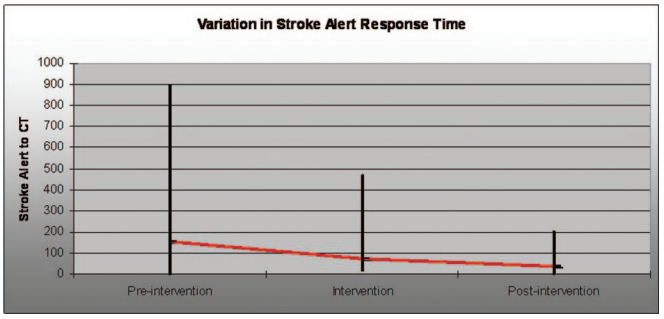
Background: Between 4-17% of all stroke patients have onset of symptoms while hospitalized. Delays in recognition and assessment are common. Research suggests in-hospital stroke alerts have greater delays compared to those in the ED. At University of Colorado Hospital (UCH), median time from in-hospital stroke alert to brain imaging was found to be 2-3 times longer than those in the ED and exceeded the benchmark of 25 minutes suggesting need for process improvement. **Purpose:** The In-Hospital Stroke Alert Improvement Project was designed to identify and rectify delays in recognition and assessment of new neurologic deficits developing in hospitalized patients. **Methods:** The In-Hospital Stroke Alert Improvement Project consisted of 6 core elements: Mapping of existing process, system re-design to address unreliable or slow steps, standardization of communication, in-hospital stroke alert checklists, rigorous measurement, and real time feedback. Root cause analysis during the pre-intervention phase (9/2008 - 2/2009) was performed using interviews with stroke team members, staff, and direct observation of alerts. Bottlenecks identified included IV access, transportation, correct test ordering, and CT notification. An interdisciplinary team developed and implemented solutions to identified barriers during the intervention phase (3/2009 - 5/2009). Checklist cards were created for both the stroke team and nursing clearly defining roles and how to execute each step in the in-hospital stroke alert. CT technicians were provided stroke alert notification pages, the stroke team assumed responsibility for transportation, a thrombolytic kit was assembled in pharmacy, and rapid response nurses were made available to respond anywhere tPA was to be given. Real time measurement and feedback was implemented. Change in stroke alert response times were tracked for 6 months (6/2009 - 11/2009) after the change implementation period. **Results:** Median and variation in times from the time a stroke alert was called to CT were significantly reduced. Median time to CT was reduced from 69 to 30 minutes (p<0.03). Variation in stroke alert to CT time was reduced from maximum of 819 minutes in the pre-intervention phase to 198 minutes in the post-intervention phase. (See Variation in Stroke Alert Response Time graph). **Conclusions:** The In-Hospital Stroke Alert Improvement Project successfully reduced in-hospital delay in time from the stroke alert to CT imaging. The methods used have potential for successful implementation in other hospitals.



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Th P184

Foley Catheterization and Urinary Tract Infections in Patients Hospitalized with Stroke

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Introduction: In conditions other than stroke, most hospital-acquired UTIs are related to bladder catheterizations, which occur in 15-25% of all hospitalized patients. The frequency of catheterization and catheter-associated UTI in patients hospitalized with stroke are not well documented. **Methods:** We utilized data on 105 randomly selected patients with ischemic stroke in QUISP, a randomized quality improvement trial focused on secondary stroke prevention, conducted between January 2004 and September 2006 in 14 hospitals in a Northern California managed care plan. Charts were abstracted for dates of Foley catheterization, days with fever (>38.4° C), laboratory and prescription information. We examined the association between Foley catheterization and UTI and between UTI and outcome (hospital length of stay, discharge disposition, recurrent stroke, or re-hospitalization). Definite UTI was defined by the CDC criteria for public reporting of hospital-acquired symptomatic UTI, including a positive culture and fever. Because records of other UTI symptoms were not available, likely UTI was defined as fever plus any of the following: urinalysis with positive nitrites, leukocyte esterase or pyuria, physician diagnosis of UTI, or appropriate treatment of UTI with antibiotics. Adjustments were made for age, gender, race, and cardiovascular risk factors. All analyses were conducted using generalized estimating equations to adjust for within and between hospital variances. **Results:** Of 105 patients, 40 (38%) had Foley catheters placed during their hospital admission. The mean duration of catheterization was 3.6 days (range 1-9 days). Women were more likely than men to have catheters placed (46% vs. 24%, p=0.02), but demographics and past medical history did not differ significantly. Eleven patients with (28%) and 4 patients without (6%) catheters had positive cultures (p=0.002). Catheterized patients were more likely to have a definite UTI (10% vs. 2%, p=0.05) or a probable UTI (20% vs. 6%, p=0.003). In multivariable analysis, there remained a trend toward prediction of definite UTI (OR 5.40, 95% CI 0.61-48.0) as well as probable UTI (OR 3.20, 95% CI 0.83-12.36) in catheterized patients. Foley catheterization was independently associated with an increase in length of stay (OR 1.45 95%CI 1.10-1.91) and increased likelihood of discharge to a facility other than home (OR 2.55, 95% CI 1.02-6.37). **Conclusions:** Compared to general medical patients, stroke patients are more likely to have Foley catheters placed during hospital admission, and catheters are associated with a trend toward greater likelihood of symptomatic

UTI, longer length of stay, and discharge to a facility other than home. Further research is needed to evaluate the appropriate indications for Foley catheter placement in stroke patients.

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Th P185

Analysis Of The Predicting Factors In The Deterioration Of Acute Ischemic Stroke On Demographic, Clinical Characteristics And Neuro-radiological Findings

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Introduction:; One third of patients with acute ischemic stroke develop early neurological worsening, a situation associated with increased mortality and long-term functional disability. The underlying basic mechanisms involved are not completely understood, although biochemical factors have been suggested. It is important to prevent patients with acute ischemic stroke from deteriorating. Age, blood pressure, diabetes mellitus, clinical symptoms, and duration of symptoms have been reported to be correlated with stroke after TIA. We investigated the predicting factors for the deterioration of acute ischemic stroke within 1 week from onset. Methods; We retrospectively investigated 537 patients who were admitted within 2 days of the occurrence of an acute ischemic stroke, between April 2007 and March 2009. Deterioration of neurological findings was defined as the worsening of 3 points or more on the National Institute of Health Stroke Scale (NIHSS) score during admission to the hospital within 1 week. We retrieved the demographic and clinical characteristics of stroke patients, medications, stroke subtypes, and functional status upon discharge. All variables with a $P<0.2$ on univariate analysis were entered into logistic regression analysis. Result; Out of 537 patients, deterioration was noted in 64 patients (11.9%; deterioration group). Multivariate analysis demonstrated that the factors associated with worsening were the history of myocardial infarction (MI) ($p<0.001$), NIHSS score 8 or more at onset ($p<0.001$), increase of WBC count ($P=0.035$), LDL-chol 140mg/dl or more ($P=0.002$) and HbA1c 7% or more ($P=0.006$). In the deterioration group, Branch artheromatous disease was more frequent than the non-deterioration group, and over 90% of patients with deterioration either were discharged to nursing home care or died. In radiological analysis, multivariate analysis demonstrated that the factors associated with worsening were internal carotid artery occlusion ($p<0.001$), middle cerebral artery occlusion at M1-2 portion ($p<0.001$), striate-capsular infarction ($P=0.030$), pontine infarction ($P=0.047$) and the 15-30mm size of lesion ($P=0.011$). **Conclusion:** Deterioration in patients with stroke was more likely to occur in those with high LDL levels, high HbA1c level on admission, history of MI and high NIHSS scores. It is important to predict deterioration in patients with minor ischemic stroke and those with many risk factors for deterioration should be given the best possible treatment. Careful attention should be paid to acute stroke patients with these risk factors.

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Th P186

Moderate Blood Pressure Reduction does not Reduce Cerebral Blood Flow in Acute Ischemic Stroke

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Background: Elevated blood pressure is common after stroke and is associated with poor prognosis. Early treatment is controversial due to concerns that this may reduce cerebral blood flow (CBF) in the ischemic penumbra. It has been hypothesized that nitric oxide donors may increase CBF in stroke patients. We aimed to assess the CBF response to acute BP reduction with labetalol and the nitric oxide donor nitroglycerin. **Methods:** Patients presenting with ischemic stroke, <72 hours after onset were enrolled. Those with mean arterial pressure (MAP)>100 mmHg received nitroglycerin (sublingual/topical) or intravenous labetalol, aiming for MAP reduction of 10%. Patients with MAP ≤ 100 mmHg were not treated. All patients underwent MRI with Perfusion (PWI) and Diffusion-weighted (DWI) imaging before and after BP treatment. PWI deficit and DWI lesion volumes were measured planimetrically. **Results:** Of 28 patients enrolled, 22 had MAP>100 (median 115.5 mmHg, IQR=19.91) and 6 had MAP of ≤ 100 (median=93.33 mmHg, IQR=9.75). The median time between first and second perfusion was 24 min (IQR= 63.5). In treated patients, mean penumbral CBF was not affected by antihypertensive therapy (pre-treatment 31.7 ± 11.5 vs post treatment 33.1 ± 11.4 ml/100g/min, $p=0.685$). Similarly, ischemic core CBF (28.7 ± 11.9 vs 30.2 ± 11 ml/100g/min, $p=0.659$) and hemispheric CBF (39.0 ± 6.2 vs 39.6 ± 5 ml/100gr/min, $p=0.698$) were not affected by treatment. The change in penumbral CBF in patients treated with antihypertensives (median= -2.1, IQR= 9.3 ml/100g/min) was not different from that in untreated patients (median= 3.7, IQR=15.2 ml/100g/min, $p=0.502$). Similarly, the change in ischemic core CBF (median= -2.7, IQR=11.6 vs 3.5, IQR=15.0 ml/100g/min, $p=0.538$) and hemispheric CBF (median= -2.4, IQR=12.3 vs 3.9, IQR=16.6 ml/100g/min, $p=0.502$) was similar in treated and untreated patients. There was no correlation between change in MAP and change in penumbral CBF ($R=0.07$, $p=0.74$). Patients who received nitroglycerin did not show improvement in penumbral CBF (median CBF change= -0.5, IQR= 12.2 ml/100g/min) relative to those who did not receive nitroglycerin (median CBF change= -3.0, IQR= 10.7 ml/100g/min, p= 0.30). There was no difference in DWI lesion volume growth, between patients receiving antihypertensives (median= 0.3, IQR= 4.3) and those who were not treated (median =3.8, IQR= 12.5, $p=0.71$). Patients who were treated with antihypertensives did not show worsening of neurological status by day 7 (median NIHSS change=-1, IQR=2.3) relative to those who were untreated (median NIHSS change = 3, IQR=12, $p=0.67$). **Conclusion:** Antihypertensive therapy does not result in further reductions in penumbral, core or hemispheric CBF in acute stroke. Nitroglycerin treatment does not appear to be associated with an improvement in CBF. These results support the safety of moderate blood pressure reduction in the early post stroke period.

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Th P187

The Brush Sign on 3-Tesla T2*-Weighted MRI as a Potential Predictor of Hemorrhagic Transformation after tPA-Induced Recanalization

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Background: The brush sign (BS) is the hypointensity findings of medullary veins depicted on 3-Tesla T2*-weighted MRI. The brush sign is reported to be seen in patients with ischemic stroke due to major cerebral artery lesions. However, the clinical relevance of the brush sign in acute stroke patient remains unclear. We assessed the hypothesis that the brush sign detected before treatments correlates with poor outcome after thrombolysis. **Methods:** We enrolled patients with anterior circulation ischemic stroke who had major artery occlusions and were treated with IV t-PA from October 2005 to June 2010. We classified the patients into two groups according to the presence of BS: the patients positive for the brush sign (P-BS) and the patients negative for the brush sign (N-BS). We investigated the differences in the clinical outcomes (NIHSS and mRS) and MRI findings (recanalization and hemorrhagic transformation) between the two groups. **Results:** The subjects consisted of 30 consecutive patients (male 14; mean age, 74 years). Eight patients (27%) had ICA occlusions, 14 (47%) had M1 occlusions, and 8 (27%) had M2 occlusions. Of the 30 patients, 22 (66%) were classified as P-BS and 8 (34%) were as N-BS. NIHSS scores had no significant difference between P-BS and N-BS (median NIHSS on admission, 15 vs 12, $p=0.170$; 24 hours after t-PA, 11 vs 4, $p=0.170$). Good outcome (mRS 0 to 1) at discharge was 23% in P-BS and 50% in N-BS ($p=0.195$). Recanalization was observed in 13 (59%) patients in P-BS and 7 (88%) patients in N-BS ($p=0.210$) at 24 hours after t-PA. Of the 20 patients with recanalization, hemorrhagic transformation on MRI were observed more frequently in P-BS than in N-BS (69% vs 14%; $p=0.057$). **Conclusions:** The brush sign may predict the hemorrhagic transformation after recanalization in the patients treated with IV t-PA.

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Th P188

Acute-phase Hyperglycemia Negatively Impacts Outcome and Recovery of Ischemic Stroke

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Introduction: Hyperglycemia is a frequent accompaniment of acute ischemic stroke. It is uncertain whether hyperglycemia negatively influences stroke outcome or simply is a marker of stroke severity. Clinical trials investigating strict control of acute hyperglycemia failed to show positive results on stroke outcome. Objectives: To define the impact of acute-phase hyperglycemia on outcome and clinical recovery after acute ischemic stroke. Main hypothesis: Hyperglycemia on admission and during hospitalization will correlate negatively with recovery after acute ischemic stroke at discharge (DC) and subsequent outpatient (OPD) follow-up. **Methods:** We analyzed prospectively collected data from the stroke registry of a large acute-care tertiary hospital. Demographic data, stroke risk factors, admission NIHSS score, DC and OPD modified Rankin score (mRS) were recorded. Serum glucose (Glu) data were obtained directly from the hospital electronic medical record system. Spearman correlation coefficients between admission-, 24-hour-, and entire hospitalization mean- glucose values and discharge and outpatient mRS were computed. We then categorized Glu values as: hyperglycemia (Glu >120 mg/dL), normoglycemia (Glu >50 and <120 mg/dL), and hypoglycemia (Glu 12, the OPD mRS was 0-3. The study was approved by the Institutional IRB. **Results:** We studied 245 patients. The mean age was 67 (±13) years, 49% were women, 66% were African-Americans. There were significant correlations between: admission Glu (r: 0.23, $p=0.0004$, $n=223$), 24-hour Glu (r:0.25, $P<0.0001$, $n=223$), the mean hospitalization Glu levels (r:0.26, $P<0.0001$, $n=223$) and DC mRS. There were significant correlations between admission Glu (r:0.20, $p=0.0038$, $n=196$), 24-hour Glu (r:0.22, $P<0.0013$, $n=196$), the mean hospitalization Glu levels (r:0.27, $P<0.0001$, $n=196$) and OPD mRS. There was strong correlation between the occurrence of hypoglycemia at any time during hospitalization and DC mRS (r;0.26, $p=0.0018$, $n=135$). On univariate logistic regression analysis, there was a negative impact of hyperglycemia during hospitalization on good stroke recovery [OR:0.29 (CI:0.15-0.55), $P<0.0001$]. The occurrence of hypoglycemia was also associated with poor clinical recovery [OR for good recovery:0.02 (CI: 0.003-0.21), $P<0.001$). **Conclusions:** Acute-phase hyperglycemia has a negative impact on outcome and clinical recovery from acute ischemic stroke. The occurrence of hypoglycemia at any point during hospitalization for acute ischemic stroke also influences negatively stroke recovery. Clinical trials should aim at producing a sustained normoglycemic effect.

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Th P189

Early Neurological Deterioration And Capillary Glucose Levels In Acute Stroke

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Background: Early neurological deterioration (END) is a common event that occurs in up to 20% to 40% of acute ischemic stroke (IS). Also, hyperglycemia is a common finding in acute IS patients and it has been associated with poor outcome. Our objective was to analize the relationship between END and hyperglycemia, and its implication on functional outcome. **Methods:** Post hoc analysis of the GLIAS (GLycemia In Acute Stroke) study, a multicenter, prospective and observational cohort study of 476 acute IS patients. Capillary finger-prick glucose was determined on admission and during the first 48h. For the purpose of this analysis, we recorded capillary finger-prick glucose on admission and 3 times a day during the first two days. We considered hyperglycemia as levels ≥155 mg/dl, since it was the threshold level associated with poor outcome in the GLIAS study. We have defined END as a decrease of one or more points in the Canadian Neurological Scale (CNS). Outcome (modified Rankin Scale, mRS) was evaluated at 3 months. **Results:** Of the 476 patients studied, 93 (19,53%) have developed END. There were no significant differences in demographic data and vascular risk factors. Patients with END have had higher body temperature (36,55°C ± 0,65 vs 36,26°C ± 0,49; p=0,001), stroke severity (CNS 6; 4,5-8 vs 4; 2-8; p=0,011) and more early computed tomography signs (75,3% vs 58,1%; P<0,001). According to stroke etiological subtypes patients with END have had more frequently large vessel disease. When we have analyzed those patients with maximum capillary glucose within 48 hours ≥155 mg/dl, there were no differences in the frecuency of END development (35,2% versus 26,9%; p=0,129). END was associated with poorer outcome (mRS>2 62,5% vs 28.3%; P<0,001) than those without END. Combination of hyperglycemia and END was significantly associated with poorer outcome than those without hyperglycemia and END (mRS>2 85,7% vs 25%; P<0.001) and higher mortality (34,15% vs 5,77%, P<0,001). Cox model confirmed that the presence of END and hyperglicemia is associated with higher mortality risk at 3 months, compared with not developing any of these two characteristics (hazard ratio 7,17; P<0,001)**Conclusions:** END is a common observation in acute IS patients that is associated with poorer outcome and higher mortality. However, the combination of hyperglycemia and END was significantly associated with worse outcomes and higher mortality.

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Th P191

Lower Admission Hemoglobin Levels are Associated with Larger Stroke Volumes and Greater Infarct Expansion

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Hemoglobin tetramers are the major oxygen carrying molecule within the blood. We hypothesized that lower hemoglobin level and its reduced oxygen-carrying capacity would associate with an increased risk of infarction within the penumbra of acute ischemic stroke patients. We studied 135 consecutive patients with acute ischemic stroke and perfusion brain MRI. We explored the association of admission hemoglobin and estimated viscosity with initial infarct volumes on acute images and the volume of infarct expansion on follow-up images. Bivariate analyses showed a significant inverse correlation between hemoglobin and initial DWI volume ($r = -0.20$, $P = 0.02$), final infarct volume ($r = -0.22$, $P = 0.01$) and absolute infarct growth ($r = -0.20$, $P = 0.02$). Estimated viscosity measurements were not significantly associated with these metrics. Multivariable linear regression modeling revealed that hemoglobin remained independently predictive of larger infarct volumes acutely and at follow-up ($P < 0.001$). Lower hemoglobin levels were also associated with greater infarct expansion ($P < 0.05$) after adjusting for other known variables that influence infarct growth. Hemoglobin level at the time of acute ischemic stroke predicts both larger infarcts and increased infarct growth, whereas estimates of whole blood viscosity do not. This raises the possibility that blood transfusion in a subset of acute stroke patients may be worthwhile investigating as a therapy.

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Th P192

Swallowing Screens in Patients after Stroke: A Systematic Review

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Objective: We performed a systematic review of standardized swallowing screening protocols in patients with acute stroke to assess ease of administration, reliability, and validity. **Methods:** Screening was defined as a brief assessment by someone other than a speech language pathologist (SLP) of patients' ability to swallow safely, namely whether the patient could eat or needed further evaluation of swallowing function. Criteria for review included: patients were in the early stage of hospitalization for acute stroke, screening items were described in sufficient detail, reliability was measured, and criterion validity was assessed. We searched MEDLINE, EMBASE and Cochrane databases with the strategy: (swallow* OR dysphagia) AND (screening OR evaluation OR assessment) AND (stroke OR cerebrovascular accident). Additional references were located by reviewing bibliographies of relevant papers, references for guideline publications, and manual search of the table of contents for the journals *Stroke* and *Dysphagia* for the past five years. **Results:** We found 730 papers in the MEDLINE search, of which 64 were reviewed in detail. From review of these papers and other sources, including the same search in EMBASE, we identified 36 papers detailing a protocol for non-SLP professionals to screen swallowing. Of these, seven met criteria detailed above: the Standardized Swallowing Assessment (SSA), the Massey Bedside Swallowing Screen, the Gugging Swallowing Screen (GUSS), a swallowing screen conducted by emergency physicians, the Toronto Bedside Swallowing Screen (TOR-BSST©), the modified Mann Assessment of Swallowing Ability (MMASA), and the Acute Stroke Dysphagia Screen (ASDS). Four screens were designed to be administered by nurses; two by physicians; and one by any specifically trained health care professional. Six of the seven included assessment with water swallows, one in conjunction with pulse oximetry. The gold standards used were clinical evaluation by an SLP (n=3), videofluoroscopic evaluation (n=1), fiberoptic endoscopic evaluation (n=1), and clinical observation and chart review for indications of dysphagia and complications (n=2). Where provided, administration time ranged from two to ten minutes. Inter-rater reliability ranged from k of 0.76 to 0.9. Sensitivity of these instruments ranged from 76 to 100%, and specificity from 56 to 100%. **Discussion:** Despite recommendations for their use by several organizations, few swallowing screens were available that met even minimal criteria. Three of the seven protocols that met criteria reported limited reliability testing or were described as preliminary with small sample sizes limiting their generalizability. Further work is needed to achieve the goal of swallowing screens to reduce the risk of aspiration pneumonia after stroke.

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Th P193

Correlation Of Neuroanatomical Location And Dysphagia Pattern By Using Videofluoroscopic Function Scale In Patients With Acute Ischemic Stroke

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Background & objectives Dysphagia is a common neurological sign and a main cause of aspiration pneumonia, which is a fatal complication in acute stroke patients. Recently, the videofluoroscopy study (VFSS) is considered to be an useful way of measuring severity and predicting prognosis of the dysphagia. We investigated the correlation between the location of brain lesion and dysphagia pattern by using subitems of videofluoroscopic functional dysphagia scale. Methods Subjects were acute ischemic stroke patients with dysarthria or dysphagia. The sites of brain lesion were classified to unilateral cortex, subcortex, cortex with subcortical extension and brainstem. All patients were underwent diffusion weighted magnetic resonance image and videofluoroscopic functional dysphagia scale were measured within 30 days. The parameters rated during the VFSS were lip closure, bolus formation, reside in oral cavity and oral transit time, triggering of pharyngeal swallow, laryngeal elevation, nasal penetration, residue in valleculae, residue in pyriform sinuses, coating of pharyngeal wall after swallow and pharyngeal transit time. For the analysis of correlation of lesion sites and parameters, Kruskal-Wallis and Mann-Whitney tests were performed. Results Sixty nine subjects were enrolled (M=48, F=21). Total score for oral phase and score for residue in oral cavity were different depending on lesion sites(oral phase $p < 0.05$, residue in cavity $p < 0.01$). The oral phase score, especially residue in oral cavity, in patients with cortex, subcortex and cortex-subcortex involvement was higher than patients with brainstem involvement (mean score 5.00, 2.83, 2.85 and 0.24, respectively). Score for residue in oral cavity in patients with cortex-subcortex involvement was higher than patients with brainstem involvement (mean score 1.10 vs 0.29, p **Conclusion:** The oral phase score in patients with cortex, subcortex and cortex-subcortex involvement was higher than patients with brainstem involvement in this study. The subitems of videofluoroscopic functional dysphagia scale may be useful to evaluate the correlation of neuroanatomical location and dysphagia pattern in acute ischemic stroke patients.

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Th P194

The Cleveland Clinic Experience: Stroke And Timing Of Valve Surgery In Infective Endocarditis

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Background: The incidence of stroke in patients with infective endocarditis (IE) is 10-20%. The timing of surgery in IE complicated by stroke is difficult because surgery can exacerbate the

patient's neurologic condition. The risk of peri-operative stroke in these patients is unclear. **Objective:** To determine the optimal timing of valve surgery in patients with IE and stroke. Method: Cohort study of peri-operative neurological complications in patients with IE and history of prior stroke admitted at Cleveland Clinic from 2007 to 2009. Subjects were identified from the Cleveland Clinic Cardiovascular Information Database, and stratified by the timing of their stroke in relation to surgery: 0-7 days before surgery (Group 1), 8-14 days (Group 2), 15-30 days (Group 3), 31-90 days (Group 4), and >90 days (Group 5). **Result:** Of the 364 patients admitted to Cleveland Clinic with IE during this period, 99 had prior stroke, including 35 (9.6%) who had stroke within 14 days, and 64 (17.5%) who had stroke greater than 14 days. Seventy were included in final analysis. The overall incidence of peri-operative stroke in IE subjects with any prior stroke was 10% (7 of 70) and tended to occur more frequently in the subjects with recent stroke: 3 (4.3%) in Group1, 1 (1.43%) in Group 2, 1 (1.43%) in Group 3, 0 in group 4, and 2 (2.9%) in Group 5. Thirteen of prior strokes were associated with hemorrhages. Eight (11.3%) occurred in Group 2: 4 hemorrahagic conversion without shift, 2 petechial, 1 subarachoid hemorrhage, 1 abscess. The MCA and PCA territories were commonly involved both in the pre- and peri-operative strokes. The mechanism of peri-operative stroke was commonly cardioembolic (71%), with the one hemorrhagic conversion (14.2%). The average length of stay for the study cohort was 24 days, and was not significantly different in patients with peri-operative stroke. **Conclusion:** In this large single-center cohort of IE patients and prior stroke, the incidence of peri-operative recurrent stroke was highest in subjects with recent stroke occurring within 7 days of surgery (5.7%) and declined if surgery was delayed for at least 7 days (1.43%). Peri-operative hemorrhagic stroke was surprisingly rare, occurring mostly in subacute strokes (8-14 days), and most of these were hemorrhagic conversion of previous embolic stroke, not primary hemorrhages. Given these findings, recent stroke does not need to be considered a contraindication for valve surgery in IE patients.

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Th P195

The level Of Creatine Kinase BB in CSF Correlates With Brain Mri Abnormalities In Post Cardiac Arrest Resuscitated Patients

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Objective: To assess the association of the biomarker creatine kinase-BB (CK-BB) in cerebrospinal fluid and brain MRI in relation to the prediction of awakening after resuscitation from cardiac arrest. **Methods:** Retrospective cohort of patients admitted to Harborview Medical Center in Seattle, Washington between the years of 1998 and 2006. Medical records were reviewed of patients with cardiac arrest either from primary cardiac causes or secondary to respiratory causes and who had a brain MRI. Neurological examination on admission, SSEP results and CK-BB levels were also recorded. SSEPs and CK-BB were not tested in all patients, nor on all the same patients. An abnormal brain MRI was defined as a radiology read of any abnormality. Abnormal SSEPs were either slow or absent. These were compared with if the patient awoke or not. Statistics were nonparametric. **Results:** 35 patients were identified, with mean age of 50.3 (SD 16.9), 34% female. The arrest was primary cardiac in 28, respiratory in 6, and unknown 1. MRI of the brain was performed an average of 7.6 days (SD 5.3) after resuscitation and was abnormal in 19 (54%). CK-BB in CSF was measured in 15 patients and ranged from 8-1764 U/L. SSEP was performed in 18 patients, 9 were abnormal, but only 2 with bilateral absent cortical responses. Out of the 35 patients 16 awoke. MRI abnormality was not associated with awakening ($P = 0.25$). There were correlations between SSEP results and awakening ($P = 0.046$), CK-BB levels and awakening ($P = 0.02$), and CK-BB levels and MRI results ($P = 0.048$). The 4 patients with minimal CK-BB levels all had normal MRIs and awoke. The 2 patients with the highest CK-BB levels (965, 1764 U/l) had severe and diffuse MRI abnormalities, prolonged SSEPs, and neither awoke. Intermediate levels of CK-BB abnormality showed a less consistent relationship to MRI findings. **Conclusion:** Despite small numbers, our results represent a proof in principle that a biomarker with a continuous association with severity of brain injury after resuscitation from cardiac arrest (CK-BB) is correlated with brain MRI findings. To the best of our knowledge this is the first study to compare CK-BB levels and brain MRI in post arrest patients. Further research, especially in the hypothermia treatment era, is needed to examine this correlation and its possible utility in prognosis in the post resuscitation cardiac arrest patient.

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Th P196

Surgical Variability and Radiological Predictors of Outcome or Reoperation in Patients that Undergo Hemicraniectomy for Malignant Middle Cerebral Artery Infarction

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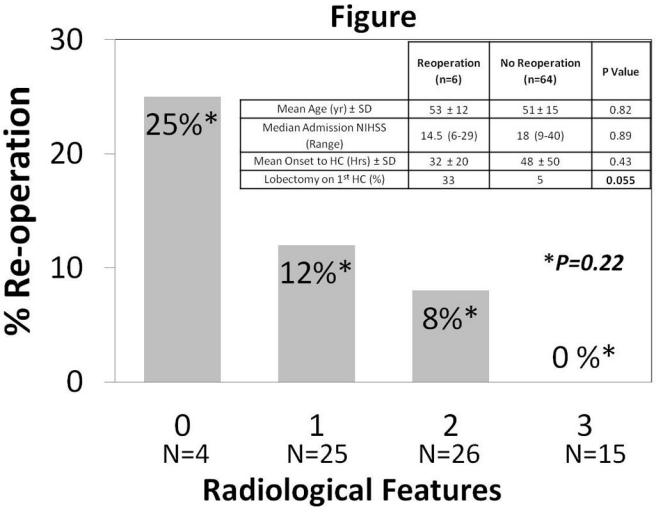
Objective: Hemicraniectomy (HC) has been shown not only to be lifesaving but it also improves clinical outcomes in the setting of malignant middle cerebral artery infarction (MMCA). We hypothesized that variation in surgical technique could contribute to suboptimal decompression, potentially contributing to poor outcomes or the need for re-operation. We reviewed all cases of HC performed for MMCA at our institution to assess clinical and predefined radiological features (RF) that may influence clinical outcomes or need for re-operation. **Methods:** We retrospectively reviewed our registry from 07/2003 to 02/2010 and identified consecutive patients diagnosed with MMCA that underwent HC. Two independent neuroradiologists reviewed all pre and post-operative CT scans and documented three predefined RF extrapolated from published surgical recommendations: 1) removal of bone flap >12 cm; 2) removal of bone ≤ 2cm to the sagittal suture; 3) bone removal within 1cm of the middle cranial fossa floor. Outcome measures included good clinical outcome defined as discharge mRS of 0-4, and need for re-operation for progressive malignant edema. **Results:** We identified 70 patients that met our inclusion criteria, with a median age of 52 years (16-80) and median admission NIHSS of 18 (6-40). Age was the only clinical factor that correlated with good outcome, (mean age 46yrs_good outcome vs mean age 54yrs_poor outcome, $p=0.04$) and we found that 96% of the HC patients achieved 1 out of the 3 RF, 56% achieved 2 out of the 3 RF, but only 26% achieved all 3 RF. No clinical factor other than lobectomy during initial HC, showed a trend towards a need for re-operation ($p=0.055$). There was an observed trend towards re-operation when fewer RF were achieved (Figure). **Conclusions:** Despite recommendations on surgical technique for HC, only 1 out of 4 patients received complete decompression. Incomplete decompression may be associated with need for re-operation, but is not associated with short-term clinical outcomes. Younger patients are more likely to achieve a good outcome after HC for MMCA, and lobectomy during initial HC may increase the need for re-operation. Our study is limited by its retrospective nature, small sample size, and lack of long-term outcomes but suggests that standardization of surgical technique may obviate the need for re-operation.

Figure



	Reoperation (n=6)	No Reoperation (n=64)	P Value
Mean Age (yr) ± SD	53 ± 12	51 ± 15	0.82
Median Admission NIHSS (Range)	14.5 (6-29)	18 (9-40)	0.89
Mean Onset to HC (Hrs) ± SD	32 ± 20	48 ± 50	0.43
Lobectomy on 1st HC (%)	33	5	**0.055**

Author Disclosures: T. Wu: None. J. Choi: None. E. Friedman: None. W. Ashley: None. P. Sahota: None. N. Harun: None. R. Pandurengan: None. N. Sangha: None. N.R. Gonzales: None. G.A. Lopez: None. J.C. Grotta: None. S.I. Savitz: None. A.D. Barreto: None.

Th P197

Infarct Volume of Cerebellar Strokes Predicts Neurosurgical Intervention

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Background and Purpose: The decision for neurosurgical intervention in cerebellar strokes is often based upon the degree of clinical deterioration. Past studies of cerebellar stroke have shown that infarct volume may not predict clinical deterioration. However, these studies did not use diffusion weighted imaging (DWI), and infarct volume was calculated more than 2 days from symptom onset. We addressed whether infarct volume and the percent volume of infarcted cerebellum measure on DWI within 24 hours of symptom onset predicts the need for neurosurgical intervention. **Methods:** A retrospective review was conducted of our stroke registry from 09/2003 to 06/2010. 125 patients were collected with cerebellar infarction on DWI within 24 hours of symptom onset. The patients were divided into 2 groups: surgery and no surgery. Surgical intervention was defined as either the placement of an EVD or a suboccipital decompressive craniectomy (SDC), with or without strokectomy. Volume analysis of the cerebellum and the infarct was performed using a semi-automated region of interest based analysis. Baseline characteristics were also studied. Data was analyzed using Pearson chi square, t-test and Mann-Whitney test. **Results:** Sixteen patients underwent surgical intervention and 113 patients were treated with medical therapy only. Four patients who had surgery could not be included because their MRI's were performed greater than 24 hours. Mean infarct volumes in patients who required surgical intervention compared to those who did not were 49.0 ml and 12.0 ml, respectively. Mean percent of infracted cerebellum in patients who required surgical intervention compared with those who did not were 30.3% and 8.4 %, respectively. The surgical procedures were ventriculostomy only (n=5), ventriculostomy + SDC (n=5), SDC (n=2). Nine patients underwent surgery because of subsequent, depressed mental state and 3 because of subsequent imaging findings that showed brainstem compression. There were no significant differences in baseline characteristics between the two groups. **Conclusion:** Quantitative measurement of infarct volume and percent of infarct volume on DWI within 24 hours may help to accurately identify patients with cerebellar ischemic

strokes who may require neurosurgical intervention. Measuring the infarct volume may aid clinical decisions to pursue surgical management. These results raise the need for a prospective analysis to investigate the factors that predict need for surgical intervention for cerebellar ischemic stroke.

	All Patients	No Surgery	Surgery	Level of Significance
Number of Patients	125	113	12	
Age, median (min-max)	63 (22-94)	64 (22-94)	58 (25-88)	NS
Gender, % Female	36.8	36.28	41.67	NS
NIHSS on admission, median(min-max)	5 (0-39)	5 (0-39)	4 (0-31)	NS
Hypertension %	71.7	70.5	83.3	NS
Diabetes %	30.7	28.7	50.0	NS
Hyperlipidemia %	27.6	27.9	25.0	NS
Brainstem involvement on admission%	17.27	17.7	18.9	NS
Previous Stroke/TIA%	21.8	22.4	16.7	NS
Coronary Artery Disease%	19.1	18.5.	25.0	NS
Vascular Territory %				NS
PICA	28.7	24.3	66.6	
SCA	39.1	41.8	16.7	
AICA	4.4	4.9	0.00	
2 OR MORE	9.6	8.7	16.7	
Punctate/ Embolic	18.2	20.3	0.00	
Infarct Volume (ml)				<0.001
Mean	16 (SD 21)	12.0 (SD 17.8)	49.0(SD 26.9)	
Median	5.76 (0.24-112.5)	3.77(0.24-76.8)	49.8(11.6-112.5)	
Infarct Percent Volume				<0.001
Mean	10.5 (SD 13)	8.4 (SD11.8)	30.3 (SD15.8)	
Median	3.9 (0.017-66.7)	2.7(0.017-55.7)	29.8 (8.7-66.7)	

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Th P198

Acute Stroke Causes Changes in Spleen Size Over Time

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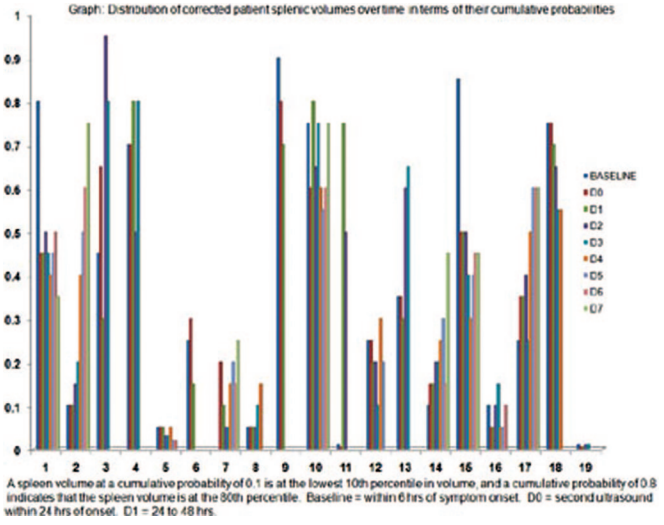
Introduction: Animal studies have demonstrated that the spleen contracts after stroke and promotes secondary inflammatory response that enhances neurodegeneration. There are no known studies on splenic changes in patients with acute stroke (AS). We conducted a prospective pilot study to evaluate changes in spleen size over time following AS. The following hypotheses were tested: ● Whether the spleen undergoes demonstrable size changes over time following AS? ● Is there clinical correlation of splenic contraction with severity of stroke? Methods Patients with AS, 18 years or older and presenting within 6 hours of onset, in absence of concomitant MI, trauma, autoimmune disease, fever, hypoxemia or hemodynamic instability were enrolled. We collected demographics, vitals and NIHSS; first splenic ultrasound (SUG) was performed within 6 hours of onset using Philips CX50 S5 MHz transducer. Splenic length, width and thickness were measured with hilum as reference point. SUG was repeated once within 24 hours of onset and then daily along with NIHSS until day 7 or discharge, whichever was earlier. Splenic volume was calculated and corrected for height, weight and gender using a published formula by Geraghty et al to determine the relative degree of splenic size changes (atrophy versus enlargement) compared to the expected normal range. Based on 5 consecutive daily SUGs in 8 healthy volunteers, splenic volume variation below 15% was considered normal. Results The clinical and SUG characteristics of 19 patients are summarized in the table. A significant increase in mean splenic volume was seen over the week (p-0.037), indicating rapid contraction and then gradual increase towards normalcy in most patients. Three patients had below 15% splenic volume change, two of whom had significant recovery (NIHSS $\leq$1) within a day. Rest of patients showed splenic contraction at first SUG or within next 6-24 hours, followed by varying degree of recovery in individual patients (figure). Most patients with severely contracted spleens ($<$1 percentile) initially had moderate to severe stroke. **Conclusions:** The spleen undergoes dynamic changes in size after AS. Stroke severity and outcome may correlate with extent of splenic contraction and recovery over time. Further studies are needed to determine the clinical significance of these findings.

Clinical Characteristics			
Type of stroke	16 Ischemic (84.21%)	3 Hemorrhagic (15.79%)	
Gender	10 Males (52.63%)	9 Females (47.37%)	
Age (years)	Mean: 65.26	Median: 63	Range: 36 – 87
Race	10 Caucasian (52.63%)	4 African-American (21%)	5 Others (26.32%)
Baseline NIHSS	Mean: 12	Median: 9	Range: 0 – 38
Splenic Ultrasound (SUG) Characteristics			
Mean (±SE) Splenic volume (cc.)	181.6 (±17.84) on first SUG within 6 hr of onset	212.32 (±16.78) on day 7	P=0.0367
Splenic Volume Change Characteristics as Related to Stroke Severity			
Type of spleen volume change	**Patient Number (%)**	**Stroke severity**	**Range of volume change**
Spleen volume decreasing over time	3 (15.79)	Mild to severe with improvement	-14.45% to -28.97%
Spleen volume increasing over time	4 (21.05)	Mild to severe	30.25% to 83.71%
Spleen volume reduces over 2-4 days then increasing/normalizes	5 (26.32)	Moderate to severe	-34.7% to 34.04%
Spleen severely contracted	4 (21.05)	Moderate to severe with improvement	-2.36% to 72.95%
Less than 15% Spleen volume change	3 (15.79)	Mild to moderate with recovery	-11.58% to 13.94%



A spleen volume at a cumulative probability of 0.1 is at the lowest 10th percentile in volume, and a cumulative probability of 0.8 indicates that the spleen volume is at the 80th percentile. Baseline = within 6 hrs of symptom onset. D0 = second ultrasound within 24 hrs of onset. D1 = 24 to 48 hrs.

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Th P199

Positional Sleep Apnea In Patients With Acute Stroke

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Background and Purpose: Supine position sleep is known to exacerbate apnea in non-stroke patients and there is a well established relationship between obstructive sleep apnea (OSA) severity and body position during sleep, a condition called positional OSA. Sleep apnea is very common after stroke, so this study aims to investigate the presence of positional sleep apnea in patients with acute stroke. **Methods:** patients with acute stroke (ischemic or hemorrhagic) were submitted to a full polysomnography, including continuous monitoring of sleep positions on the first night after admission. Severity of sleep apnea (OSA) was measured by the apnea-hypopnea index (AHI). Stroke severity was measured by the National Institute of Heath Stroke Score (NIHSS). In all patients, demographic data and vascular risk factors were recorded. The percentage of total sleep time supine was compared to severity of stroke using the Wilcoxon rank-sum test. Positional OSA was defined as an overall AHI≥5 and at least a 50% lower AHI in the lateral positions than the supine position and possible positional OSA was defined as an AHI≥5 in the supine position and no sleep recorded in any other position. **Results:** of the 66 patients (48.5% had ischemic stroke and 51.5% had hemorrhagic stroke), the mean age was 57.57±11.46 and the mean body mass index (BMI) was 26.63±5.05. The sleep apnea was present in 81.8% of the patients (AHI≥5) and the median AHI was 23.35. The median percent sleep time spent supine among all the patients was 76.2% (IQ: 57-85.6). The median percent sleep time supine was 81.6% (IQ: 71.8-87.3) in those with a higher NIHSS and 71.9% (IQ: 43.7-81.7) in those with a lower NIHSS. The NIHSS was correlated to the sleep time supine (rs= 0.445; p=0.001). The positional OSA was present in 63% of acute stroke patients and there was no difference between the stroke subtypes. **Conclusions:** Positional OSA was found in majority patients with acute stroke in our series. The correct positioning of patients in acute phase may improve OSA in acute stroke patients particularly for those with higher NIHSS.

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Th P200

Low Body Temperature Does Not Significantly Compromise Therapeutic Effect of Alteplase

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Background and Purpose: Body temperature is a modifiable risk factor in the treatment of acute ischemic stroke, early rises being associated with worse outcome at 90 days. Higher body temperature has been hypothesized to enhance performance of alteplase. Such temperature dependency would undermine future trials of induced hypothermia, however. We have examined the impact of baseline temperature on outcome according to alteplase exposure. **Methods:** We identified 5832 patients with acute ischemic stroke in the Virtual International Stroke Trials Archive, of whom 2097 received alteplase (T) and 3735 were not thrombolysed (C), according to local standard of care. Age and baseline severity were similar (68.0±13.0 versus 69.9±12.3 years, NIHSS 14.2±5.2 versus 13.0±5.6). We compared outcome in T versus C, testing for significance and extent of interaction of baseline temperature on 90 day mRS using the Cochran-Mantel-Haenszel test and estimation of odds ratios for improved functional outcome from ordinal logistic regression. All analyses were adjusted for age and baseline severity. We also examined the temperature profile over 7 days after stroke, by treatment group. **Results:** Alteplase was associated with improved outcome, OR 1.49 (95% CI 1.35-1.65, P<0.0001). Baseline temperature was not significantly associated with the estimated alteplase treatment effect, p=0.14. Point estimates for alteplase treatment effect were greatest and showed significant benefit evident in each temperature category from 35.5-37.5C, but showed a negative trend above 37.5C (Figure). Alteplase did not influence the temperature profile over the first 7 days after stroke. **Conclusion:** There is no evidence of an influence of body temperature on alteplase treatment response. These controlled but non-randomized results offer preliminary reassurance that induction of modest hypothermia should not compromise the therapeutic effect of alteplase in acute ischemic stroke, but require prospective confirmation.

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Th P201

Baseline Creatinine Levels Are Not Needed Prior to CTA/CTP Imaging in Acute Ischemic Stroke Evaluation

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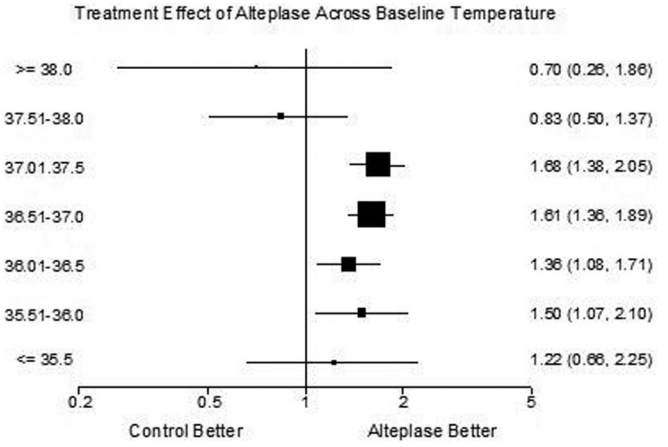
Objective: Computerized tomography perfusion imaging is emerging as an important adjunct to acute stroke therapeutic decision making. However, at many centers CTA/CTP imaging is not performed until Creatinine levels are obtained resulting in potential delays in treatment. We sought to determine the renal safety of CTA/CTP at a single stroke center. **Methods:** Using an IRB-approved prospectively collected acute ischemic stroke (AIS) database, we identified patients who had CTA and/or CTP (total volume 140ml Optiray™ contrast) as part of initial evaluation during a 2year period. Patients who received subsequent contrast, other than cerebral angiography, were excluded. All AIS patients receive hydration via 1-2liter NS bolus and infusion of ≥150cc/hr. Data collected included patient demographics, DM, HTN, chronic kidney disease (CKD), use of Metformin, ACE-I, ARB, and/or diuretics, baseline and highest Creatinine values in the following 5days. An increase of Creatinine >25% from baseline was considered significant. **Results:** 91 patients (54% men) with mean age of 61±13.5years were included, of whom 31(34%) had cerebral angiograms with 109.3±42ml of additional contrast. DM and CKD were reported in 31(34%) patients and 69(75%) patients had HTN. Forty-five patients (49%) were on Metformin, ACE-I/ARB, and/or diuretics. The mean baseline Creatinine was 0.95±0.41. No patient had >25% increase in Creatinine and no patient needed dialysis. There was no clinically or statistically significant difference in baseline vs. peak Creatinine in 60(66%) patients who had CTA/CTP only (0.9±0.28 vs. 0.86±0.37, p=0.47) or in the 31(34%) patients having additional contrast (1.05±0.56 vs. 1.04±0.65, p=0.93). Similarly, no significant difference existed between baseline and peak Creatinine in patients with DM and CKD (0.94±0.45 vs. 0.93±0.51, p=0.92) or in those who were on Metformin, ACE-I/ARB, and/or diuretics (0.96±0.43 vs. 0.90±0.43, p=0.48). **Conclusion:** Emergent CTA/CTP and DSA are safe with no increase in follow-up Creatinine even in patients with DM and CKD or those who were on Metformin, ACE-I/ARB, and/or diuretics. We do not know if our hydration protocol contributed to the lack of observed renal toxicity. If confirmed by larger studies, our results suggest that baseline Creatinine values are not needed prior to obtaining emergent CTA/CTP in acute ischemic stroke patients.



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Th P202

Does Gender Influence The Evolution Of Patients Treated With Intraarterial Procedures?

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Background: Previous studies have suggested gender differences in the response to intravenous thrombolysis for acute stroke. We aimed to evaluate whether gender differences may also influence recanalization, early and long-term outcome and mortality in acute stroke patients treated with intraarterial (IA) reperfusion procedures. **Methods:** Consecutive stroke patients treated with IA procedures between September 2006 and August 2010 were analyzed. Baseline clinical characteristics, different endovascular approaches and response to endovascular procedures (recanalization, clinical evolution, hemorrhagic transformation, mortality and functional outcome) were evaluated according to gender. Recanalization was defined as TIMI 2-3. Clinical improvement was considered if a decrease in NIHSS >4 points was achieved, and good functional outcome if modified Rankin scale at 3 months was ≤2. **Results:** A total of 121 patients were included; mean age 70.4±12.1 sd and 57(47.1%) were women(W). W were older (74 vs 67.2; p=0.002), presented more atrial fibrillation (61.4% vs 39.1%; p=0.014) and previous treatment with coumadin (35.7% Vs 15.6%; p=0.01). No gender differences were observed in baseline NIHSS score (median W 19 vs men(M) 20; p=0.946), symptoms to groin-time (W 217.5 min vs M 232.8 min, p=0.512) or door to groin-time (W 85.3 min vs M 75.7 min, p=0,25). The occluded vessels and clot locations were also similar in both groups. Rate of pre-treatment with iv tPA was lower in W (47.3% vs 67.64%, p=0.047). During IA procedure 10.2% W vs 10% M were treated with tPA alone, 18.4% vs 34% with isolated mechanical procedures and 71.7% vs 56% required more than one IA technique to achieve recanalization (p=0.199). Recanalization rate after IA procedures was similar between W and M (72.7% vs 71.7%, p=0.899) and occurred at a comparable symptoms-to-recanalization time (W 329.9min vs M 338.1min, p=0.778). No differences were found in clinical improvement at discharge (W 47.1% vs M 49.1%, p=0.830), hemorrhagic transformation (34.6% vs 30.4%, p=0.637), symptomatic intracranial hemorrhage (3.7% vs 10.3%; p=0.274) or in-hospital mortality (32.1% vs 35% p=0.745). At 3 months, 31.9% of patients achieved a good outcome in both genders (p=1). **Conclusions:** Despite the older age and the higher prevalence of atrial

fibrillation, W had similar response to endovascular reperfusion therapies than M. W received more frequently primary IA therapy, because the higher rate of previous anticoagulant therapy.

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Th P203

Neural Stem Cell Engraftment Peaks at 3 Days After Intraarterial Delivery in a Mouse Hypoxic-Ischemic Stroke Model

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Intro: With its minimal invasiveness and ability to target a wide area of the brain, intra-arterial (IA) neural progenitor cell (NPC) transplantation has emerged as a potent therapeutic avenue for stroke. However, the effects of timing of transplantation on cell delivery efficiency remain unknown. In this study, we transplanted NPCs at specific time points after stroke to evaluate cell engraftment and viability with in-vivo bioluminescent imaging. **Methods:** Mouse NPC's (5x105 in 5μl saline) harboring a reporter gene construct containing renilla luciferase were delivered to the brain via the ipsilateral carotid artery at 6 hours, 24 hours, 3, 7 and 14 days after hypoxic-ischemic stroke in Bl6 mice (N=10 per group), using a microneedle. Cell engraftment was monitored by in-vivo bioluminescence imaging (BLI) for luciferase activity, performed immediately and 4 days after IA injection. Stroked brain homogenates were analyzed using quantitative RT-PCR for the chemokine CCL2 and adhesion molecule VCAM1 to investigate the mechanism of cell recruitment. Western blotting was performed to corroborate RNA expression data. **Results:** Cell engraftment was significantly higher when NPCs were injected at 3 days after stroke (1.86 x 10 6 photons/s/cm 2/sr) as compared to 6 hours (3.87 x 10 5 photons/s/cm 2/sr) and 14 days (5.51 x 10 5 photons/s/cm 2/sr) ($p<0.01$). NPCs transplanted at three days post-stroke also demonstrated greatest survival when imaged at 4 days after IA injection ($p<0.01$). Quantitative RT-PCR showed that CCL2 expression in the ipsilateral brain as compared to naïve brains was significantly upregulated at 3 days (520.9 fold regulation) after stroke as compared to 6 hours (32.5 fold regulation), 5 days (422.1) and 14 days (323.8) after stroke. VCAM-1 expression in the ipsilateral brain was significantly upregulated at 24 hours (4.055 fold regulation) after stroke compared to 6 hour (0.245 fold regulation) after stroke. Western blotting data revealed a peak in VCAM expression at 3 days post stroked with bands having a relative intensity of 1.14 as compared to 6 hours (0.95), 5 days (0.36), and 14 days (0.88). Preliminary cell counts revealed a significant peak in cell homing to the injured brain ($p<0.05$) compared to 6 hour and 14 day time points. **Conclusion:** Intravascular transplantation of NPCs 3 days after stroke resulted in significantly higher delivery of NPCs to the area of injury and highest degree of cell survival at 4 and 7 days after injection. The observed differences in cell engraftment may be attributed to a favorable environment for NPC migration as evident by the secretion pattern of chemoattractant factors and adhesion molecules such as CCL2 and VCAM-1 in the injured brain.

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Th P204

Mechanical Thrombectomy by the Penumbra System has the Potential to Improve Neurological and Functional Outcomes in Japanese Patient with Acute Ischemic Stroke

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Introduction: Mortality from acute ischemic stroke in Japan is known to be much lower than that reported in the West. In Japan, IV rt-PA therapy has been approved since 2005, and endovascular intervention is indicated in patients who are either contraindicated to, or failed IV rt-PA therapy. However, mechanical thrombectomy devices, such as the Merci Retriever or Penumbra System are not approved, and it remains controversial if mechanical thrombectomy has a role for acute stroke intervention in Japan. **Methods:** This study was a retrospective review of 1176 acute stroke patients from 13 hospitals in the JR-NET2 and SAMURAI registry group. The goal was to select those who would qualify for mechanical thrombectomy therapy but were never treated. These patients (N=334) had large vessel occlusions who presented within 8 hours from symptom onset with a NIHSS score of at least 8 and not eligible for IV rt-PA therapy. Their outcomes were then compared with matched patients pooled from the Penumbra Pivotal and POST trials* who were treated by the Penumbra System (N=143). The primary endpoints were all cause mortality, poor functional outcome as defined by a modified Rankin Scale (mRS) score of >5 and good functional outcome as defined by a mRS score of <2 at 90 day post-procedure. **Results:** Table.

	JAPANESE PATIENTS (N=334)	POOLES PENUMBRA PATIENTS* (N=143)
Age (mean)(years)	77	64
Female	48%	46%
Baseline NIHSS (median)	20	17
Mortality at 90 Days	36.2%	30.1%
mRS 5-6 at 90 Days	62.3%	39.2%#
mRS $\leq$ 2 at 90 Days	12.0%	31.5%#

** Stroke 2009;40:2761-8. JNIS 2010;In Press.*

 # P<0.01 from a 2-tailed Fisher's Exact test.

Conclusion: These results suggest that patients with large vessel occlusion, eligible for mechanical thrombectomy in Japan, who present within 8 hours from symptom onset and with a NIHSS score of at least 8 could potentially get benefits from treatment by the Penumbra System.

Author Disclosures: N. Sakai: None. K. Toyoda: None.

Th P205

Long-term Clinical Outcome Following Endovascular Reperfusion Therapy In Severe Ischemic Stroke Patients

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Object The purpose of our study was to investigate long-term clinical outcome following endovascular reperfusion therapy in severe ischemic stroke patients with occlusions of the internal carotid artery (ICA) or the middle cerebral artery (MCA), and to find predictors of favorable clinical outcome. Methods We retrospectively analyzed the acute stroke patients 1) who were admitted to our institution from 2004 to 2009, 2) with serious neurological symptoms of GCS of 12 or less or NIHSS score of 10 or more, 3) who had total occlusion of the ICA or MCA displayed by MRA, and 4) who underwent emergency reperfusion endovascular therapy within 6hours from stroke onset. We investigated patient's baseline features, emergency MRI finding, stroke subtypes, successful recanalization defined as TIMI2 or 3, onset-to-treatment time (OTTT), NIHSS score on admission (AD-NIHSS),and the 7th day (7D-NIHSS), and mRS at 3 months (3M-mRS). We defined favorable clinical outcome as mRS of 0-2, and assessed predictors for favorable clinical outcome by using logistic regression analysis. We evaluated factors for long-term survival with cox proportional hazard model. Results Fifty nine patients were analyzed. Their median age was 77, women were 26 patients, median follow-up period was 6 months (range: 1-72 months), median AD-NIHSS was 18, median DWI-ASPECT score was 7, median OTTT was 2.67 hours, fifty two patients had cadiogenic stroke, successful recanalization was achieved in 33 patients (56.0%), median 7D-NIHSS was 10, and median 3M-mRS was 3. Logistic regression analysis demonstrated that successful recanalization (OR11.9, 95%CI 2.08-67.93, P=0.005) was the independent predictor of favorable clinical outcome (3M-mRS of 0-2) . Successful recanalization following endovascular reperfusion therapy (OR9.57 95%CI1.47-62.10 P=0.018) was the independent significant predictor for long-term survival free from any death. In patients with and without successful recanalization, cumulative survival probability at 1 year free from any death was 83.1% and 60.4% (p= 0.002), respectively. **Conclusion:** In severe ischemic stroke patients who underwent endovascular reperfusion therapy for the ICA or MCA occlusion within 6hours from onset, successful recanalization was the significant predictor for favorable 3M-mRS of 0-2 and long-term survival.

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Th P206

Endovascular Treatment Outcomes in Acute Stroke Patients with Distal MCA lesions: A single center experience

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Objectives: To assess the safety and efficacy of endovascular treatment modalities in acute ischemic stroke patients with distal MCA lesions**Background:** Endovascular treatment modalities have been shown to be efficacious in acute ischemic strokes resulting from proximal middle cerebral artery (MCA) lesions. Data regarding their utility in treating distal MCA clots such as M2 and M3 branches is limited. **Methods:** Retrospective chart review was performed in 190 consecutive patients who underwent endovascular treatments for acute ischemic stroke at our center between 2005 and 2009, n=39 patients had distal MCA (M2 and M3) branches occlusion. This study included 22 males and 17 females with mean age of 69.25±12.75). In our study group, 84.6% (n=33) were hypertensive, 35.9% (n=14) were diabetic, 61.5% (n=24) had hyperlipidemia and 30.7 % (n=12) had atrial fibrillation. The mean NIHSS on admission was 14.64 and that on discharge was 8.71. The primary outcome measures following the intervention were intracranial hemorrhage (ICH) rate, mortality and recanalization rate. **Results:** In our study group 73.1% (n=30) patients had lesions in the M2 branches, 23% (n=9) in M3 and 3.9% (n=2) in M4 branches. 92.3% (n=36) of these patients were treated with IA tPA. In addition, one patient received mechanical thrombectomy using Penumbra device. Of the other 3 patients, one had recanalization with mechanical clot disruption, one had spontaneous improvement of symptoms during the procedure and one had attempted mechanical thrombectomy with penumbra device. None of the patients had MERCI clot retrieval, angioplasty or stenting. Partial-to-complete recanalization (TIMI 2-3) was achieved in 64% (n=25) patients. Post procedure symptomatic hemorrhages were found in 9.7% (n=4) patients. The mortality rate was 19.5 % (n=8) in our study group. **Conclusions:** Emergent

endovascular therapy is a relatively safe and efficacious strategy for patients with acute ischemic stroke secondary to distal MCA clots in our experience.

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Th P207

Acute Stroke Trials in the 1st decade of the 21th Century

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Background: Instructed by past successes and failures, numerous acute ischemic stroke trials have been conducted during the 1st decade of the 21th century. The evolution of trial designs during this epoch has not been systematically delineated. **Methods:** Systematic search of MEDLINE and clinical trial registries was performed to identify all acute ischemic stroke trials published between Jan 2000 and Dec 2009. Data for trial designs, interventions, baseline characteristics, and results were abstracted and analyzed. **Results:** 104 acute ischemic stroke trials were identified, enrolling 36,059 patients (median, IQR: 117, 41-403), including 9 phase 1, 56 phase 2, 7 phase 2b/3a and 31 phase 3 trials. A total of 66 agents or interventions were tested. Fifty trials tested neuroprotectives, 38 reperfusion therapies, 7 antithrombotics, and 9 others. Eighty-three (79.8%) trials were randomized, including 62 double-blind, 14 PROBE-design, 2 single-blind, and 5 non-blinded. Initial stroke severity was measured by NIHSS in 88 (84.6%) trials and employed as an inclusion criterion in 85 (81.7%) trials. Modified Rankin Scale was the most common outcome scale, employed in 74 trials, of which 20 used analytical techniques other than a simple mRS dichomization. Intravenous TPA was tested or allowed to be combined with tested interventions in 27 trials. Baseline characteristics of enrolled patients were: mean age, 67.6±5.0; male, 54.9%; median NIHSS (IQR), 13 (9.5-14.9); median onset to treat, 5.5 h (4.1-12.3). Twenty-five trials were early terminated due to futility, safety concerns, slow enrollment or other reasons. Among phase 3 trials, 5 (16%) were positive on the primary efficacy outcome. However, two failed on replication (NXY-059 and ancrod); one tested statin withdrawal rather than new therapy addition; and one was single-center, open-label, evaluator-blinded (minocycline). Intravenous TPA between 3-4.5 h from onset was the only well-validated positive trial. Hemicraniectomy for malignant infarction, though individual trials failed to meet the primary efficacy endpoints, was another intervention of which the efficacy was demonstrated by a pooled analysis. **Conclusion:** Acute ischemic stroke trials during the opening decade of the 21th century were larger in size, had earlier treatment initiation, and used more nuanced outcome analysis than previously. RCT results added intravenous TPA between 3-4.5 h and hemicraniectomy for malignant infarction to the arsenal of proven therapies for acute ischemic stroke.

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Th P208

Ascertaining the Impact of Distal Embolization in Recanalization Therapies for Acute Ischemic Stroke

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Background: Endovascular recanalization therapies (ERT) are evolving to expand options for treatment of acute ischemic stroke. While these procedures have higher rates of recanalization than IV tPA, they are associated with higher rates of symptomatic hemorrhage and mortality. Another possible complication of recanalization therapy, either intravenous or intra-arterial, is distal embolization (DE). We investigated the clinical impact of DE in patients treated with various methods of recanalization therapy. **Methods:** Ischemic stroke patients from 2005 to 2010, treated with either IV tPA alone or ERT with or without IV tPA, were identified in a prospectively maintained database. Post-treatment MR imaging for all patients was evaluated for changes consistent with DE. Catheter angiograms for ERT patients were evaluated for evidence of DE. Successful recanalization (SR) for ERT patients was defined as TICI 2b or 3, and recanalization for IV tPA patients was determined using post-treatment MRA. Variables analyzed included demographics, clinical history, laboratory and imaging findings, method of recanalization, initial NIHSS, and discharge modified Rankin Score (mRS). **Results:** Among 18 patients treated with IV tPA only, the mean age was 67.2 (range 41-97), 55.6% were female, and median initial NIHSS was 11.5. Among 50 ERT patients, mean age was 67.4 (range 29-95), 62% were female, and median initial NIHSS was 18.5. For ERT patients, affected vessels were: ICA - 26%, M1 MCA - 62%, and other - 12%. For IV patients, vessels were: ICA - 11%, M1 MCA - 28%, and other - 61%. Therapies for ERT patients were Merci retriever alone in 50%, Merci retriever plus IV or IA tPA in 27%, IA tPA alone in 6%, and other in 17%. SR was achieved in 32% of ERT. Recanalization was seen on post-treatment MRA in 40% of those receiving IV tPA. SR was seen in 70% of ERT patients with final mRS 0-2, and 23% of those with final mRS 3-6 (P=0.012). DE was seen in 46% of ERT patients and 13% of IV tPA patients. DE was not more common among ERT patients who achieved SR than those who did not, 36% vs 28% (P=0.76). DE after recanalization was seen in 50% of IV tPA patients. For ERT patients, new DWI lesions consistent with DE were seen in 60% of those with final mRS 0-2, and 32.5% of those with mRS 3-6 (P=0.22). For IV tPA patients, new DWI lesions were seen in 0% of those with discharge mRS 0-2 and 37.5% of those with discharge mRS 3-6 (P=0.24). The mean discharge mRS of ERT patients was lower in those with DE, 3.2 vs 4.1 (P=0.03). DE was more common in ERT patients with non-disabled (mRS 0-2) than disabled outcomes, 80% vs 37.5% (P=0.04). For ERT patients who had both DE and SR, 60% had final mRS 0-2 and 7.5% had final mRS 3-6 (p<0.001). **Conclusions:** Distal embolization occurs in nearly half of patients treated with endovascular recanalization therapy. Good functional outcomes are associated with the presence of DE, likely because DE indicates recanalization of occluded vessels.

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Th P209

Eligibility Determinations By "Witnessed Onset" and "Last Seen Normal" Principles are Not the Same Among Acute Ischemic Stroke Patients Undergoing Endovascular Treatment

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Background: Acute ischemic stroke treatment is guided by therapeutic windows. These windows are decided upon the moment of witnessing the stroke onset or when the patient was last seen normal. However, "last seen normal" principle is likely to overestimate the time interval between symptom onset and treatment. **Objective:** To compare outcomes between eligibility determination by "witnessed onset" and "last seen normal" principle among acute ischemic stroke patients undergoing endovascular treatment. **Methods:** Consecutive patients with acute ischemic stroke who underwent emergent endovascular treatment over five years were included. A univariate analysis was performed comparing patients who had a "witnessed onset" of stroke symptoms and patients in whom the moment they were "last seen normal" was considered the time of onset. Patient characteristics and outcomes were compared between the two groups including age, admission National Institutes of Health Stroke Scale score (NIHSSS), discharge NIHSSS, discharge modified Rankin scale (mRS), and in-hospital mortality. **Results:** A total of 172 patients, mean age ± standard deviation (SD) 67±15.3 years and mean National Institutes of Health Stroke Scale Score (NIHSSS) ±SD of 15.4±6.3 had a witnessed stroke time of onset (Group A). 41 patients, mean age ±SD 61.1±15.5 and mean NIHSSS ±SD 14.1±6.4 underwent endovascular treatment based on the time the patient was last seen normal (Group B). There were no significant differences in baseline characteristics, admission NIHSSS, proportion of patients in whom the NIHSSS improved ≥4 points or returned to 0 (A=64.5%, B=78.1%; p=0.098), and in whom discharge modified Rankin Scale was 0-2 (A= 32.9%, B= 36.6%; p=0.66). There was a significant difference in the median time interval between symptom onset or last seen normal and microcatheter placement in the cerebral circulation (A= 299 minutes, B= 563 minutes; p=<0.001). The rate of symptomatic intracerebral hemorrhage was lower in group B (7% vs 0%; p=0.08) and there was a trend to a significantly higher in hospital mortality in patients with witnessed acute ischemic stroke symptom onset (A= 23.3%, B=9.8%; p=0.051). **Conclusion:** There appears to be differences in outcomes between patients treated based on eligibility determination using witnessed stroke symptom onset or last seen normal symptom principles. Future guidelines must consider these two patient populations in a separate context.

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Th P210

Comprehensive Stroke Centers Do Not Experience the Weekend Effect for Intra-Arterial Therapy

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Background: Epidemiologic studies have shown that patients admitted on weekends are less likely to undergo necessary invasive cardiac procedures, contributing to the higher mortality rate seen in weekend admissions. Little is known about how this "weekend effect" influences intra-arterial therapy (IAT). The purpose of this study was to investigate time to treatment and outcome in patients receiving IAT on weekends as compared to weekdays. **Methods:** Data from UT Houston and UAB IAT databases were examined. Patients lacking time of admission data were excluded. The remaining patients were divided into those arriving on a weekend (17:01 Friday to 08:59 Monday) and those arriving on a weekday. Demographics, NIHSS, admission glucose, and time to treatment were examined. Primary outcomes including mortality, favorable discharge disposition (home or inpatient rehab), and length of stay, symptom onset to IAT treatment times, recanalization rates and sICH were compared between weekend and weekday admissions. **Results:** A total of 392 consecutive patients were screened (299 UT, 93 UAB). 392 patients met inclusion criteria. 33% percent (129/392) arrived on a weekend. Demographics and outcomes are shown in Table 1. After adjusting for age, baseline NIHSS and admission glucose, weekend admission was not a significant independent predictor of sICH (OR=0.91, 95% CI=0.44-1.87, p=.80), favorable disposition (OR=1.11, 95% CI=0.66-1.85, p=.70), favorable mRS at discharge (OR=1.12, 95% CI=0.61-2.07, p=.71), or death (OR=0.89, 95% CI=0.48-1.63, p=.70). **Conclusions:** Our study found no weekend effect on intra-arterial therapy. Our results may not be generalizable, however, as our experience reflects centers with

24/7/365 stroke team coverage and response to the ED. Emergency medical services (EMS) should consider delivery of patients to centers that provide equal coverage on weekends and weekdays.

Table 1	Weekday Admissions	Weekend Admissions	p value
Age, median (min-max)	61.8±14.8	60.7±14.3	.477
Gender, % male	55.9%(147/263)	55.0%(71/129)	.873
Race/Ethnicity, %			
African American	25.9%(68/263)	39.5%(51/129)	
Asian	4.9%(13/263)	2.3%(3/129)	.039
Caucasian	62.0%(163/263)	51.2%(66/129)	
Hispanic/Mexican	7.2%(19/263)	7.0%(9/129)	
NIHSS, median (min-max)	17(0-40)	18(0-40)	.041
Admission glucose, median (min-max)	76-388	79-355	.53
IAT patients treated with IV t-PA, %	61.8%	55.6%	.24
Symptom onset to IAT, median (min-max)	318(81-5421)	300(126-5938)	.745
Successful recanalization (TICI ≥2b), %	67.6%(171/253)	66.7%(84/126)	.857
Length of stay (LOS), median (min-max)	7(1-71)	7(1-48)	.619
Favorable discharge disposition (Home or Inpatient Rehab), %	47.8%(122/255)	47.7%(61/128)	.972
Discharge mRS, median (min-max)	4(0-6)	4(0-6)	0.86
Discharge mRS 0-1, % (excellent outcome)	14.2%(35/247)	16.3%(20/123)	.594
Discharge mRS 0-2, % (good outcome)	22.7%(56/247)	23.6%(29/123)	.845
sICH, %	11.0%(29/263)	10.9%(14/129)	.959
In-hospital mortality, %	22.7%(56/247)	21.1%(26/123)	.738

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Th P211

Safety and Efficacy of Early Blood Pressure Reduction in Acute Ischemic Stroke: An Interim Analysis of VENTURE Trial

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Background and purpose: The management of blood pressure (BP) in acute stage of ischemic stroke has been a matter of debate. Based on the equivocal evidence and marked variations in clinical practice, we designed a prospective, randomized, open-labeled, blinded endpoints, multi-center study to evaluate the Valsartan Efficacy oN modesT blood pressUre REduction in Acute Ischemic Stroke (VENTURE). **Methods:** Eligible patients were randomly assigned to receive valsartan or no anti-hypertensive agents during 7 days after symptom onset by the central computerized system. Inclusion criteria were 1) age older than 18 years, 2) admission within 24 hours from onset, 3) treatment initiation within 48 hours, 4) NIHSS 2-21, and 5) Systolic BP 150-185 mmHg. Primary endpoint was death or dependency measured as modified Rankin Scale (mRS) score ≥ 3 at 90 days. Safety endpoints were early neurological deterioration within 7 days and mortality at 90 days. Thirty centers have participated in this trial since October 2008. We conducted planned interim analysis after capture of 50% of primary endpoint from all enrolled patients. Analysis was based on intention to treat. This study is registered, number NCT00874601. **Results:** At the time of interim analysis, the adjudicated primary endpoints were obtained from 147 patients of the valsartan group and 143 patients of the control group were evaluated in this interim analysis. During the first 7 days, BP reduction was greater in valsartan group than in control group: mean reduction of diastolic BP was 2.82 mmHg (95% confidence interval [CI] -4.94 ~-0.88, p=0.005); and mean reduction of systolic BP was 1.93 mmHg (95% CI -7.06 ~0.72, P=0.055). However, there was no difference in the primary endpoint, combined death or dependency at 90 days, between valsartan (n=34, 23.4%) and control (n=35, 24.6 %) groups (risk ratio [RR] 0.94, 95% CI 0.55-1.61; p=0.812). In addition, the safety endpoints, early neurological deterioration within 7 days, mortality at 90 days, did not differ between the two groups (RR 1.86, 95% CI 0.83-14.17; p=0.13). **Conclusion:** This interim analysis shows that early BP reduction with valsartan did not increase dependency or mortality at 90 days. VENTURE trial will continue to establish the efficacy and safety of modest BP reduction in patients with acute ischemic stroke.

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Th P212

Imaging Criteria as a Surrogate Marker for Outcomes after Intra-arterial Thrombolysis.

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Background: We sought to determine which neuro-imaging parameters during intra-arterial (IA) thrombolysis can predict good functional recovery. **Methods:** With institutional approval from each center (Saint Louis University and University of Pittsburgh Medical Center), we retrospectively reviewed cases of anterior circulation acute ischemic stroke treated with IA thrombolysis from January 2006 to March 2010. We excluded patients who sustained a symptomatic intracerebral hemorrhage or who did not have available pre-treatment neuro-imaging. We also excluded those without a pre-treatment collateral score based on the protocol described below. We assessed time from symptom onset to end of procedure as well as imaging parameters including: the extent of infarction, based on the Alberta Stroke Program Early CT Score (ASPECTS), site of angiographic occlusion, succesful recanalization (defined as a Thrombolysis in Myocardial Infarction score of ≥2), and extent of intracranial collaterals. Collaterals were stratified according to a previously published classification system based on the most proximal reconstitution of the middle cerebral artery (MCA) segments. Hence, any reconstitution of the M1 segment was given a score of 1, any reconstitution upto the M2 segment was given a score of 2, etc. A score of 5 represented absent collaterals. Other parameters studies were recanalization with an ASPECTS score > 8 and recanalization with a collateral score ≤2 and ≤3 respectively. Our endpoint was good functional outcome defined as a modified Rankin Score ≤2. A step-wise logistic regression analysis was performed to determine imaging predictors of a good outcome. **Results:** A total of 83 patients were reviewed with complete imaging assessments. The mean National Institutes of Health Stroke score was 12 (s.d. 4). Treatment was completed within 545 minutes (mean, s.d. 338 minutes). Of these 83 patients, 20 had concomitant tandem occlusions of the internal carotid artery (ICA) origin and either the intracranial ICA or M1 or M2 MCA segments. Other sites of occlusion included M1 MCA only (34), M2 MCA only (7), and intracranial ICA only (22). Recanalization occurred in 49 patients (59%). Good outcome was observed in 22 patients (26%). In the regression model, duration of ischemia, baseline ASPECTS score, site of occlusion, extent of collaterals, and successful recanalization did not predict good recovery. Only recanalization in the setting of a pre-treatment ASPECTS score > 8 predicted good outcome (OR 5.4, 1.8-16 95% CI, p=0.002). **Conclusions:** Good outcome after IA thrombolysis is likely to occur when patients with minimal signs of infarction are selected for therapy. This study suggests that imaging-based criteria may be more meaningful for IA thrombolysis patient selection than time-based assessments. Successful recanalization in selected patients may serve as a surrogate marker for subsequent studies.

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Th P213

Soft Hyperdense Lesions on CT Scan after Endovascular Treatment in Acute Ischemic Stroke of the Anterior Territory: a Sign of Successful Recanalization and Good Outcome

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Pérez de la Ossa N, Ribó M, Pagola J, Millán M, Gomis M, Silva Y, Aleu A, Rodríguez-Campello A, Cuadras P, Álvarez-Sabín J, Dávalos A. Soft Hyperdense Areas on CT Scan after Endovascular Treatment in Acute Ischemic Stroke of the Anterior Territory: a Sign of Successful Recanalization and Good Outcome. Hyperdense lesions (HDL) on CT scan 24h after endovascular treatment (EVT) may differ from those observed after intravenous thrombolysis since contrast extravasation contribute to the lesions. We aimed to assess the patterns of HDL and their predictive value on clinical outcome. **Methods:** Retrospective analysis of 109 patients with anterior territory AIS treated with EVT in two comprehensive stroke centers. CT scans at 24h were reviewed by two independent observers and HDL were classified according to location, morphology and maximum Hounsfield units as (1) soft HDL within the infarct area (HU65) and (3) subarachnoid HDL. Good outcome at 3 months was considered as a Rankin scale 0-2. **Results:** 35/109 (32.1%) patients showed HDL: soft HDL in 12 (11%), bright in 15 (13.8%) and subarachnoid in 8 (7.3%). Age, gender, risk factors, prior antithrombotic therapy, vital signs, site of arterial occlusion, early CT signs of ischemia and bridging therapy with iv tPA were not different between groups, but admission serum glucose levels were higher in all HDL groups compared with the non-HDL group (p=0.02). Good outcome at 3 months was achieve in 40% of non-HDL, 64% of soft, 0% of bright and 25% of subarachnoid HDL patients (p=0.004). Using non-HDL as reference group, soft HDL pattern had an OR 7.9 (IC95% 1.4-44.8) of good outcome, and bright and subarachnoid HDL patterns combined had an OR 6.9 (IC95% 0.8-61) of poor outcome after adjustment for stroke severity and serum glucose. Non-HDL and soft HDL patterns were associated with a similar rate of complete recanalization (57% vs 68%), higher than in bright (13%) and subarachnoid (37%) patterns (p=0.01). Accordingly, hypodensity volume at 24 h was smaller in the non-HDL (median 25mL) and soft (26mL) groups than in the bright (100mL) and subarachnoid (187mL) groups (p=0.005). **Conclusion:** Soft HDL on 24h follow-up CT after EVT are associated with higher rate of complete recanalization and good clinical outcome. In contrast, bright parenchymal and subarachnoid HDL may be considered as clinically significant complications of the endovascular procedure.

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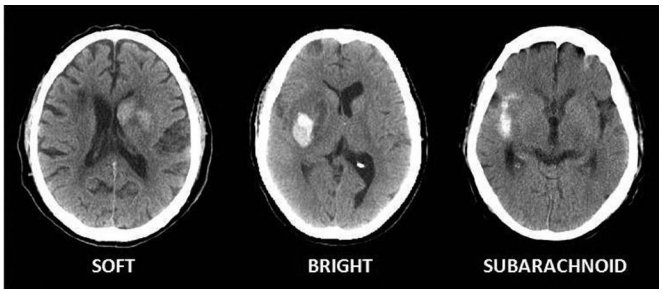

Th P214

Successful Endovascular Acute Stroke Intervention Prevents Infarct Core Growth

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Objective: CT perfusion (CTP) imaging has been widely applied in patients with acute ischemic stroke for assessing penumbral tissue aiding in decision-making on whether or not endovascular therapy (ET) should be initiated. However, there is a paucity of data showing that successful recanalization prevents infarct growth in those with baseline penumbra. We sought to determine if successful ET can prevent lesion growth. **Methods:** Using an IRB-approved prospectively collected interventional registry, we identified consecutive patients with anterior circulation strokes during a 2year period treated with ET who also had interpretable CTP and 24-48hour post-ET follow-up CT (patients with follow-up MRI were excluded). Data collected included demographics, admission NIHSS, glucose, and blood pressure, IV-lytic and ET technique, time from stroke onset to ET, and final recanalization (TIMI) grade. Only patients with CBF lesion 20% larger than CBV lesion and ischemic core (defined as CBV $<$50% of contralateral normal side) 1/3 MCA territory were offered ET. For outcome assessment, ABC/2 volume calculation was obtained from CBV slices and compared with the corresponding follow-up CT slices showing the final infarct. **Results:** Twenty patients (65% women) with a mean age of 63$\pm$19years were identified. Mean admission NIHSS, glucose, and blood pressure were 18$\pm$4, 146$\pm$47mg/dl, and 152/79$\pm$25/18mmHg respectively. The mean time to ET was 6.9$\pm$4.2hours. All received endovascular embolectomy in addition to IV-tPA in 5(20%) or IA-tPA and/or GPIIb/IIIa antagonist in 8(40%) patients. There was no statistically significant difference in baseline demographics and endovascular techniques between 14 patients (70%) who achieved recanalization (TIMI 2-3) and 6(30%) who did not (TIMI 0-1). No statistically significant infarct growth existed in patients with recanalization (13.5$\pm$8.5cm^3 CBV vs. 11.4$\pm$8.1cm^3 follow-up CT, p=0.54). However, in patients who did not recanalize (TIMI 0-1) there was a significant increase in final infarct volume (15$\pm$5.73cm^3 vs. 28.4$\pm$10.3cm^3, p=0.034), which was similar to the initial CBF volume (21.7$\pm$8.7cm^3 vs. 28.4$\pm$10.3cm^3, p=0.30). **Conclusion:** In our experience, successful ET was associated with tissue salvage in patients with acute ischemic stroke. CTP data can be used to predict the final infarct size in patients with ischemic stroke and may be helpful in therapeutic decision making. These results need to be validated in future studies.

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Th P215

The Internal Maxillary Artery is the Key External to Internal Carotid Collateral in Carotid Occlusion

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Background and Purpose: Carotid occlusion is present in 10-15% of acute stroke patients. The risk of recurrent stroke in this condition is related to the adequacy of collateral supply. A number of external carotid to internal carotid artery anastomoses have been described. No previous study has delineated the frequency of these anastomotic sites in carotid occlusion. **Methods:** We retrospectively identified subjects with carotid occlusion diagnosed on digital subtraction angiography between July 2009 and June 2010. We collected data on demographic variables; past medical history; and the cause of occlusion. The type of external to internal carotid artery anastomosis was categorized into one of 9 categories based on review of the digital subtraction angiogram. Patients were also divided into those with ipsilateral ischemic symptoms and those with no ischemic symptoms. **Results:** Thirty-seven patients were identified; the average age was 57 +/- 12 years and 22 (59%) were male. Twenty-one patients (67%) had external to internal carotid artery anastomoses; all of these were through branches of the internal maxillary artery. Eleven (52%) anastomoses arose from the mandibular segment of the internal maxillary artery (middle meningeal to recurrent meningeal artery = 7; middle meningeal to inferolateral trunk = 4; accessory meningeal to vidian artery = 1) and 9 arose from the pterygopalatine segment (artery of the foramen rotundum to pertrous internal carotid = 4; other pterygopalatine branch to ophthalmic = 5). Those presenting with ischemic symptoms were numerically less likely to have external to internal carotid collaterals (13/28; 46% versus 3/9; 33%; NS). **Conclusion:** External to internal carotid artery anastomoses are numerically more common in those presenting incidentally than in those presenting with ischemic stroke symptoms. The internal maxillary artery branches were the source of collateral supply in all patients in who external to internal carotid artery anastomoses were identified. This important potential source of hemispheric collateral must me carefully evaluated in patients with atherosclerotic carotid occlusion and those being considered for therapeutic internal maxillary or internal carotid sacrifice.

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Th P216

Mutant Erythropoietin without Erythopoietic Activity is Neuroprotective Against Ischemic Injury

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EPO has robust neuroprotective effects both in animal models of ischemic brain injury and stroke patients. However, treatment of stroke with EPO requires large doses and multiple administration, which may potentially result in multiple high risk factors for stroke patients. Alternate strategies to reduce erythropoietic activity and other potential side effects of EPO will greatly improve its clinical applications for the treatment of stroke patients. We have successfully generated a novel mutant EPO (MEPO) containing a single amino acid mutation which completely lacks erythropoietic activity. The objective of this study is to test the neuroprotective effect of MEPO in the clinically relevant middle cerebral artery occlusion (MCAO) model. Both an *in vitro* EPO-dependent proliferation assay and an *in vivo* mouse model assessed the loss of erythropoietic activity. MEPO completely lost the ability to induce myeloid proliferation, even at high concentration (100U/ml, equivalent to 25 nM). MEPO does not induce increased hemoglobin concentration even when continuously present at high concentrations for 4 weeks, while wild-type EPO increases hemoglobin concentration significantly at week 2 and 4, indicating a loss of erythropoietic function. To determine whether MEPO has neuroprotective effects, we first tested it in the primary neuronal culture model of NMDA neurotoxicity. Primary cortical neurons were pretreated with MEPO at 1U/ml, and then challenged with 200 μM of NMDA. Pre-treatment with MEPO significantly decreased the necrotic cell death as determined by LDH release and the number of neurons that contained condensed apoptotic-like nuclei following NMDA toxicity. The neuroprotective effects of MEPO were further determined in the murine model of focal ischemia and reperfusion. Intraperitoneal administration with MEPO (5000U/kg) at the onset of post-ischemic reperfusion significantly reduced the infarct volume ($p<0.01$ versus vehicle), and improved neurological deficit scores assessed at 72 hr following ischemia ($p<0.05$), with a similar efficacy as the wild type EPO. MEPO does not change physiological parameters and cortical blood flow. Taken together, our study shows that MEPO is non-erythropoietic, but neuro-protective against ischemic brain injury. Thus, MEPO may be potentially used as a safe therapeutic agent in stroke as well as in other neurological diseases.

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Th P217

Evidence of Bias and the Bias of Evidence in Neurothrombectomy for Stroke

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Background: Endovascular therapies for acute ischemic stroke, including neurothrombectomy, have been limited by evidence for safety and efficacy. Randomized controlled trials (RCTs) provide a means to establish these critical aspects, yet these studies are shaped by regulatory agencies and guidance documents. We analyzed the United States Food and Drug Administration (FDA) guidance document on neurothrombectomy to ascertain levels of evidence for each element in proposed use for developing clinical trial protocols. **Methods:** Details of the most recent guidance document on neurothrombectomy were analyzed to identify specific elements. These variables were classified as selection criteria, baseline stroke features, randomization, angiography details, baseline clinical measures, imaging methodology, adverse events, outcome parameters, and analysis techniques. Literature search identified all publications on endovascular therapy prior to and after the 2007 guidance document. AHA/ASA levels of evidence (A-C) were established for each variable. **Results:** Identified guidance document variables included 22 selection criteria, 9 baseline stroke features, presence of randomization, 7 angiography details, 3 baseline clinical measures, 8 imaging methods, 15 adverse events, 17 outcome parameters, and 5 on analysis techniques. Levels of evidence for use of these 87 variables were determined from 78 reports (n=2,743) before and 54 reports (n=2,535) after the 2007 guidance was issued. No evidence was available for 11/87 (13%) and only level C for 26/87 (30%) of variables in the 2007 guidance. After 2007, 6/11 (55%) criteria without evidence remained devoid of further data. Previous level C variables remained without more data in 24/26 (92%), yet level B was attained in 2 after 2007. Increased levels of evidence were established for 4 selection criteria, 1 baseline clinical measure, 1 imaging method, and 1 type of adverse event. At present, 42/87 (48%) of variables in the 2007 guidance have level A evidence, 11/87 (13%) level B, 28/87 (32%) level C, and 6/87 (7%) no evidence. **Conclusions:** Only limited evidence was available for 43% of variables stipulated in the 2007 guidance on neurothrombectomy. Trial design considerations that are limited in prior evidence or biased may erroneously alter data from subsequent studies. Evidence for interventional strategies is increasing but such emerging data should be used to continually revise regulatory guidance and future stroke trial design.

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Th P218

Rapid Formation Of Cerebral Microbleeds After Carotid Artery Stenting

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Background A recent study showed that new microbleeds (MBs), comprising small areas of signal loss on T2*-weighted gradient-echo (GRE) MRI, can develop rapidly after acute ischemic stroke. We hypothesized that MBs may develop rapidly after carotid artery stenting (CAS), and investigated the frequency of new MBs after CAS. Methods We retrospectively examined 78 consecutive patients who underwent CAS for carotid stenosis and MRI before and after CAS between April 2009 and June 2010. We defined new MBs as those that newly appeared on follow-up GRE MRI. Results Among the 78 patients, 21 (26.9%) had baseline MBs and 9 (11.5%) developed new MBs. Among the 9 patients with new MBs, 6 had no MBs on baseline MRI and 3 had MBs on baseline MRI. The presence of baseline MBs was not significantly associated with the formation of new MBs (P=0.696). **Conclusions:** The results of this study suggest that new MBs can develop rapidly after CAS. Therefore, particular attention should be paid to patients at risk of cerebral hyperperfusion, which is a cause of cerebral hemorrhage. Further studies are required to investigate the factors associated with the formation of new MBs after CAS.

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Th P219

The Usefulness Of DWI-aspect Score As A Predictor Of Short And Long-term Clinical Outcome Following Emergency Reperfusion Therapy In Severe Acute Ischemic Stroke Patients

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Object: It is unclear whether or not DWI findings on admission in patients presenting serious neurological symptoms due to acute internal carotid artery (ICA) or middle cerebral artery (MCA) occlusions can predict their clinical outcome following reperfusion therapy. The purpose of our retrospective study was to investigate whether or not DWI-Albert stroke program CT (ASPECT) score before initiating reperfusion therapy can be a predictor of clinical outcome. Methods We retrospectively analyzed the ischemic stroke patients 1) who were admitted to our institution from 2004 to 2009, 2) with serious neurological symptoms of GCS of 12 or less, or NIHSS score of 10 or more, 3) who had total occlusion of the ICA or MCA displayed by MRA, and 4) who underwent emergency reperfusion therapy including intravenous rt-PA therapy or endovascular therapy within 6 hours from stroke onset. Patient's baseline features, MRI/DWI findings before initiating reperfusion therapy using DWI-ASPECT score, MRA findings, stroke subtypes, onset-to-treatment time (OTTT), NIHSS score on admission (AD-NIHSS),and the 7th day (7D-NIHSS), and mRS at 3 months (3M-mRS) were evaluated. We used univariate and multiple regression analysis to assess whether or not 7D-NIHSS and 3M-mRS were correlated with patient's baseline features, DWI-ASPECT score, stroke subtypes, OTTT and AD-NIHSS. Result Seventy six patients were analyzed, median age was 77, women were 37, median follow-up period was 6 months(range: 1-72 months), median AD-NIHSS was 18, median DWI-ASPECT score was 7, median OTTT was 2.67 hours, seventeen patients underwent intravenous rt-PA therapy within 3hours, and fifty-nine patients endovascular reperfusion therapy. Median 7D-NIHSS was 10,median 3M-mRS was 3.5. DWI-ASPECTscore on admission was significantly correlated with 7D-NIHSS and 3M-mRS (rs=-0.39,pysis demonstrated the DWI-ASPECTscore was the only independent predictor for 7D-NIHSS (β=-0.39 t=-3.36, P=0.001), and also one of the independent predictors for 3M-mRS (β=-0.28 t=-2.53, P=0.014) . **Conclusion:** In severe ischemic stroke patients who underwent emergency reperfusion therapy for the ICA or MCA occlusion within 6 hours, DWI-ASPECTscore before initiating the therapy was the independent predictor for NIHSS score on 7th day and mRS at 3month following reperfusion therapy. The higher DWI ASPECT score can predict favorable 7-day and 3-month clinical outcome.

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Th P220

Does Arrival By Ambulance Predict Acute Stroke Intervention In Young Adults?

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Background: The incidence of stroke in young adults is less common and increasing age is a potent risk factor for stroke. It is important to identify young patients presenting with stroke symptoms to the ED to institute intravenous t-PA or intra arterial intervention and minimize long term disability. **Objective:** We hypothesized that arrival to ED by ambulance would increase the chances of acute stroke intervention with intravenous t-PA or intra arterial procedures. We also assessed other variables as predictors of receiving acute stroke therapy, including initial presentation to a Primary Stroke Center (PSC). **Methods:** Seventy seven patients aged 15-49 years diagnosed with ischemic stroke by vascular neurologists and followed at a Comprehensive Stroke Clinic from 2001-2010 were enrolled into the study. Data was collected on age, race, gender, arrival to ED by ambulance, whether brain MRI was done within 48 hours of admission, if the initial hospital at presentation was a PSC and intervention by intravenous t-PA or intra arterial procedures. **Results:** Seventy seven patients with mean age of 37.9 years were reviewed which included 57.1% women. Caucasians composed 57.1%, African Americans 37.7% and 3.9% were others. 48.3% of patients arrived by ambulance, 53.2% got MRI brain within 48 hours of admission, and 23.4% initially presented to a PSC. Twelve (15.8%) patients had acute stroke intervention - 7 intravenous tPA, 3 IA tPA and 2 mechanical thrombectomies. The results of the univariate analysis by Fisher's exact test are listed in the table

	Number included in analysis	Intervention (12)	No intervention (64)	P values
age	76	37.8±8.3	37.9±8.3	0.94
Male sex	76	5(41.7)	27(42.2)	0.97
Black race	73	6(50.0)	23(37.7)	0.52
Arrived by ambulance	60	9(90.0)	20(40.0)	0.005*
MRI within 48 hours	62	3(27.3)	30(58.8)	0.09
Initial presentation to a PSC	76	3(25.0)	14(21.9)	1.00

Multivariable analysis (n = 57) showed that the age (p = 0.991), male sex (p = 0.894) and primary stroke certification (p = 0.937) was not significantly associated with patients getting acute stroke intervention. Arrival by ambulance was significantly associated with acute stroke intervention in young adults (p = 0.016). Patients who received intervention were less likely to get MRI within 48 hours of admission (p = 0.049). **Conclusion:** Young adults with stroke symptoms were more likely to receive acute stroke intervention if they arrived by ambulance. Factors such as increased awareness of stroke symptoms, patient's decision to call 911, evaluation of patients by EMS personnel and their communication to the ED staff for preparedness and prompt action on arrival may play a role in increased rate of stroke intervention in young stroke patients who arrive by ambulance to the ED. Larger, multi-center studies should address whether PSCs are more likely to provide either IV thrombolysis or interventional therapies.

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Th P221

Anterior Circulation Large Vessel Occlusion Stroke Presenting With Mild Symptoms. Clinical Outcomes And Safety Of Intravenous Thrombolysis And Endovascular Treatment

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Background: While intravenous thrombolysis (IVT) for stroke presenting with mild symptoms (SPMS) is an accepted paradigm in most centers, there is considerable heterogeneity in practice regarding endovascular treatment (EVT) for SPMS not responding to or ineligible for IVT. We sought to assess IVT and EVT for SPMS due to anterior circulation large vessel occlusion (ACLVO) with regard to safety and clinical outcomes. **Methods:** Retrospective analysis of thrombolysis databases in two university hospitals. Patients with ACLVO confirmed by transcranial Duplex or angiography and NIHSS score <8 treated either with IVT only or with EVT were selected. Successful recanalization was defined as TIMI 2 or 3 in the EVT group and as TIBI 4, 5 or improvement of 1 or more in the TIBI scale in the IVT group. Symptomatic intracerebral hemorrhage (SICH) was defined as PH2 with neurologic deterioration, and favorable outcome as modified Rankin score of <3 at 3 months**Results:** Thirty-seven patients were treated with IVT only and 23 patients were treated with EVT (in 8 cases EVT followed IVT due to lack of recanalization). Median [quartiles] age was 73 [60,77] in the IVT group and 62 [52,66] in the EVT group ($p=0.021$), and median NIHSS score before treatment was 6 [4,7] and 4.5 [2,6] ($p=0.068$), respectively. Distribution of the site of occlusion in IVT/EVT groups was M1 30%/43%, M2 67%/13%, terminus ICA 3%/17% and tandem ICA-MCA 0%/26% ($p=0.001$). Recanalization at 2 hours after treatment occurred in 64.3% of the IVT and in 90.5% of the EVT group ($p=0.047$). SICH appeared in 10.8% and 5.3% ($p=0.491$), favorable outcome was recorded in 70.3% and 73.3% ($p=0.789$) and mortality in 10.8% and 15.8% ($p=0.444$). After exclusion of M2 occlusions in each group similar results were obtained. **Conclusions:** Patients with stroke presenting with mild symptoms and anterior circulation large vessel occlusion show high rate of favorable outcome and low mortality whether treated with IVT or EVT. Successful recanalization was more frequent with endovascular therapy. In these selected patients, treatment with EVT appears to have similar safety profile and outcomes than IVT only. Larger, prospective studies are needed to confirm these preliminary findings.

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Th P222

Early Ischemic Lesion Recurrence Pattern In The Borderzone Region After Thrombolysis

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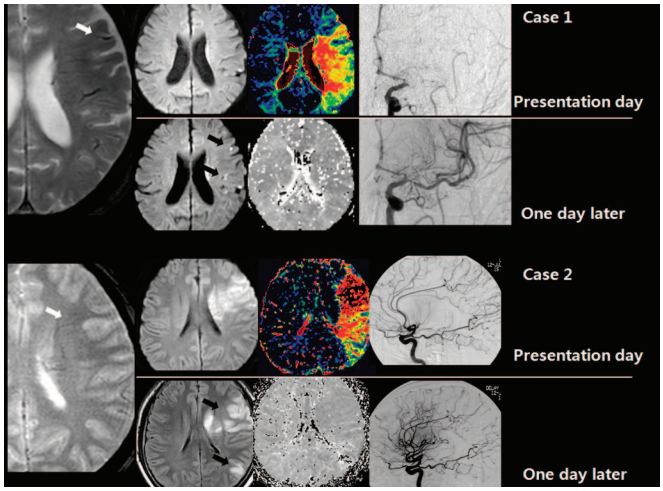
Background : The ischemic penumbra is defined as ischemic tissue which is functionally impaired and is at risk of infarction and has the potential to be salvaged by reperfusion. The possibility of penumbral region would be highest in the borderzone territory in ischemic stroke, and this be continued after thrombolysis. **Methods:** From Samsung Acute Stroke Registry, 35 patients with middle cerebral artery stroke were included, who were treated by combined intravenous and intra-arterial thrombolysis or intra-arterial thrombolysis within 6 hours of symptom onset and they underwent brain MRI including diffusion-weighted and perfusion-weighted imaging and follow up MRI at 1st and 7th day. We analysed the early ischemic lesion recurrence pattern in the borderzone region in the good recanalization group (TIMI 2 or 3) and divided these lesions into cortical borderzone and deep subcortical borderzone infarction. Results : Ischemic lesion recurrence in the borderzone region developed in the 14 patients of the 21 patients shown good recanalization. All these patients except one showed clinical improvement on NIHSS scores (improvement range 1 to 14). Cortical borderzone (CBZ) recurrence lesions were seen in patients with slow antegrade/retrograde collateral flow($N=8$) and isolated deep subcortical borderzone (IDSBZ) recurrence lesion in patients with fast collateral flow($N=6$). These patients with borderzone lesion recurrence in the good recanalization group showed residual stenosis in occlused vessel or focal incomplete recanalization after thrombolysis on angiography, and the recurrence lesion developed around dark vessels on T2*-weighted gradient echo imaging. The patients with CBZ recurrence lesion showed larger diffusion-perfusion (Tmax$\geq$8 sec) mismatch (69.5 ± 46.5 vs 46.7 ± 40.2, $p=0.014$) and initial NIHSS scores (13.8 ± 4.4 vs 11.8 ± 3.9, $p=0.217$) than the patients with IDSBZ recurrence lesion. **Conclusion:** Early ischemic lesion recurrence pattern in the borderzone region represents temporal and spatial progression of the penumbra even though good recanalization and vessel flow status before and after thrombolysis. Figure legend : Isolated deep subcortical borderzone infarction recurrence is seen on follow up diffusion weighted imaging and residual stenosis on angiography in case 1 patient. Cortical borderzone infarction recurrence and salvaged lesion are seen on follow up diffusion weighted imaging in case 2 patient.



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Th P223

Early Benefit of Thrombolysis is Limited to Strokes of Minor and Moderate Severity

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Introduction: A large number of parameters have been identified as predictors of early outcome in patients with acute ischemic stroke. The present work analyzes a wide range of demographic, metabolic, physiological, clinical, laboratory and neuroimaging parameters in a large population of consecutive patients with acute ischemic stroke and aims to identify independent predictors of early clinical course. Subjects and**Methods:** We used prospectively collected data from the Acute STroke Registry and Analysis of Lausanne (ASTRAL). All consecutive patients between 01/2003 and 12/2008 admitted to our stroke unit and/or intensive care unit with ischemic stroke within 24 hours after onset of symptoms were analyzed. Univariate and multivariate analysis was performed to identify significant association with NIHSS score at admission and 24 hours. We also sought for any interactions between identified predictors. **Results:** 1446 patients were included in the analysis. In multivariate analysis, NIHSS at 24 hours was associated with NIHSS at admission ($\beta=1$, $P<0.001$), initial glucose ($\beta=0.05$, $P<0.002$) and thrombolytic intervention ($\beta=-2.91$, $P<0.001$). There was a significant interaction between thrombolysis and NIHSS at admission ($p<0.001$), indicating that the latter does not improve early clinical course in patients with severe stroke. **Conclusions:** Thrombolytic treatment, lower initial glucose and lower initial stroke severity predict favourable early clinical course. However, the effect of thrombolysis was limited to minor and moderate stroke, and was absent in patients with severe stroke.

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Th P224

Facilitated Recanalization Observed During Endovascular Treatment of Tandem Extracranial Carotid and Intracranial Occlusions: Incidence and Clinical Outcomes

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Background: The optimal treatment method for tandem occlusions (TO) of the extracranial internal carotid artery (ICA) and intracranial arteries is not well established. One approach consists of proximal followed by distal recanalization, during which the process of facilitated recanalization (FR) may be observed. FR involves spontaneous intracranial recanalization immediately following proximal revascularization, thereby obviating the need for intracranial intervention. We aimed to evaluate the incidence of this phenomenon in a cohort of TO patients treated via endovascular means at our center. **Methods:** Consecutive patients with TO of the ICA origin and an intracranial artery (i.e. ICA terminus, M1 middle cerebral artery [MCA], or M2 MCA) were identified in the UPMC endovascular acute stroke database. In all cases, treatment approach consisted of proximal revascularization with angioplasty and stenting followed by, if necessary, intracranial recanalization. The incidence of FR and clinical outcomes in the FR versus non-FR group was analyzed. Endpoints were successful recanalization (TIMI $\geq$ 2), parenchymal hematoma (PH), and good clinical outcome (mRS $\leq$ 2) at 3 months. **Results:** Of

77 identified TO patients, all of whom received proximal stenting, 18/77 (23.4%) patients experienced FR. Successful recanalization was observed in 18/18 (100%) patients in the FR group vs. 42/59 (71.2%) patients in the non-FR group ($p<0.01$). FR was more likely to occur with tandem M1 or M2 MCA occlusions than with carotid terminus occlusions (OR 5.5, 95% CI [1.15, 26.1], $P<0.01$). PH occurred in 3/18 (16.6%) FR cases vs. 6/59 (10.2%) non-FR cases ($p=0.52$). Good clinical outcome was achieved in 9/18 (50.0%) FR patients vs. 23/59 (39.0%) non-FR patients ($p=0.78$). **Conclusions:** In TO patients treated with endovascular therapy consisting of initial proximal recanalization, FR occurs in nearly a quarter of patients in whom further (intracranial) intervention is no longer necessary. FR is associated with a statistically significant higher incidence of successful recanalization and a non-statistically significant higher incidence of good clinical outcome compared to patients without FR. FR represents one of the advantages of proximal recanalization as the first step in endovascular treatment of TO.

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Th P225

MRI Turn-Around Time for Acute Stroke Imaging Remains Unchanged Over a 2 Year Time Period

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Introduction: Advanced MRI imaging for acute ischemic (AIS) stroke is increasingly used for patient selection for endovascular therapy (ET) beyond the 3-4.5h window. Such studies increase the door-to-groin puncture time. The amount of time added and whether it decreases with practice over time is unclear. Hypothesis: We hypothesized that time added by advanced MRI imaging will decrease over time with practice. **Methods:** We analyzed MRI turn-around times in the MRI In Acute Management of Stroke (MIAMIS) study. MIAMIS is a single university center retrospective study that has enrolled consecutive suspected AIS patients with presenting NIHSS $>$ 5 or aphasia with acute stroke 0 - 14 hours from symptom onset undergoing emergent MRI imaging for possible ET. The MRI protocol included diffusion, perfusion, FLAIR, gradient echo and brain MR angiogram. No systematic review of MTAT was done on an ongoing basis. The MRI turnaround time (MTAT) was defined as MRI order time to time of last MRI image. We retrospectively analyzed MTAT over four consecutive six month time periods. We also analyzed the time taken for the actual MRI protocol as time taken from first image to last image. Statistical analysis was done with SPSS ver16.0 using one-way ANOVA. **Results:** From February 2008- February 2010, 87 patients (45 F, 42M) underwent acute advanced MRI selection for ET at our university medical center. Patients were evaluated by a neurology attending at 0 - 8 hours and 8-14 hours from symptom onset in 81 patients (94.2%) and 7 patients (5.8%) respectively. The mean age was mean age 67 (range 28 - 92) and median NIHSS 18 (range 6 - 29) within 14 hours of symptom onset. The overall MTAT was a mean of 99.5 ± 54.7 minutes. The MTAT in minutes was 87.5 ± 28.33, 85.4 ± 21.01, 114.5 ± 20.05, 101.2 ± 51.4, during the time periods of Feb'08-July'08, Aug '08-Jan'09, Feb'09-July'09, Aug '09-Jan'10 respectively. There was no significant difference in the MTAT amongst these time periods. The time from first to last MRI image in minutes for the overall time period was a mean of 27.7 ± 24.5 and 29.9 ± 9.9, 26.1 ± 12.3, 24.7 ± 8, 29.1 ± 15.2 over the same time periods as above. Again there was no significant difference amongst these times. **Conclusions:** The time added by advanced MRI imaging is substantial and remains constant despite practice over time. System strategies to shorten MRI order to MRI start time and technical advances to shorten time for MRI sequences are needed to decrease the delay added by advanced imaging.

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Th P226

Different Clinical Evolution and Infarct Volume across Final TIMI grades in Endovascular Reperfusion Therapies for Acute Stroke. Should we Redefine Recanalization End-points in IA Trials?

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Background: Endovascular reperfusion trials for acute stroke show up to 60-80% recanalization(RE) rates but good functional outcome in only 30-40% of cases. Definition of RE is usually considered as final Thrombolysis In Myocardial Infarction(TIMI) 2-3 score. We hypothesized that clinical course, infarct volume and outcome vary widely across TIMI grades in successful RE as defined in IA trials. Patients&Methods: Consecutive patients treated with IA reperfusion therapy after acute intracranial occlusion were analyzed. Vascular occlusion and RE were classified according to TIMI grade. Infarct volume was measured on 24h CT. Early clinical evolution was determined by NIHSS at baseline, after 24h and at discharge. Clinical improvement was defined as a decrease $\geq$4 from baseline NIHSS. Long-term outcome was evaluated by modified Rankin Scale at 3months(Good functional outcome: mRS$\leq$2). **Results:** 120 patients were included; 56(46.6%) female, mean age 70.5 ± 11.8y and median baseline NIHSS 19 (IQR 15-23). Arterial occlusions were: 62(51.6 %) MCA, 42(35.8%) TICA, 13(10.8%) BA and 2(1.7%) PCA. At the end of IA procedure, 81(67.5%) patients achieved RE defined as TIMI 2-3. Patients who RE had better clinical evolution after 24h(55.6 vs 16%), at discharge(64.4 vs 12%), smaller infarct(mean 111.6 ± 153 vs 239.8 ± 168.2 cc), lower mortality(25.3 vs 56.7%) and better functional outcome(41.5 vs 3.8%) than patients who didn't ($p<0.01$). However, significant differences between TIMI grades were detected in the RE group(Table). Patients who achieved TIMI 3 had 5-times smaller infarct and 2-times better early clinical course than those with TIMI 2a. The rate of futile RE (RE without achievement of good functional outcome) was: 81%, 70.4% and 36.4% in TIMI 2a, 2b and 3 respectevely ($p<0.01$).In patients who RE, achievement of TIMI 3 independently predicted good functional outcome after adjusting for baseline NIHSS and time to RE(OR 5.8; 95% CI 1.4-23.9; $p=0.014$). **Conclusion:** RE after endovascular treatment is associated with clinical improvement but relevant differences are detected between TIMI grades. Patients with TIMI 2a have 2-times more frequently futile RE than TIMI 3 patients. More strict RE end-points in IA reperfusion trials are required to refine the translation of RE into good clinical outcome after endovascular procedures.

N (%)	TIMI 2a 21 (17.5)	TIMI 2b 27 (22.5)	TIMI 3 33 (27.5)	p A: TIMI 2a vs 2b B: TIMI 2b vs 3 C: TIMI 2a vs 3
Improvement after 24h	5 (23.8)	13 (48.1)	24 (72.7)	A: 0.163 **B: 0.017*** **C: 0.001***
Improvement at discharge	9 (42.9)	17 (62.9)	26 (78.8)	A: 0.221 B: 0.151 **C: 0.017***
Infarct volume	252.3±54.7	77.6±25.3	49.7±17.3	A: 0.221 B: 0.358 **C: 0.003***
Mortality	7 (33.3)	9 (33.3)	3 (9.1)	A: 0.995 **B: 0.038*** **C: 0.038***
mRS≤2	4 (19)	8 (29.6)	21 (63.6)	A: 0.381 **B: 0.031*** **C: 0.006***

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Th P227

2D-3D Computational Fluid Dynamics Add Novel Dimension to Recanalization Scores in Acute Middle Cerebral Artery Occlusion

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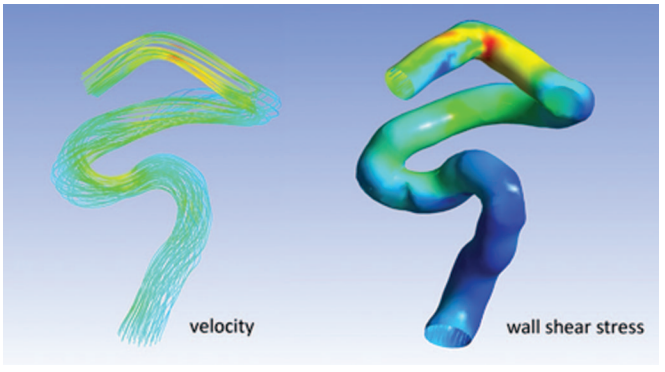
Background: Angiographic scores for recanalization, or restoration of arterial patency in proximal segments after endovascular therapy, remain limited to categories of either partial or full. Hemodynamic changes at the site of recent thrombosis and catheter manipulation are unexplored. We implemented a method to convert static 2D, or standard biplane, angiography images to 3D and run computational fluid dynamic (CFD) calculations to depict subtle hemodynamic features in recanalized segments of the proximal (M1) middle cerebral artery (MCA) in acute stroke. **Methods:** Consecutive acute ischemic stroke cases treated with endovascular therapies for M1 MCA occlusion were analyzed. A single angiography frame from corresponding AP and lateral projections was used from a subset of 40 cases with angiographic scores of full recanalization, or Arterial Occlusive Lesion (AOL) of 3. Dedicated software was used for 3D reconstruction of orthogonal biplane images followed by post-processing with the Vascular Modeling Toolkit. Numeric simulations conducted with ANSYS CFX on a Cray supercomputer rapidly provided 3D images of velocity streamlines, wall shear stress, and shear strain rate. **Results:** Hemodynamic simulations from the AOL 3 recanalization cases following endovascular therapy revealed numerous distinctions on an individual case basis. Uniform velocity streamlines and evenly distributed shear stress was noted in some cases, yet other cases revealed focal abnormalities.



Such subtle hemodynamic perturbations were not evident on review of the standard biplane angiography images. Interestingly, downstream perfusion showed considerable variability despite "full" proximal recanalization at AOL 3. **Conclusions:** 2D-3D conversion of biplane angiography images may be used to generate CFD calculations of velocity, wall shear stress and shear strain rate from routine angiograms. 3D depictions of subtle hemodynamic abnormalities may distinguish seemingly identical cases of AOL 3 recanalization. The impact of these hemodynamic features on downstream perfusion remains to be explored.

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Th P228

Poorer Outcomes and Mortality in Elderly Patients treated with Intra-arterial Therapies for Acute Ischemic Stroke

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Background: Intra-arterial therapies for acute ischemic stroke are more commonly being used. While these therapies improve recanalization and are generally thought to improve outcomes, the relative benefit in the elderly population >/= 80 years of age) is unknown. As the population ages and increasing numbers of elderly patients are being seen, it is important to assess the impact of intra-arterial therapies in this population. **Objective:** To assess procedural factors and outcomes, particularly mortality, in elderly patients undergoing intra-arterial therapies for acute ischemic stroke. **Methods:** From a prospective maintained database, patients undergoing intra-arterial therapy for acute ischemic stroke at Cleveland Clinic Foundation from June 2007 - February 2010 were retrospectively reviewed. Demographic information, imaging characteristics, procedural factors, and periprocedural and long-term outcomes were collected. Univariate and multivariate analysis was performed (JMP, SAS, Cary, NC)**Results:** 77 patients (median age 79, 55% females) had outcome data and were included in the analysis. 43 (56%) patients were >/= 80 years. Characteristics and baseline NIHSS were similar between the elderly group (age >/= 80 years) and non-elderly group, with the exception of a large proportion of atrial fibrillation seen in the elderly group (62.5% vs. 43.9%, $P<0.05$). Intravenous tissue plasminogen activator (tPA) was less commonly received by the elderly patients (17.6% vs. 31.0%, $P<0.05$). Elderly patients had the Penumbra aspiration device (Penumbra Inc., Alameda, CA) more commonly attempted as the first device (54.6% vs. 18.2%, $P<0.05$). Stroke etiology was less commonly large artery atherosclerosis (16.1% vs. 51.5%, $P<0.05$) and more commonly cardioembolic (77.4% vs. 40.5%, $P<0.05$). Discharge NIHSS score (17 vs. 8, $P<0.05$), discharge modified Rankin scale score (4.1 vs. 2.5, $p< 0.05$), and mortality at 90 days (42.4% vs. 18.4%, $P<0.05$) were higher in the elderly group. In multivariate analysis, age (OR 4.5) and having not received IV tPA (OR 4.8) were significant predictors of increased mortality ($p<0.05$). **Conclusion:** Elderly patients treated with intra-arterial therapy appear to have significantly worse outcomes as compared to non-elderly patients. Prospective studies and randomized trials focusing on this subgroup are required to assess the best treatment strategy in this population.

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Th P229

Safety of Periprocedural Heparin in Acute Ischemic Stroke Endovascular Therapy: The Multi MERCI Trial

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Background: There are limited data on the safety of periprocedural heparin in acute ischemic stroke endovascular therapy. **Methods:** We performed a post-hoc analysis of patients enrolled in the Multi MERCI trial to compare baseline characteristics and clinical outcomes between patients who received periprocedural heparin (HEP+) with patients who did not receive periprocedural heparin (HEP-). **Results:** Of 164 patients enrolled in the Multi MERCI trial, 51 (31%) had documentation of periprocedural heparin use (n=24) or non-use (n=27); median dose of periprocedural heparin was 3000 U. Baseline and procedural characteristics were similar between the two groups though HEP+ patients were more likely to have vertebral or basilar occlusion than HEP- patients (16.7% vs 0%, p=0.04). There was no significant difference in rates of all intracerebral hemorrhage, symptomatic intracerebral hemorrhage, parenchymal hemorrhage type 2, clinically significant procedural complications or 90-day mortality between the two groups. In multivariable analysis, a 90-day good outcome (mRS 0-2) was associated with age (OR, 0.92; 95% CI, 0.86 to 0.98; p=0.0104), final revascularization success (OR, 6.86; 95% CI, 1.39 to 33.81; p=0.0179) and periprocedural heparin use (OR, 5.89; 95% CI, 1.34 to 25.92; p=0.0189). **Conclusions:** In this small subgroup of the Multi MERCI trial, periprocedural heparin use in acute ischemic stroke endovascular therapy was not associated with increased rates of intracerebral hemorrhage or 90-day mortality. The improved 90-day good outcome among patients undergoing mechanical thrombectomy combined with periprocedural heparin requires further study in a larger cohort.

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Th P230

Multiple Merci Passes And Endovascular Treatment Outcomes: A Single Center Experience

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Objectives: To evaluate the safety and efficacy of mechanical thrombectomy in acute ischemic stroke (AIS) patients using multiple attempts of the MERCI device. Background: The MERCI retrieval device is an FDA approved clot retrieval device used to treat AIS. Often patients need more than one attempt using this device to achieve revascularization of the occluded vessel. There is little data regarding the influence of the number of attempts on outcomes. **Methods:** Retrospective chart review was performed between 2005 and 2009 of patients with AIS. Patients who underwent treatment with MERCI device were selected for further review (n=37). We divided our study population into three groups - those who had one pass, 2 passes, or greater than 2 passes of the MERCI device for thrombectomy. This study included 13 males and 24 females with mean age of 67.8±14.96. 89.2% (n=33). The primary outcome measures following the intervention were recanalization rate, intracranial hemorrhage (ICH) rate and mortality rate. **Results:** All the patients had lesions in the anterior circulation (16 internal carotid and 21 proximal middle cerebral artery). 29 received intra-arterial tPA in addition to MERCI and 22 received a combination of IV and IA tPA. Penumbra device was used additionally in 6 patients - 1 each being in group 1 and 2, while 4 patients were in Group 3. Amongst our study group, 40.5% (n=15) had one pass (group1), 27% (n=10) had 2 passes (group 2), 32.4% (n=12) had 3 or more passes (group 3). Group 1 (Pass 1): Partial-to-complete recanalization (TIMI 2-3) was achieved in 80% (12/15) patients. Post procedure symptomatic hemorrhages were found in 13 % (n=2) patients. The mortality rate was 20 % (n=3). Group 2 (2 passes): Partial-to-complete recanalization (TIMI 2-3) was achieved in 70% (7/10) patients. Post procedure symptomatic hemorrhages were found in 30% (n=3) patients. The mortality rate was 20 % (n=2). Group 3 (>2 passes): Partial-to-complete recanalization (TIMI 2-3) was achieved in 66% (8/12) patients. Post procedure symptomatic hemorrhages were found in 33% (n=4) patients. The mortality rate was 41.6 % (n=5). **Conclusions:** Patients in whom revascularization is achieved with one attempt of the MERCI device tend to have better out comes than those requiring multiple passes and had lesser rates of symptomatic hemorrhages and mortality.

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Th P231

Initial Assessment of CT Perfusion Parameters to Determine Thresholds for Infarct Core, Ischemic Penumbra, and Benign Oligemia in Patients undergoing Endovascular Revascularization Therapy (ERT)

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Background and Purpose: CT Brain Perfusion (CTP) is emerging as a powerful tool in guiding stroke therapy. Limited studies have shown CTP parameter (MTT, CBF, CBV) thresholds that differentiate ischemic penumbra from infarct core. The purpose of this study is to determine CTP parameter thresholds (MTT, CBF, CBV) that differentiate infarct core, penumbra, and benign oligemia in patients undergoing ERT. **Methods:** A retrospective review of a prospective clinical database for patients receiving ERT was performed from 05/01/07 through 12/31/09. Among 14 patients found, five patients were excluded secondary to absence of perfusion imaging. The remaining 9 who underwent CTA and CTP on presentation, and delayed noncontrast CT (NCT) or MRI, >24 hrs after stroke were divided into either the persistently occluded group or the revascularized group, based on results from catheter angiography immediately post-intervention. CTP source images were processed by Philips Extended Brilliance Workshop 3.5.0.2254 with anterior cerebral artery as the Arterial Input Function and superior sagittal sinus as the Venous Output Function. A MATLAB graphic user interface developed by our research team was used to co-register perfusion maps with delayed final infarct NCT or MRI. For both groups, the final infarct was outlined as region of interest (ROI) on the NCT or MRI. For the occluded group, the region that survived ($n_{ROI}=32$) was defined as benign oligemia (BO) while the region that infarcted ($n_{ROI}=35$) represented the original penumbra (P) and infarct core (IC). In contrast, for the revascularized group, the region that survived ($n_{ROI}=35$) encompassed the original benign oligemia and penumbra while the final infarct ($n_{ROI}=22$) was defined as the infarct core. In addition, contralateral regions with normal perfusion were used for normalization. **Results:** In the occluded group, ROI's that demonstrated absolute CBV > 3.5 (ml/100g) and CBF > 30 (ml/min/100g) trended towards survival in absence of revascularization (benign oligemia). Relative values did not appear to demonstrate any predictive trends. For the revascularized group, ROI's with absolute CBV > 3.0 and CBF > 20 were potentially salvagable (penumbra). Relative CBV < .7 and CBF < .3 were also potentially salvageable following successful ERT. (Figure 1)

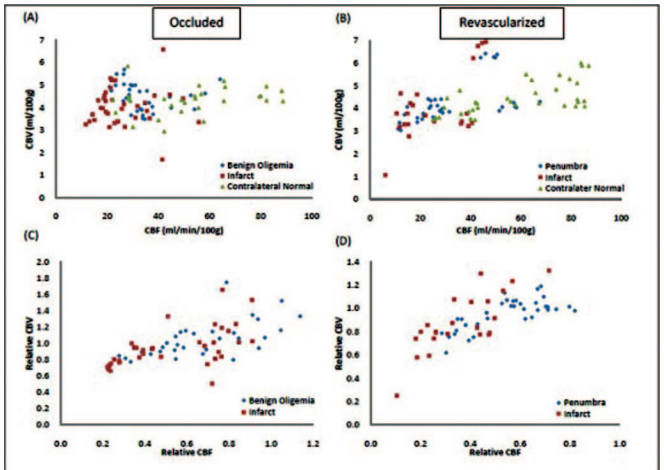

Figure 1: Scatterplots of (A) absolute and (C) normalized CBV vs. CBF for occluded patients; similar scatterplots (B)(D) for revascularized patients.

Conclusions: CBV and CBF may have the potential to differentiate infarct core from ischemic penumbra in patients undergoing ERT. Further prospective study of these parameters in patients experiencing successful revascularization will be required to further refine these thresholds.

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Th P232

Endovascular and Surgical Management of Symptomatic Rotational Vertebral Artery Compression Resulting from Cervical Spondylosis

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Background: Cerebral ischemia due to cervical spondylosis causing vertebral artery (VA) compression during rotation of the head has been rarely described in literature. The authors describe endovascular and surgical management of three patients with symptomatic rotational VA compression from cervical spondylosis. **Methods:** From 2003 to 2010, the authors encountered three patients who presented with vertebrobasilar insufficiency (VBI) or stroke and demonstrated VA compression during dynamic VA angiogram performed with the patient's head turned to the right, left, and in neutral position. We reviewed the pre-operative computed tomography (CT) scan of cervical spine to identify the cervical spondylotic bone spur and the level of the VA foramenal compression. We reviewed the angiographic and clinical outcome as determined by Modified Rankin Scale (mRS) at 90 days. **Results:** Pre-operative CT scan of the cervical spine showed that all three patients (mean age 60.6 + 3.2) had compression of VA by cervical spondylotic bone spur at the level of the C4-5 uncinate process. Two patients developed left VA compression and near occlusion when the head was turned to left beyond 30 degrees during VA angiogram. One patient developed near occlusion of the right VA when the head was turned to right beyond 30 degrees. Two patients underwent endovascular stent placement in the symptomatic VA. One of these patients had intra-procedural complication of transient thrombosis of the stent requiring intra-arterial thrombolysis with complete recanalization. Second patient treated with stent developed recurrent symptomatic rotational VA compression at 6 months requiring angioplasty followed by left posterior cervical C4-5 and C5-6 foraminotomy at 2 years. The third patient underwent left posterior cervical C4 facetectomy and C3-5 lateral mass fixation. All patients had immediate angiographic resolution of rotational VA compression after initial treatment. Favorable outcome (mRS of 0-1) at 90 days was observed in two patients. The mean clinical follow up period was 23 + 21 months (range 3 to 41 months) with no recurrent stroke. **Conclusions:** Endovascular stent placement and open surgical decompression of VA may be performed to treat symptomatic rotational compression of VA due to cervical spondylosis. Dynamic cerebral angiogram or computed tomographic angiogram (CTA) should be performed for accurate diagnosis. Open surgical decompression of VA with or without fusion may provide more long-term durability than endovascular treatment using stents.

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Th P233

Cerebral Blood Volume Reversibility Within Infarcted Lesions: The Need for Lengthened Scan Times

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Objective: During the first few hours of stroke onset, the use of multimodal neuroimaging to delineate penumbra from dead tissue could aid in the crucial decision to use thrombolytics. This study examined the temporal profile of CT perfusion (CTP)-derived cerebral blood volume (CBV) within confirmed infarcted lesions from admission, 24 hours and 5-7 days post stroke to determine if reduced CBV could normalize. **Methods:** Twelve patients underwent a NCCT, CTP/CTA scan within 6 hours of stroke onset, CTP/CTA at 24 hours, and CTP, NCCT at 5 to 7 days post stroke. Final infarct volumes were manually traced on 5 to 7 day NCCT images. These infarct regions of interest (ROIs) were superimposed onto admission, 24 hour and 5 to 7 day post CTP-derived perfusion weighted (PW) and CBV functional maps. Using custom software, PW maps were used to segment gray and white matter in the infarct ROIs. A weighted average CBV for gray and white matter was calculated from the averages of all infarct ROIs. Additionally, intra-patient CBV differences were observed. At each time point, time-density curves (TDC), taken from the ipsilateral hemisphere of each patient, were examined for truncation of the contrast wash out phase; CBV is underestimated when TDC truncation is present. **Results:** CBV (mean ± stdev; ml/100g) for gray and white matter within infarcts at admission and 24 hours and 5 to 7 days were 1.8±0.71, 1.6±0.27, 1.8±0.51 and 1.1± 0.47, 1.2±0.46, 1.2±0.44, respectively when averaged over all patients. Unpaired t-tests showed no significant differences in CBV between time points for both brain tissue types ($p > 0.05$). However, a repeated measures ANOVA displayed a statistically significant within-subjects effect ($p < 0.05$) with a Greenhouse-Geisser correction. These differences were observed in patients whose TDC was truncated at any time point. **Conclusion:** Within tissue that progressed to infarction, we showed that CTP derived CBV, averaged over all patients, remained consistently low out to 7 days. Examining within patient differences, CBV was underestimated with increasing TDC truncation. We speculate this truncation is not physiological, and likely associated with insufficient scan time length. As such, low CBV lesions do not normalize and, when scan time is properly managed, could aid with final infarct volume quantification.

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Th P234

Post-intervention TCD Examination May Predict Outcome In Acute Ischemic Stroke Patients With Successful Intra-arterial Intervention

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Background and Purpose: Arterial recanalization has been associated with improved outcomes after intravenous and intraarterial (IA) acute stroke therapy. We hypothesize that transcranial Doppler (TCD) finding after IA intervention might provide an important predictor of short-term clinical outcome among those with recanalization. **Methods:** From a prospective registry of acute ischemic stroke patients who underwent IA therapy, patients treated with internal carotid artery (ICA) or middle cerebral artery (MCA) lesions with follow-up TCD examination within 3 days after IA intervention were retrospectively analyzed. Only those with recanalization at thrombolysis in myocardial infarction (TIMI) flow grade 2 or better in MCA territory were included. TCDs were conducted to assess the mean flow velocity (MFV) of the MCA, and findings were classified into two categories based on thrombolysis in brain ischemia (TIBI) grading system: Poor Flow group was defined by TIBI grade ≤3 with MFV diminished by ≥30% compared to contralateral MCA. Normal Flow group included patients without decreased MFV compared to contralateral MCA (TIBI >3). Poor clinical outcome was defined as in-hospital death or decompressive craniectomy. **Results:** Forty-eight subjects were included from period March 2007 to February 2010. Twenty-three (48%) subjects had ICA lesions and 25 (52%) had MCA lesions, including 2 (4%) isolated M2 lesions. TCD examination was conducted at a median of 1 day after IA intervention. Poor Flow group had 9 (19%) patients and Normal group had 39 (81%) patients. Poor Flow group was older than Normal group (78 [56-83] versus 57 [47-70], $p=0.023$). National Institute of Health Stroke Scale [NIHSS] score was 16 [6-22] in Poor Flow group and 16 [10-20] in Normal group ($p=0.959$). Gender and the frequency of ICA occlusions were similar. Residual TIMI flow grade 3 was seen in 3 (33%) patients with Poor Flow group and 14 (36%) with Normal group ($p=1.000$). Three (33%) patients in Poor Flow group and 2 (5%) in Normal group died during hospitalization ($p=0.039$). Two (22%) patients in Poor Flow group and 2 (5%) patients in Normal group underwent decompressive craniectomy ($p=0.155$). Thus, poor in-hospital outcome was significantly more frequent in Poor Flow group than Normal group (44% versus 10%, $p=0.031$). After adjustment for age, Poor Flow group was significantly associated with worse outcome (Adjusted odds ratio: 11.1, 95% confidence interval: 1.5-80.1, $p=0.012$). **Conclusion:** Residual TIBI flow grade on follow-up TCD examination after IA intervention may predict patient outcome beyond angiographic residual TIMI flow.

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Th P235

Implementation Of A Patient Selection Protocol For Intra-arterial Therapy Increases Treatment Rates In Acute Ischemic Stroke

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Background: Limited evidence supports current patient selection for intra-arterial therapy (IAT) in acute ischemic stroke (AIS) and selection strategies are highly variable. Patients who present with proximal intracranial artery occlusion (PAO), small infarct volume, and large volume of tissue-at-risk may be most likely to benefit (LTB) from intra-arterial intervention. We sought to determine characteristics of protocol adoption and treatment rates in association with implementation of a service-wide patient selection protocol for IAT. **Methods:** We conducted a retrospective review of our prospectively acquired Get With the Guidelines Stroke (GWTG-S) database from 01/2007-06/2009. All patients underwent clinical evaluation by a vascular neurologist, diagnostic neuroimaging, and laboratory testing on admission. The protocol for IAT patient selection was implemented in 03/2008. Patients were defined as LTB if they had brain imaging completed within 6 hours from last known well (LKW), had NIHSS score ≥8, baseline

infarct volume ≤ 100 cc, and evidence of PAO (internal carotid artery or middle cerebral artery M1 or proximal M2 segments). **Results:** Among the 1,348 AIS patients who presented to our hospital within the study period, 118 subjects (8.7%) met criteria for LTB (mean age 66±14.8 years; 40% women; 93% Caucasian). Of those LTB, 62 (52%) underwent IAT. There was a significant increase in rates of IAT after protocol implementation (61% vs. 40%, P<0.02). Compared with those who were not treated, patients selected for IAT were older (75±14 vs. 70.3±15 years, P<0.03), received IV tPA prior to IAT more often (58.6% vs. 41.4%, P<0.02), had shorter median LKW to arrival time (2.7 vs. 3.5 hours, P<0.02), and were less often diabetic (11.3% vs. 26.8%, P<0.03). Among LTB patients, univariate predictors of IAT were increasing LKW to arrival time (OR 0.8, 95%CI 0.6-0.9 *per hour*), increasing number of calendar months within the study period (OR 1.1, 95%CI 1.02, 1.2, *per month*), IV tPA use (OR 0.6, 95%CI 0.4, 0.9), and diabetes (OR 0.4, 95%CI 0.1, 0.9). Following multivariable adjustment, only age (OR 0.9, 95%CI 0.8, 0.9 *per year*) remained an independent predictor of IAT. The predominant reason for no IAT in the LTB group was late presentation in the intervention window or concerns about reliability of the reported LKW time (21%). There was no association between use of IAT and either the individual stroke staff involved (n=12) or their years of experience (p=0.6). **Conclusions:** Most AIS patients did not meet our criteria for LTB, and only 52% of those defined as LTB overall received IAT. Adoption of the protocol increased use of IAT over time, across all stroke staff members. Further exploration of factors associated with the reasons for non-treatment, and the impact of IAT on outcomes, is necessary.

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Th P236

Comparison of Ultrasonography and MR Images to High Risked Plaques for Carotid Artery Stenting; with a Pathological Diagnosis

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[Background] Carotid ultrasonography (CUS) has been the first choice for the indication of carotid artery stenting (CAS) for a long time, though the examination alone was difficult to fully predict the risk of complications such as re-stenosis and distal embolism. Plaque findings such as fibrous caps and intramural hemorrhages are the particularly valuable information. We used the MRI plaque imaging together to evaluate the plaque findings for comparison and the accuracy was decided by the pathological results. [Methods] We retrospectively studied consecutively 18 carotid plaque specimens from 18 patients with carotid endarterectomy and compared their findings between MRI plaque imaging and CUS. The study focused fibrous caps and intramural hemorrhage findings inside the plaques. Conventional method was used for CUS. The 1.5T MAGNETOM Avanto MRI performed PROPELLER (Periodically Rotated Overlapping Parallel Lines with Enhanced Reconstruction) sequence for plaque imaging to avoid motion artifacts and also Gd-enhancement images were performed at the plaque portions. Distinguished signal of the plaque was sub-quantitatively analyzed. The pathological diagnosis was given by an independent pathologist unaware of clinical information. [Results] The sensitivity and specificity of CUS in detection of fibrous caps were both 100%, respectively. In the other hand, the sensitivity and specificity of Gd-enhanced PROPELLER-ed MR plaque imaging were 40% and 100%, respectively. Strikingly, the sensitivity and specificity of CUS in the detection of intramural hemorrhages were only 22.2% and 100%, respectively, when the sensitivity and specificity of Gd-enhanced PROPELLER-ed MR plaque imaging were 77.8% and 100%. The accuracy of the Gd-enhanced PROPELLER-ed MR plaque imaging in the detection of intramural hemorrhage was significantly higher in comparison to that obtained using CUS. Also from the pathological results, Gd-enhanced MR images could detect the inflammation inside the vulnerable plaques meanwhile the CUS could not detect well enough numbers in contrary. **Conclusions:** Plaques accompanied with fibrous caps, CUS showed higher detection than MR plaque images, but with intramural hemorrhages seen in vulnerable plaques, which most complications might occur, the enhanced MR plaque images with PROPELLER sequence showed higher accuracy for diagnosis. This concludes that plaques with inflammation are only detected by the MRI, and even with Doppler CUS, the resolution of intramural hemorrhages has its limits. We suggest to use the MR plaque imaging with Gd-enhanced PROPELLER sequence together with the CUS to prevent the complications for high risk CAS cases.

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Th P237

Thrombolysis In Cerebral Ischemia/tici Vs. Thrombolysis In Myocardial Ischemia/ Timi Scores As Assessment Tool For Recanalization In Endovascular Therapy For Acute Stroke Due To M1 Mca Occlusion

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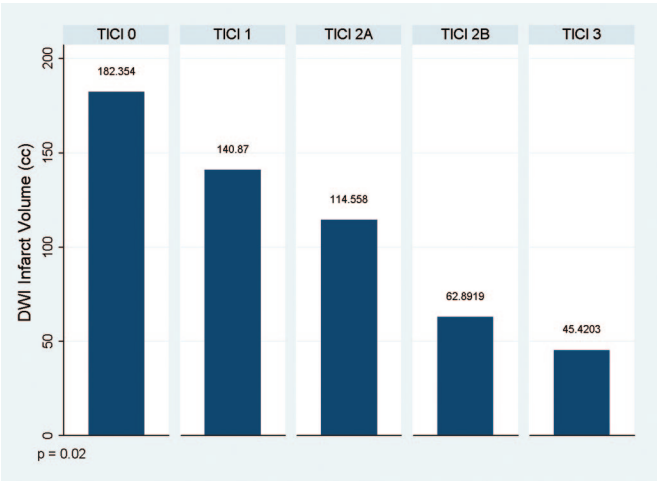
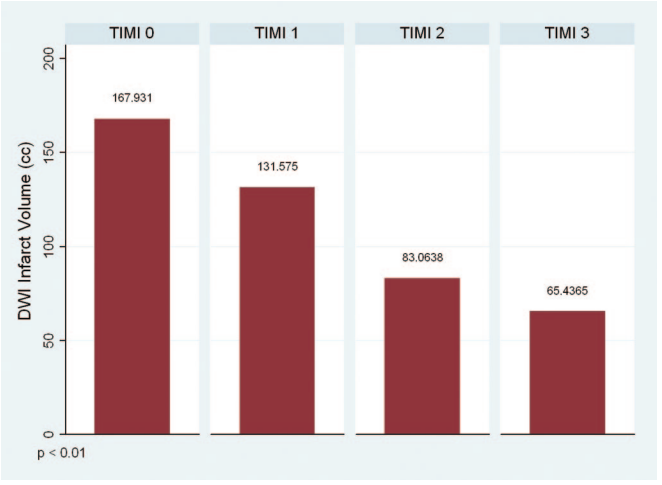
Introduction: There is considerable debate whether TIMI scores vs. TICI scores should be used as recanalization outcome mesurement for endovascular acute stroke trials. We sought to compare these two scoring methods with respect to clinical outcomes and final infarct volumes in a homogenous patient population with M1 MCA occlusion who underwent follow-up MRI imaging. **Methods:** Retrospective review of a prospectively acquired endovascular stroke database was performed. Patients with M1 MCA occlusion and available DWI MRI on follow-up were selected. Collected data included baseline risk factors, clinical and imaging characteristics. Prospectively collected TIMI scores were obtained at the time of the procedure by the treating interventionalist. TICI scores were obtained subsequently by blinded investigators. Post treatment DWI volumes obtained by a blinded investigator using a semiautomated method, and 90 day modified Rankin scores (mRS) were reviewed. Successful recanalization was defined as TIMI grade 2 & 3, TICI grade 2a, 2b or 3 or altenatively as TICI 2b or 3 only. Clinical outcome was considered favorable if 90 day mRS was ≤ 2. **Results:** Between November 2002 and April 2010, we identified 178 patients. TIMI grade 2 & 3 recanalization was achieved in 144 (80.9%) patients. Overall 76 (45.8%) patients had favorable outcomes. A high correlation between TIMI and TICI scores was noted (spearman 0.79, P<0.0001). By TIMI scores, succsesfull recanalization was achieved in 144/178(81%) of patients. By TICI with 2a as cutoff in 150/178(84.27%) and with 2b as cutoff in 98/178 (55%) of patients. In univariate and multivariate analyses all recanalization cutoffs were found to be significantly associated with outcomes (for TIMI23 OR 12.65, 95% CI 2.08-76.72, p=0.006, for TICI2a OR 11.75, 95% CI 1.8-75.6, p=0.009, for TICI 2b OR 9.08, 95% CI 2.7 - 30.5, P<0.0001) A strong corelation between both TICI and TIMI scores and final infarct volumes was found (see graphs). **Conclusion:** Our results indicate that TIMI and TICI scores are highly correlated both with respect to clinical outcomes and with respect to final infarct volumes. The concern that TIMI scores do not adequately reflect tissue reperfusion status post endovascular therapy for acute stroke could not be substantiated by our findings.





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Th P238

Pre-stroke Dementia Is Associated With Poor Outcomes After Thrombolysis Among The Elderly

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Background. Many physicians are reluctant to initiate thrombolysis in acute ischemic stroke (AIS) patients over age 80. We sought to determine whether pre-stroke dementia contributed

to poor outcomes after thrombolysis in these patients. **Methods:** We retrospectively identified all AIS patients age $\geq$ 80 yr who received IV or intra-arterial thrombolysis (IAT) in our Get With the Guidelines Stroke (GWTG-S) database from 2/02-12/09. Vascular risk factors, symptomatic ICH (sICH) and discharge destination were abstracted from the full medical record, using GWTG-S definitions. Dementia was recorded when listed in the past history or when under medical treatment. The primary outcome was discharge destination dichotomized into "good" (discharge to home or rehabilitation facility) vs. "poor" outcome (discharge to skilled nursing facility, hospice, or death). Statistical analyses were Wilcoxon rank sum or Fisher's Exact test, and multivariate logistic regression (with variables $P<0.2$), as appropriate. **Results:** There were 154 AIS patients age $\geq$ 80 who received either IV tPA (n=110), IAT (n=54), or both (n=11). Mean age was 85.8 $\pm$ 4.6 years (range 80-103), 13.6% had pre-stroke dementia, 31.2% were men, 88.3% were white, and 98% were ambulatory prior to admission. Median NIHSS score on admission was 16 (IQR 11-20). Ten patients (6.5%) had sICH, of whom 3 (30%) had pre-stroke dementia, 6 (60%) received IV tPA alone, 2 (20%) received IAT alone, and 2 (20%) received both. Good outcome occurred in 84/154 (54.5%) patients, of whom 64 (59%) received IV tPA, 22 (41%) received IAT, and 3 (3.5%) received both. In-hospital mortality rate was 35% (57% in IV tPA, 54% in IAT, and 11% in IV+IAT group). In univariate analysis, the odds of good outcome were decreased with increasing age (OR 0.94 per year above 80, 95%CI 0.1-1.01), NIHSS (OR 0.89 per point, 95%CI 0.84-0.95) as well as with sICH (OR 0.08, 95%CI 0.01-0.7), IAT (OR 0.4, 95%CI 0.2-0.8), and pre-stroke dementia (OR 0.4, 95%CI 0.1-0.9). There was a trend for good outcome among the elderly who received IV tPA (OR 1.7, 95%CI 0.83-3.4). Following adjustment for age, NIHSS, sICH, IV tPA, IAT, and pre-stroke dementia, only NIHSS (OR 0.9 per point, 95%CI 0.85-0.96) and dementia (OR 0.3, 95%CI 0.11-0.94) independently predicted the decreased odds of good outcome. Furthermore, in a multivariable logistic regression model, only pre-stroke dementia was an independent predictor of in-hospital mortality (OR 13.1, 95%CI 1.2-146) among the elderly treated with thrombolysis. **Conclusions:** Among the elderly, diagnosis of pre-stroke dementia is a powerful independent predictor of poor outcome and in-hospital mortality. This study emphasizes the importance of incorporating dementia into the baseline stroke assessment when considering likely outcomes after thrombolysis. These data warrant future prospective investigations to determine efficacy of acute thrombolysis in the elderly.

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Th P239

Mild Strokes with Large Vessel Occlusion

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Background and Objective: Large vessel occlusion strokes are associated with high mortality (oddsodds ratio-4.5 [95% CI, 2.7 to 7.3; $P<0.001$]) and severe disability. Intravenous (IV) tissue plasminogen activator (rt-PA) results in good outcomes in only 19% patients with large vessel occlusion (internal cerebral artery and middle cerebral artery). Randomized controlled trials studying the role of mechanical embolectomy and intra arterial rt-PA have excluded patients with NIHSS less than 8 (mild ischemic strokes (MIS)). Some cases presenting with MIS symptoms may be harboring a large vessel occlusion and may worsen during hospitalization secondary to stroke progression or recurrent stroke resulting in higher morbidity and mortality. We share our center's experience in the aggressive treatment of MIS patients with large vessel occlusion. Methods We identified cases of ischemic stroke eligible for IA rt-PA or mechanical intervention by time criteria with NIHSS score <8 admitted to Saint Luke's Stroke Center from March, 2006 through April, 2010.We studied the type of intervention done and the outcome. Outcome was defined based on discharge disposition. Discharges to home with or without home health or inpatient rehabilitation were defined as good outcomes. Discharge to nursing homes or hospice homes or death were defined as poor outcomes. Univariate analysis including t-test, Chi-square, and Fisher Exact test was used when appropriate. Results Thirty five mild ischemic strokes (female to male: 1.1:1 and a mean age of 65$\pm$15 yrs ranging from 33 to 86 yrs) were included in this study. Percent of patients treated with IA rt-PA, mechanical embolectomy using the Merci Retriever and a combination of two were 60, 14 and 26 respectively. Only 4 patients (12%) deteriorated as measured by a change of 3 or more points on NIHSS at 24 hours from admission. Five patients (15%) had NIHSS worsening $\leq$2 points. There were no in-hospital mortalities. Internal carotid artery occlusion was seen in 29% patients who underwent angioplasty and stenting. Eighty six percent patients had good outcome. **Conclusion:** Large vessel occlusions can present as mild strokes. Aggressive treatment of these patients can result in good outcome. Randomized controlled trials are needed to test the safety and efficacy of IA rt-PA and mechanical intervention in this patient population.

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Th P240

Subacute Angioplasty And/or Stenting For The Stroke Patients Deteriorating Due To Vertebrobasilar Stenosis

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Background: When acute stroke patients deteriorated neurologically due to vertebrobasilar stenosis, it is not established how to treat them in a subacute stroke stage and how to improve their clinical outcome. The purpose of our retrospective studies was to investigate the feasibility, safety, and effectiveness of subacute angioplasty and/or stenting for the stroke patients deteriorating due to vertebrobasilar stenosis. **Methods:** Included for our retrospective analysis were patients (1) who were admitted in our institution within 72 hours of stroke onset from August 2004 to August 2009, (2) without large diffusion-weighted imaging lesions, (3) with vertebrobasilar stenosis (the degree of stenosis $>$ 50%) and (4) who developed neurological deterioration within 7 days of onset despite intensive medical treatment (an increase of 2 or more points on the National Institutes of Health Stroke Scale (NIHSS)). Some patients gave written informed consent and underwent endovascular treatment (ET) of angioplasty and/or stenting for the vertebrobasilar stenosis from 7 to 14 days after onset (group E) and others not (group C). NIHSS on admission, 7-day NIHSS after admission, NIHSS on discharge, time from onset to admission, hospitalization periods and 3-month modified Rankin Scale (mRS) were investigated between two groups and procedural success rate in group E. **Results:** During study periods, 12 patients were included for analysis. Among them, 4 patients underwent ET (group E) for the vertebrobasilar stenoses, which were successfully dilated. The procedural complications did not occur, whereas other 8 patients did not undergo ET (group C). There were no significant differences in NIHSS on admission, 7-day NIHSS after admission, NIHSS on discharge, time from onset to admission and hospitalization periods between two groups, whereas 3-month mRS (median) was 1.5 in group E and 3.5 in group C ($p<0.05$). **Conclusion:** Subacute angioplasty and/or stenting for the stroke patients deteriorating due to vertebrobasilar stenosis may be feasible, safe and effective in achieving favorable long-term clinical outcome.

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Th P241

Elderly Chronic Stroke Survivors Benefit From Aerobic Treadmill Exercise: A Randomized, Controlled Trial

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Objective: To investigate the effects of 3 months aerobic treadmill training in geriatric chronic stroke survivors on cardiovascular fitness and endurance walking (primary endpoints), and on short distance gait speed, balance, functional leg strength, self-rated mobility and quality of life (secondary endpoints). Design: Randomized-controlled trial (with crossing-over of control patients, www.clinicaltrials.gov: NCT00614224) with 1-year follow-up. Setting: Outpatient rehabilitation center in a large German city. **Methods:** 38 stroke survivors aged 60 years or older with mild to moderate residual hemiparetic gait disturbance were enrolled 6 or more months after their stroke. Participants were randomized to receive 3 months (3x/week) progressive, high intensity aerobic treadmill exercise (TAEX) or conventional care physiotherapy (1-3x/week). Primary outcome measures were cardiovascular fitness (VO2 peak) and sustained walking capacity in 6-minute-walks (6MW). Secondary measures were gait velocity in 10-m walks, Berg Balance Scale, functional leg strength (5 chair-rise), self-rated mobility (Rivermead Mobility Index, RMI) and quality of life (SF-12). **Results:** Thirty-six participants completed the study (18 TAEX, 18 controls). The trial was positive in its primary endpoints: TAEX but not conventional care improved peak exercise capacity (relative improvement in VO2 peak, 30% vs. -1%, $P<0.0001$) and 6MW (22% vs. -1%, $P<0.0001$). Likewise, maximum walking speed (13% vs. -6%, $p=0.01$), RMI ($p<0.05$) and the mental subscore of the SF12 ($p<0.05$) improved more after TAEX than control. Gains in VO2 peak ($r2=0.2$, $p=0.008$) but not gains in measures of walking correlated with the degree at which training intensity (percent heart rate reserve) could be progressed in the individual participant. In contrast, better walking was related to the individual progression in treadmill velocity and training duration (6MW: $r2=0.52$; $P<0.0001$; maximum walking speed: $r2=0.37$; $p=0.0001$). VO2peak and 6MW performance was still higher one year after the end of training as compared to baseline, but for endurance walking (6MW) lower than immediately after training ($p=0.002$). **Conclusion:** This randomized controlled trial demonstrates that aerobic treadmill exercise effectively improves cardiovascular fitness, gait, balance and quality of life in geriatric chronic stroke survivors. Fitness improves as a function of training intensity, gait improves by the number of repetitions (=steps) as can be expected for task-specific exercises. Therapy effects were maintained at 1-year follow-up.

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Th P243

Trials and Tribulations of Multi-Site Recruitment for the Interdisciplinary Comprehensive Arm Rehabilitation Evaluation (ICARE) Trial

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Background: The primary objective of ICARE is to improve outpatient therapy for arm paresis. We are conducting a phase III, single-blind, multi-site, randomized controlled trial to investigate the effectiveness of the Accelerated Skill Acquisition Program (ASAP), a 30-hour dose of arm-focused therapy initiated during the early post-acute outpatient interval. Research

Objective: To compare the effects of ASAP to a dose-equivalent usual and customary arm therapy group and a observation only usual and customary group on functional outcomes at 12 mos post randomization. To achieve this we must randomize 360 participants at multiple sites across 3 regional centers (California, Georgia, Wash DC). Since initiating ICARE, we completed a 9-mo (08/01/08-5/31/09) start-up to procure enrollment feasibility, and 13 mos of active recruitment activities (06/23/09-08/11/10). To meet our proposed objectives, we must randomize 3 patients/center/month and continue that pace for ~ 44 mos. Method: Working with our Data Management and Analysis Center (DMAC), we developed a comprehensive real-time tracking system to enable enrollment projections from start-up census data and early screening activities. Activities from 01/01/09 to 04/19/09 showed a total of 422 Express Chart Screens (ECS), representing an aggregate number of all new stroke admissions to inpatient rehabilitation units. From this, we estimated an aggregate annual stroke admission rate of 1447, which was 20% lower than the 2007 proposal estimate. Early low recruitment over the first 4 months was due to additional observed variations from our original proposal including: 1) continuously shortening inpatient rehabilitation stays; 2) patients discharged home directly from acute stroke unit; 3) Non-English language as sole reason for ECS exclusion is 14.1% aggregate; > 50% at one site with a majority Spanish language. These data combined with knowledge that approximately 80% of all clinical trials fail to meet recruitment goals provided impetus for the following: 1) expand enrollment window from original 1-3 mo to 14-106 days post-stroke; 2) support a Spanish translation effort; and 3) expand recruitment targets, including acute care. **Results:** Across 3 centers, we have performed 2979 ECS from varied sources now including 40.2% from acute, 56.8% from inpatient rehab; and we randomized 107/135 expected. Compared to an initial 4-mo 4.25/mo average randomization rate, the last 9 mos yielded an aggregate 9.4/mo rate. **Conclusion:** Close vigilance of site-specific and global fluctuations in recruitment, combined with a proactive and nimble administration and DMAC oversight are necessary to determine effective strategies for longer-range objectives. Carefully reasoned changes in recruitment strategies and close monitoring of dynamic changes in healthcare for stroke is essential for success in contemporary multi-site rehabilitation trials.

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Multiple linear regression of rehabilitation outcome (Total FIM scores at discharge) on clinical factors

Clinical Factors and ischemic stroke subtypes	β	B	p-value	R^2
All ischemic stroke				
NIHSS scores on admission	-0.653	-2.813	<0.001	
Age	-0.292	-0.788	<0.001	0.565
PVH scores	-0.126	-3.861	0.003	
Lacunar				
NIHSS scores on admission	-0.362	-2.208	0.041	0.429
Atherothrombosis				
NIHSS scores on admission	-0.669	-2.612	<0.001	0.590
Age	-0.482	-1.322	<0.001	
Branch Atheromatous Disease (BAD)				
NIHSS scores on admission	-0.550	-2.556	<0.001	0.558
Age	-0.397	-0.794	<0.001	
Artery to artery embolism				
NIHSS scores on admission	-0.708	-3.095	<0.001	0.728
PVH scores	-0.256	-9.065	0.015	
Cardiogenic embolism				
NIHSS scores on admission	-0.648	-2.993	<0.001	0.627
Age	-0.379	-1.224	<0.001	

Independent variables (clinical factors) : sex, age, NIHSS scores, the presence of medications used to treat diabetes mellitus (DM), hypertension (HTN) and hyperlipidemia (HL), infarction on right side / left side / both sides, periventricular hyperintensity (PVH) scores, history of stroke / ischemic heart disease, deep white-matter hyperintensity (DWMH) scores, the existence of stenosis ≥50% or occlusion of any large vessel in MRA (all assessed on admission) .

β: standardized regression coefficient, B: unstandardized coefficient
R^2: coefficient of determination

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Th P244

Severity, Age, and Leukoaraiosis affect Rehabilitation Outcomes of Inpatients with Different Types of Ischemic Stroke

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Background and Purpose: We investigated the clinical factors affecting rehabilitation outcomes of inpatients with ischemic strokes of different etiologies. **Methods:** Subjects were 314 ischemic stroke patients (196 males, 118 females; age 71.7±12.4 years; length of hospitalization 84.6±26.3 days) transferred from stroke units or emergency units for inpatient rehabilitation at Kami-iida Rehabilitation Hospital (January 2007-December 2009). National Institutes of Health Stroke Scale (NIHSS) scores and head-MRI/MRA were assessed for all patients on admission. Functional Independence Measure (FIM) scores were measured both on admission and discharge. **Results:** Stroke etiologies were as follows: lacunar (LI) in 27 patients; atherothrombosis (AT) in 49; branch-atheromatous-disease (BAD) in 90; artery to artery embolism (A to A) in 33; cardiogenic embolism (CE) in 64; undetermined embolism (unable to differentiate between A to A and CE) in 40; the 11 remaining patients were not categorized. The NIHSS scores for patients with a definite diagnosis on admission were: 5.07±3.28 in LI; 11.41±6.24 in AT; 8.74±4.12 in BAD; 9.06±5.04 in A to A; and 9.65±5.98 in CE. The FIM scores at discharge were: 97.19±18.78 in LI; 83.57±23.85 in AT; 98.38±18.33 in BAD; 90.09±23.41 in A to A; and 83.91±27.98 in CE. MRI demonstrated high periventricular hyperintensity (PVH) scores in the LI and A to A patients (LI; 2.19±0.60, AT; 1.46±0.78, BAD; 1.45±0.73, A to A; 1.63±0.69, CE; 1.16±0.68). MRA demonstrated high rates of stenosis (≥50%) or occlusion with intracranial arteries in the AT and A to A patients (LI; 9/27 [33.3%], AT; 38/49 [77.5%], BAD; 18/90 [20.0%], A to A; 28/33 [84.8%], CE; 27/64 [42.2%]). A multiple linear regression over all disease types revealed that NIHSS scores on admission (β=-0.653, B=-2.813, P<0.001), age (β=-0.292, B=-0.788, P<0.001) and PVH scores (β=-0.126, B=-3.861, p=0.003) (R^2=0.565) clearly affected rehabilitation outcome (FIM scores at discharge), especially in A to A patients [NIHSS scores (β=-0.708, B=-3.095, P<0.001); PVH scores (β=-0.256, B=-9.065, p=0.015) (R^2=0.728)]. A multiple linear regression on the data from A to A patients also showed that, based on large-vessel arteriosclerosis, ischemic stroke rehabilitation outcome appeared to be influenced by leukoaraiosis. **Conclusion:** Our study revealed that severity, age, and leukoaraiosis at the start period of rehabilitation affect inpatient rehabilitation outcomes with ischemic stroke patients.

Th P245

Correlation of Circadian and Homeostatic Changes in the Sleep-Wake Pattern with Quality of Life in Chronic Stroke Patients

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Background and Objective: Stroke patients can incur a loss of functional autonomy due to physical limitations from the stroke. They have persistent neurological deficits that impair daily activities, sensory disturbances and cognitive impairments that disrupt the quality of life. However, the impact on sleep-wake patterns to quality of life has not been considered as an important measure of therapeutic intervention. It is known that brain injuries can impact on both circadian and homeostatic sleep-wake processes. The manner in which these changes contribute to the quality of life in the stroke population needs to be more fully investigated. Thus, the aim of this study was to evaluate circadian and homeostatic changes in chronic stroke patients and then correlate with their quality of life. **Methods:** The study analyzed 22 chronic stroke patients (55±12 yrs) and 24 healthy subjects (57±11yrs) of both genders. The instruments used were the NIHSS, IQSP, SF-36 and acthimetry assessment. Data were analyzed using the Student's t-test, Mann-Whitney, ANOVA and Spearman Correlation. **Results:** Findings of the study showed significant difference in sleep quality between patients and healthy, in which patients on average had a poor quality of sleep (patients: 8.4 ± 3.4; healthy: 6.2 ±2.5; p= 0.0001). With the analysis of quality of life, significant differences were also found between stroke patients and healthy subjects for all variables (p<0.01). With the analysis of quality of life, significant differences were also found between stroke patients and healthy subjects for all variables (p<0.01). Correlations showed associations between all components of quality of life and sleep quality (p<0.01). Among the circadian variables, the highest correlations were found between quality of life and the sum of activity (R=0.48) with changes in the amplitude of the rhythm for the stroke patients (p<0.01). Regarding the homeostatic variables, sleep efficiency showed the highest coefficients (Table 1). **Conclusions:** Results suggest impairment of the circadian and homeostatic control of the sleep-wake cycle initiated mainly by the decreased level of activity from the stroke injury; thus, compromising the patients' quality of life. Therefore, it is suggested that the concerns of quality of life related to the temporal varation of activity and sleep efficiency be considered in the evaluation of stroke patients. This may provide for greater efficacy of treatment and therapeutic outcome.

Table 1: Correlation and p values between Quality of Life and Circadian and Homeostatic variables.

	Circadian (sum of activity)		Homeostatic (efficiency)	
SF-36	*R*	*p*	*R*	*p*
PF	0.403	0.0001	-0.16	0.003
RP	0.403	0.0001	-0.18	0.001
BP	0.239	0.0001	-0.26	0.001
GH	0.166	0.011	-0.22	0.001
VT	0.210	0.001	-0.24	0.001
SF	0.477	0.0001	-0.18	0.001
RE	0.439	0.0001	-0.18	0.001
MH	0.254	0.0001	-0.23	0.001

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Th P246

Dysphagic Pattern According to Stroke Location

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Introduction: Stroke patients show several patterns of dysphagia. The location of stroke is suggested as one of the determining factors of the dysphagia pattern. **Objective:** We assessed the hypothesis that the pattern of dysphagia is different according to the location of stroke lesions. Method: Two hundred ten patients with post-stroke dysphagia underwent a Video-fluoroscopic Swallowing Study(VFSS). The pattern of dysphagia was assessed with parameters of swallowing process in each phases of swallowing. The character of the brain lesions were classified into infarction and hemorrhage by brain MRI or CT findings, and the location of the brain lesions was subdivided into right and left hemisphere, brainstem, and cerebellum. The dysphagia patterns of VFSS were analyzed according to stroke locations. **Result:** In oral phase of swallowing, patients with left hemisphere or cerebella stroke showed more frequent abnormal coordination of oral transfer ($p<0.05$). Delayed pharyngeal swallowing was seen more frequently in patients with stroke of the left hemisphere or brainstem ($p<0.05$). Drooling and biting were not different according to stroke locations. In pharyngeal phase, the range of laryngeal excursion decreased in brainstem or cerebella stroke. Bolus retention in vallecular and piriform sinuses were more frequent in left hemisphere stroke ($p<0.05$). Pharyngeal motility was reduced in patients with brainstem or cerebella stroke. Patients with brainstem stroke had a higher incidence of upper esophageal sphincter opening dysfunction($p<0.05$). Aspiration was not different according to stroke locations. **Conclusion:** The pattern of dysphagia was different according to stroke locations. These results suggest that dysphagia patterns can be predicted by stroke location, and it will be beneficial to make therapeutic plans for dysphagia rehabilitation.

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Th P247

Gender Differences Post Stroke In The Stroke Unit. Women Were More Often Aphasic

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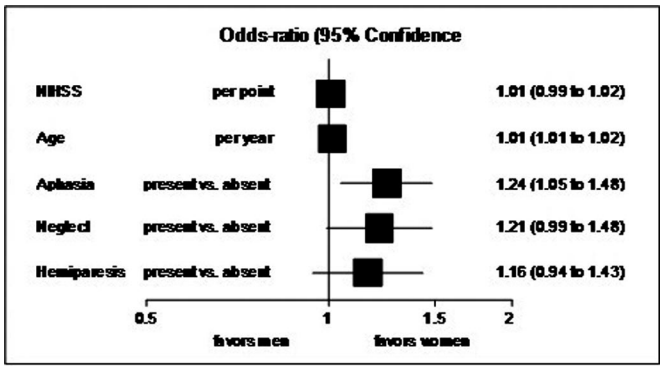
Background: Women with acute stroke are usually older, have more atrial fibrillation and higher NIH-Stroke Scale (NIHSS) scores. We wanted to know if the stroke patients in our stroke unit differ regarding stroke symptoms evaluated with the NIHSS. **Methods:** Between 1998 and 2006 we prospectively collected demographic data and detailed NIHSS scores from any patient admitted to our stroke unit. For this analysis we included every stroke patient with persisting symptoms and excluded patients with bilateral lesions. The remaining data set contains 3,048 patients. Univariate (Mann-Whitney U, t- or Fisher's exact test) und multivariate (logistic regression) analyses were applied using gender as dependent and age, NIHSS, type and site of stroke, aphasia, neglect, dysarthria, paresis and previous stroke in history as independent variables, in those variables having a p-value of variate tests. **Results:** 1,218 women and 1,830 men were included in the analysis. Women had severe strokes more frequently (median NIHSS 10 vs. 8, $P<0.0001$), were older (mean age 66.6 vs. 64.5 years; $P<0.0001$); were more often aphasic (46.0% vs. 40.1%; $P<0.0001$), more often showed a neglect (26.5% vs. 21.9%; $p=0.004$) and more often had a paresis (81.7% vs. 77.4%; $p=0.004$). There were no differences regarding type or site of stroke, presence of dysarthria or stroke in the history. Only age and aphasia remained as significant differences between men and women in this multivariate analysis (see figure). **Conclusion:** In this analysis we discovered that women admitted in our stroke unit with acute stroke, had a significantly higher rate of aphasia then men. There were no major differences regarding other relevant stroke symptoms. This could be an indication of gender differences of language function networks in a German population. The data gathered could prove to be useful in estimating future resources for language therapy in stroke unit patients.



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Th P248

Is The Efficacy Of Low-frequency RTMS Combined With Intensive Occupational Therapy Influenced By Baseline Severity Of Upper Limb Hemiparesis In Post-stroke Patients?

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Background and purpose: Recently,15-day protocol of low-frequency repetitive transcranial magnetic stimulation (rTMS) and intensive occupational therapy (OT) has been applied as a therapeutic tool for post-stroke patients with upper limb hemiparesis at our department. So far, the intervention seems to be a safe and feasible approach, since all patients completed the protocol without any adverse effects. In addition, the intervention produced some functional improvement in almost all patients. The purpose of the study is to clarify the difference of clinical efficacy of the combination treatment featuring rTMS among post-stroke patients with various baseline severities of upper limb hemiparesis. **Subjects and methods:** Fifty-two post-stroke patients with upper limb hemiparesis (age at intervention: 57 ± 19 years, time between onset and intervention: 52 ± 31 months) were studied. In all subjects, motor recovery of the affected upper limb was considered to have reached a plateau state at admissions, and baseline severity of upper limb hemiparesis at admission was categorized as Brunnstrom stage 3-5 for hand-fingers. During 15-day hospitalization, each patient was scheduled to receive 22 sessions of 20-minute low-frequency rTMS to the non-lesional hemisphere and 120-minute intensive occupational therapy consisting of one-to-one training and self-training. Motor function of the affected upper limb was evaluated with Fugl-Meyer Assessment (FMA) and Wolf Motor Function Test (WMFT) on the day of admission and discharge. For WMFT performance time, natural logarithm of the time was calculated to normalize the distribution of the data. According to Brunnstrom stage for hand-fingers at admission, subjects were divided into 3 groups such as Stage 3 group ($n=13$), Stage 4 group ($n=20$) and Stage 5 group ($n=19$). Among these 3 groups, the extent of changes in the measures with the intervention were compared. **Results:** Although significant score increase in FMA was found in all groups, Stage 4 group showed significantly larger score increase in FMA as compared with other 2 groups (2.5 points in Stage 3 group, 5.1 points in Stage 4 group, 2.3 points in Stage 5 group. all $p < 0.05$). Similarly, natural logarithm of WMFT performance time significantly decreased in all groups. However, the difference in decrease of the natural logarithm was significant between Stage 3 group and Stage 4 group, and between Stage 3 group and Stage 5 group (0.04 in Stage 3 group, 0.41 in Stage 4 group, 0.35 in Stage 5 group. all $p < 0.01$). **Conclusions:** The extent of motor improvement of the affected upper limb with the intervention was significantly influenced by baseline severity of upper limb hemiparesis after stroke. It seems that optimal candidates for the intervention are post-stroke patients with upper limb hemiparesis which is categorized as Brunnstrom stage 4-5 for hand-fingers.

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Th P249

Comparison of High and Low Dose Oral Corticosteroid Therapy on Complex Regional Pain Syndrome Type I after Brain Injury

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Introduction: Complex regional pain syndrome (CRPS) type I is a disabling complication in patients with hemiplegia from brain lesion. It usually hinders functional recovery of involved upper extremity of hemiplegic patients. **Objective:** We assessed the hypothesis that there would be no difference of treatment efficacy between high and low dose oral corticosteroid therapy on CRPS type I after brain injury, and investigated the value of three phase bone scan(TPBS) as a follow-up marker for severity of CRPS type I. Materials and**Methods:** 17 hemiplegic patients diagnosed as CRPS type I after brain injury(stroke=13, traumatic brain injury=4) were randomly treated with high dose(60mg, N=7) or low dose(15mg, N=10) oral corticosteroids(prednisolone) for 2 weeks. Clinical efficacy of treatment was measured with 'severity score' and 'Kozin's classification' by a blinded expert. TPBS was also done before and

after oral corticosteroid therapy. Uptake ratio of hand and wrist was calculated by radioisotope count of affected side divided by radioisotope count of unaffected side in pooling and delayed phases. **Results:** All patients treated by high or low dose oral corticosteroids were improved on severity score($p=0.0003$) and Kozin's classification($p=0.005$). The treatment efficacy was not different between high and low dose oral corticosteroid therapy($p>0.05$). Uptake ratio of radioisotope on TPBS was not changed after treatment($p>0.05$), and showed no difference between high and low dose oral corticosteroid therapy($p>0.05$). **Conclusion:** Low dose oral corticosteroid therapy was as effective as high dose therapy on CRPS type I after brain injury. TPBS is not recommended as a follow-up marker for severity of CRPS type I.

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Th P250

Body Mass Index Predicts Outcomes in In-patient Neuro-rehabilitation

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BACKGROUND and HYPOTHESIS: High body mass index (BMI) is a risk factor for multiple co-morbidities such as diabetes, hypertension, atherosclerosis and stroke, and patients with obesity are at an even higher risk for such medical complications, which often require inpatient rehabilitation as part of management and recovery. Although the link between high BMI and co-morbidities is well established, the relationship between high BMI and recovery in inpatient rehabilitation has not been fully elucidated but we hypothesize that it is likely to be detrimental. AIM: To evaluate the impact of BMI on functional outcomes during acute in-patient neuro-rehabilitation. **Methods:** A prospective, observational study of 214 patients in an acute inpatient neuro-rehabilitation setting. Diagnoses included traumatic and non-traumatic brain injuries and strokes. Functional Independence Measure (FIM) scores were used to measure outcomes. FIM scores were measured at admission and discharge from acute inpatient rehabilitation and at 3 months follow up. BMI was recorded at admission, and correlated with the FIM change at discharge and at 3 months. Obesity was regarded as BMI $>=30$. Those with BMI 25-29 were considered overweight. **Results:** forty two percent of patients were overweight, while 27% were obese. Linear regression was used to seek an association between BMI and FIM change (i.e., the difference between discharge and admission FIM scores). Thirty percent of patients suffered a negative FIM change, i.e., a regression in FIM scores, while 70% had a positive FIM change. There was a statistically significant association between BMI and FIM change ($p=0.034$). High BMI was particularly associated with negative FIM changes ($p=0.004$). Obesity was associated with a negative FIM change ($p=0.044$). Conversely, lower BMI was associated with positive FIM changes ($p=0.018$), while obesity was not. At 3 months follow up, normal weight was associated with a positive FIM change ($p=0.04$), but there was a trend towards negative FIM changes for the obese ($p=0.078$). **Conclusion:** High BMI is associated with negative FIM change and hence a tendency towards worse rehabilitation outcomes for stroke and other neuro-rehabilitation patient, even at 3 months post discharge from inpatient rehabilitation. Greater emphasis should therefore be paid to nutritional management in primary prevention and rehabilitation practices.

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Th P251

Effect of Statins on Functional Rehabilitation Outcome in Stroke Inpatients in Convalescence Stage

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Back ground and purpose: Statin is reported to have a role to improve neurological function during acute phase of ischemic stroke. Herein, we have shown that statin may have a role to improve neurological function during the subsequent rehabilitation period in convalescence stage. **Methods:** As a retrospective study, 301 ischemic stroke patients were admitted to our institute during June 2007 to May 2009. The patients who had in-hospital rehabilitation at least 28 days were enrolled to this study. The patients were divided into statin group (age 69.3 ± 11.4 years; mean$\pm$S.D., $n=84$) and non-statin group (age 72.7 ± 12.9 years, $n=219$). Statin group was also divided into early-statin group; statin being started before or within 14 days of admission to our institute ($n=70$), and late-statin group ($n=14$); ibid., after 14 days of admission. The effects of neurological improvement were assessed by Functional Independence Measure (FIM) and Barthel Index (BI). **Results:** Cholesterol data of 2 groups were not different (T-Chol 175.4 ± 40.2, LDL-Chol 106.1 ± 34.3 mg/dl as statin group, and T-Chol 177.5 ± 3.1, LDL-Chol 109.8 ± 27.0 mg/dl as non-statin group). Systolic and diastolic blood pressure was not different (118.8 ± 1.9 and 68.8 ± 10.5 mmHg as statin group, 119.1 ± 15.9 and 69.1 ± 10.6 mmHg as non-statin group). Statin group showed a significant improvement in post-rehabilitation cognitive FIM score (25.5 ± 8.0 to 28.0 ± 7.4) as compared with that in non-statin group (24.2 ± 9.1 to 25.8 ± 8.8, $P<0.05$) and a better tendency of post-rehabilitation BI score (56.8 ± 27.0 to 77.7 ± 28.1, and 52.9 ± 28.9 to 70.5 ± 30.1, respectively, $p=0.09$). Although there were no differences on FIM gain (19.9 ± 17.2 and 18.7 ± 18.9) and BI gain (21.0 ± 15.4 and 17.6 ± 15.8). Late-statin group showed a higher improvement in cognitive FIM score gain as compared with that in early-statin group and non-statin group (5.4 ± 5.7, 1.9 ± 4.7 and 1.6 ± 6.0, respectively, $P<0.05$) and BI gain (27.1 ± 17.4, 21.2 ± 15.9 and 17.1 ± 16.4, respectively, $P<0.05$). Because early statin group had already better FIM scores in comparison to non-statin group (cognitive 26.3 ± 7.7 and motor 52.1 ± 17.9, as compared with cognitive 24.2 ± 9.1 and motor 47.2 ± 18.7, $p=0.08$ and $p=0.058$, respectively), there might be no significant gains. **Conclusion:** Statin group showed much more improvement in cognitive FIM score during post-rehabilitation periods. Because this is a retrospective study, functional scores on the admission period were not even, namely e.g., early statin group had already higher scores on the stage of admission. However, even late timing of administration of statin may have a role to improve neurological function on ischemic stroke patients in convalescence stage.

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Th P252

Use of Intelligently Controlled Assistive Rehabilitation Elliptical Trainer to Improve Walking and Fitness during Acute Stroke Rehabilitation

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Introduction: During stroke rehabilitation, patients often seek to improve walking. While sophisticated devices exist to enable the mass repetition of a gait-like movement pattern thought to be important for promoting neuroplastic changes, many patients lack access due to the expense (e.g., robotic gait trainers) or need for multiple clinicians (e.g., partial body weight support treadmill training). *ICARE*, an *I*ntelligently *C*ontrolled *A*ssistive *R*ehabilitation *E*lliptical trainer, is an affordable training device developed to address these barriers. The current study explored the feasibility of incorporating *ICARE* training into an inpatient stroke rehabilitation program. **Methods:** Ten acute stroke rehabilitation inpatients were enrolled in the *ICARE* study within 96 hours of admission (ages 39-88 years; mean admission FIM locomotion score=2). Participants *ICARE* trained 3 to 5 times/week as an adjunct to physical therapy (mean total sessions=10; range=3-25). Initial velocity (VEL), step length (SL), and body weight support (BWS) settings were customized to each participant. Total duration of exercise per session (DUR) and subsequent setting adjustments were determined based on participant's fatigue and cardiovascular response. Paired t-tests evaluated significant changes in training parameters (i.e., VEL, SL, total strides/session, DUR, and BWS) and participants' responses (i.e., HR; rating perceived exertion, RPE) between training's beginning (first two sessions averaged) and end (last two sessions averaged), as well as self-selected overground walking velocity pre and post *ICARE* training. **Results:** *ICARE* function improved from beginning to end of training as evidenced by significant increases in VEL (31 vs. 39 RPM; $P<0.001$), SL (20 vs. 25"; $P<0.001$), number of strides/session (426 vs. 778; $p=0.002$) and DUR (12.5 vs. 20.5 min; $p=0.002$), and decreases in external BWS (26 vs. 21% BW; $p=0.023$). HR (87 vs. 93 bpm) and RPE (12.4 vs. 12.6) did not change significantly between beginning and end. Overground walking velocity also improved (pre=19 vs. post=37 m/min; $p=0.007$). **Conclusions:** ICARE enabled mass practice of a simulated gait activity, as evidenced by the large number of strides/session. The augmentation of traditional therapy with ICARE was tolerated well. Important gains were noted in endurance and speed (both overground walking and ICARE training).

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Th P253

Muscle Demands of Device Assisted versus Clinician Assisted Sit-to-stand Transfers: Implications for Stroke Rehabilitation

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Introduction: Back injuries are a serious problem in the rehabilitation setting. Frequent lifting of patients during transfers increases the risk of injury. Although mechanical sit-to-stand devices are readily available in most rehabilitation settings, some team members prefer manual transfers due to perceptions that they can more effectively facilitate activation of weakened muscles. The purpose of the current study was to compare hemiparetic muscle demands during device-assisted and clinician-assisted transfers in individuals recovering from a stroke. **Methods:** Ten adults (50-82 years) engaged in acute inpatient stroke rehabilitation participated. A Vancare VeraLift 350 (V) was used for device-assisted trials. Surface electromyography (EMG) recorded activity of the hemiparetic limb's gluteus maximus, lateral hamstring, vastus lateralis, gastrocnemius, and tibialis anterior. Participants performed three device-assisted sit-to-stand conditions: 1) giving best effort (V-BE); 2) giving no effort (V-NE); and 3) physical therapist guided motions using physical and verbal assistance (V-PT). A fourth trial, with only the physical therapist's assistance (PT), was performed. The same physical therapist (36 years old, 10 year stroke rehabilitation experience) provided assistance for trials. Peak EMG was expressed as a percentage of each muscle's maximum voluntary contraction (% MVC). Duration was expressed as a percentage of the movement trial. One-way ANOVA's with repeated measures identified significant differences in EMG peak and duration across conditions (PT, V-PT, V-BE, and V-NE). When assumptions of normality were violated, Friedman's ANOVA on Ranks was performed. Bonferroni adjustments accounted for multiple comparisons. Statistical significance was defined as $P< 0.010$. **Results:** Figure 1 summarizes significant findings for the five hemiparetic limb muscles. **Conclusions:** Hemiparetic muscle

activation increased when effort was encouraged (verbally and/or manually). Ankle muscles, in general, were less active when strapped into the mechanical device than when mobile with the PT.

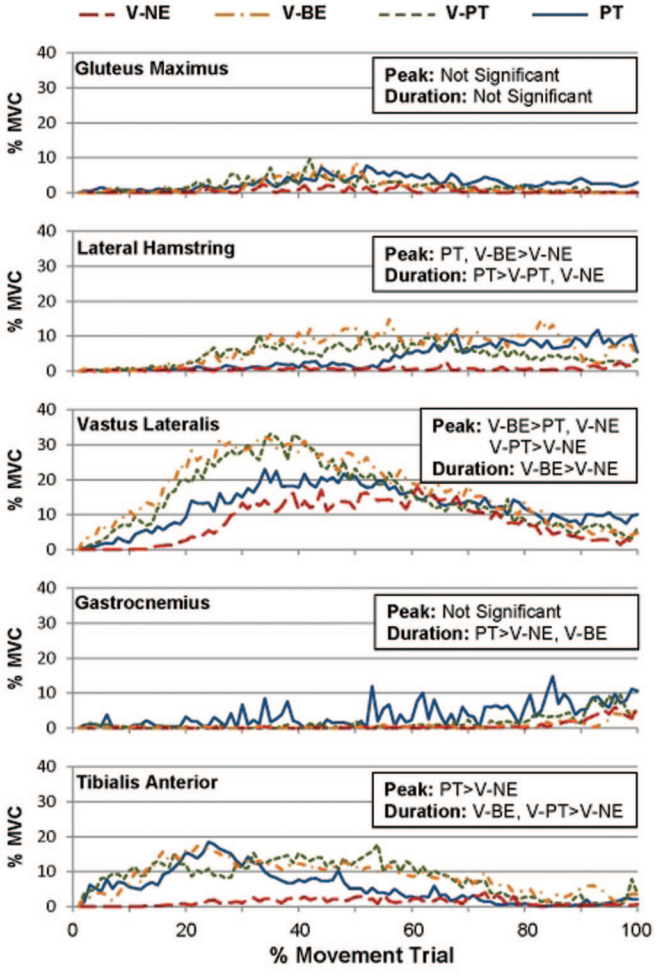

Figure 1. Ensemble EMG profiles for five hemiparetic muscles during four transfer conditions (n=10 participants).

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Th P254

Serum Uric Acid and Outcome after Ischemic Stroke. *Results from the Mexican Multicenter Ischemic Stroke Registry (The PREMIER Study)*

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Background: The relationship between serum uric acid (SUA) and stroke remains controversial and it is not clear whether the association is either circumstantial or causal. Some recent evidence supports that this routinely measured cardiovascular marker is a risk factor independently related with stroke outcome. Therefore, we aimed to examine the relationship of SUA with ischemic stroke subtypes and the clinical outcome. **Methods:** We analyzed data of patients for whom SUA was measured at hospital admittance from different geographic regions of Mexico, included in the PREMIER study (*Primer Registro Mexicano de Isquemia Cerebral*) from October 2004 to August 2006. We considered for the analyses the personal risk factors, National Institutes of Health Stroke Scale (NIHSS) at hospital arrival, comorbidities treatment, and final outcome as assessed by the modified Rankin scale (mRS) at 30-day, 3-, 6- and 12-month follow-up. **Results:** A total of 463 patients were included (52% men, mean age 68 years; range 21 to 104 years). Mean SUA at hospital admittance was 6.1 ± 3.7 mg/dl (0.36 ± 0.22 mmol/l); higher for men, as compared with women [6.6 ± 3.9 vs. 5.5 ± 3.5 (0.39 ± 0.28 vs. 0.32 ± 0.20 mmol/l); p=0.002]. A SUA of ≤4.5 mg/dl (≤0.26 mmol/l; the lowest tertile of the sample) was associated with functional independence at 30 days post-infarction in univariate analysis (mRS 0 to 1: 47.7% vs. 32.7%, for the lowest vs. higher tertiles, respectively; p=0.005), but not with stroke mortality or functional independence at 3-, 6- and 12-month follow-up. In a multivariate analysis controlled for age, gender, hypertension, diabetes, body mass index, statin, anti-hypertensive and anti-platelet therapy, previous stroke and smoking habit; a SUA of ≤4.5 mg/dl (≤0.26 mmol/l) was independently associated with 30-day functional independence (OR: 1.94, 95% CI: 1.21-3.10). Moreover, a lower SUA was also associated with a minor stroke (NIHSS of <5 points at hospital admittance: 47.3% vs. 33.4%, for the lowest vs. higher tertiles, respectively; p=0.02). We observed a trend towards higher SUA values among strokes due to large and small vessels disease, as compared with other stroke mechanisms [6.4 ± 4.1 vs. 5.5 ± 3.5 (0.38 ± 0.24 vs. 0.34 ± 0.19 mmol/l); p=0.08]. **Conclusions:** A SUA of ≤4.5 mg/dl (≤0.26 mmol/l) is independently associated with a higher chance of being functionally independent at 30 days post-stroke, possibly due through a reciprocal relationship with minor strokes. Higher SUA levels tend to be found among small- and large-vessels disease, underlying the participation of uric acid in atherotrombosis pathogenesis.

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Th P255

Caregivers Solutions to Problems Experienced in Caring for Stroke Survivors

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Background and Purpose: Stroke is a leading cause of long-term disability. Many stroke survivors return home to be cared for by untrained and unprepared new caregivers and problems surface. The research on these caregivers' successes in finding solutions to problems is limited. The purpose of this secondary analysis of data project was to identify solutions to problems that family caregivers used while caring for stroke survivors. **Methods:** These data came from a larger stroke study where biweekly interview data for 73 adult caregivers over a 1-year period were collected. Eighteen men and 55 women from northern Ohio and southern Michigan participated. These caregivers were asked about problems /challenges that they had experienced while caring for the stroke survivor. When problems were identified, the caregivers were asked what solutions they had tried to solve them. These data were analyzed using Colaizi's rigorous content analysis method. **Results:** Six themes for the caregivers' solutions to problems in caring for the stroke survivor emerged from these data and were drawn to the process dimensions in Friedemann's framework of systemic organization. Themes included: 1) getting life in order through changing behaviors or altering the environment (system maintenance in Friedemann's terms); 2) seeking medical advice and treatment (system maintenance and individuation); 3) reaching out to family, friends or community resources (coherence); 4) psychologically accepting the new normal (system maintenance and individuation); 5) hanging on to what they had (coherence); and 6) taking time for self (individuation). No differences appeared among these themes for male versus female caregivers. **Conclusions:** These caregivers of stroke survivors were doing everything in their power to preserve their lives and family system. Knowing caregivers' solutions to problems in caring for the stroke survivor can help nurses, and others, to provide them with education and problem solving strategies which assist them in adapting to their new caregiver role.

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Th P256

The Effects of Day Care Service Based on Partnership on Blood Pressure, Cognitive Function, Performance of Activities of Daily Living, Nutritional Status and Health-related Quality of Life for Older Adults with Stroke in South Korea

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Background: While adult daycare is considered a culturally acceptable model of long-term care in countries with a tradition of family-oriented caregiving, South Korea is struggling as soaring needs for developing qualified daycare services based on the needs of older adults and family caregivers. **Purpose:** The aim of this study was to examine the effectiveness of Adult Daycare Service (ADS) based on partnership for older adults with stroke and their family caregivers. **Methods:** A quasi-experimental intervention study. Older adults with stroke from two ADS centers in Korea were separately allocated to either an experimental (n=16) or a control group (n=13). Experimental group received health education and tailored rehabilitation program with their family caregivers based on partnership by trained ADS center nurses for 12 weeks. **Results:** The mean ages were 76.6 years (experimental) and 77.0 years (control). There were no significant differences in socio-demographic and clinical characteristics between two groups. Intervention participants had improved changes in diastolic blood pressure (p=.019), cognitive function (P<.001), performance of activities of daily living (P<.001), and nutritional status (P<.001). Three of the quality-of-life domains showed trends toward increased in the experimental group: physical functioning (P<.001), role physical (p=.001), and role emotional (P<.001). **Conclusion:** The ADS based on partnership had significant effects on blood pressure control and improving cognitive function, performance of activities of daily living, and nutritional status of older adults with stroke. Further research is needed to develop nursing intervention for older adults with stroke at long term care facilities as well as at home and evaluate the long

term effects of an intervention to enhance participants' adherence, health status, and quality of life for older adults with stroke.

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Th P257

Code 20 Increases Identification and Treatment of In-Hospital Stroke

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Background: Stroke is a medical emergency. In-hospital stroke (IHS) represents 6.5 - 15% of all strokes. The treatment goal for acute ischemic stroke is to reperfuse ischemic brain tissue. Delay in recognition due to comorbidities and delay in brain imaging with neurologist evaluation are common. Unlike the response for cardiac arrest, most hospitals have no organized system in place for the patient having an acute stroke while hospitalized. **Purpose:** The purpose was to increase recognition of IHS, develop an organized acute stroke code process with rapid brain imaging and interpretation, increasing treatment rates and improving patient outcomes. **Methods:** FAST test was used to teach stroke recognition to all hospital employees. An online stroke education module, in-services and dedicated stroke champions on each unit helped reinforce the teaching. The Rapid Response Team (RRT) at Hoag Hospital consists of experienced critical care RNs. Stroke symptoms, establishing a "last time seen normal", NIH Stroke Scale, treatment options and IV tPA competencies were part of a class for all RRT RNs. A "Code 20" is called by RRT for any patient exhibiting the signs and symptoms of stroke, last time seen normal within 8 hours. This code pages Stroke Team, which provides a neurologist, Stroke Unit Charge Nurse and CT. Stroke Protocol Orders are initiated. The goal is to arrive at CT scan within 20 minutes of calling the code. The RRT RN discusses treatment plan with neurologist and transfers patient to the appropriate level of care to facilitate thrombolytic therapies as needed. Restrospective ongoing analysis of RRT Code 20 calls over the time period of 5/1/2008 - 7/31/2010 was undertaken. This includes monthly reports to committee, case studies and immediate debriefing with the RNs involved. **Results:** A total of 160 Code 20s have been called since program rollout. 23% (37/160) were new IHS, 13% (21/160) were TIAs. 16% (6/37) IHS received IV tPA, 2.7% (1/37) IHS received IA tPA with Penumbra thrombectomy for a total of 19% (7/37) treatment rate for IHS. 2.5% (4/160) of Code 20s were acute ICH. **Conclusions:** RRT Code 20 is an effective tool for the management of acute in-hospital stroke. Ongoing education with real time feedback to the nurses involved with each case is needed to decrease the false positives called as Code 20s. Several other neurological emergencies were also rapidly identified and treated.

Author Disclosures: D.M. Mastrolia: None. K. Furlong: None.

Th P258

Feasibility of Screening Swallowing in Patients with Stroke Symptoms in the Emergency Department

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Background: Early detection of dysphagia is critical in acute stroke as it allows for immediate intervention thereby reducing morbidity, length of stay, and healthcare costs. Completing a swallowing screening test (SST) in the emergency department (ED) appears most logical given American Heart Association/American Stroke Association recommendations and the potential need for rapid administration of medication. Research has suggested that SSTs with trial water swallows are the most accurate in identification of patients with risk of dysphagia. Barriers to implementing a SST, particularly one with a water swallow component, in the ED are unknown **Objective:** The aims of this study were to: 1) implement a stroke dysphagia screening protocol in the ED, that included water swallows, and track clinicians' adherence with the protocol over time; 2) assemble ED nurses for focus group sessions to identify barriers and facilitator to administering a SST with water swallows; and 3) develop and implement a process improvement plan to address identified barriers to administering a SST with water swallows in the ED. **Methods:** A standard SST that incorporated water swallows was introduced in the ED. A process approach was utilized as follows: 1) education on SST administration to all ED nurses, 2) semi-structured interviews with a convenience sample of 9 ED nurses, and 3) implementation of suggestions obtained from focus groups. The number of screenings completed in the ED was tracked monthly from December 2009-June 2010. **Results:** The Cochran-Armitage Test was calculated to determine if there was a trend over time in the percent of patients who received the SST in the ED. Results indicated a statistically significant change over time, $p = 0.0173$. Barriers identified from interviews were: 1) documentation of screening in computerized record system, 2) recall of screening items during administration, and 3) inconsistent method of SST administration. To address these identified barriers, the following were implemented: 1) documentation dysphagia screening template in the electronic medical record, 2) pocket cards with SST screening items and steps for water swallow test 3) a video training module of the SST procedure, and 4) continued focused staff education with demonstration feedback. **Conclusions:** Results indicate that it is feasible to administer a SST with a water swallow component in the ED. Involvement of ED staff in the implementation process is critical to success. Supported by: Department of Veterans Affairs HSR&D RRP-09-182

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Th P259

The Benefits of Multidisciplinary Stroke Grand Rounds on Ischemic Stroke Patient Length of Stay

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Background and issues: Primary Stroke Centers employ American Stroke Association guidelines to achieve the best patient outcomes. A study by Furlong et al. (2007) states that Nursing Grand Rounds focuses on "a situation-based interpretive learning by identifying and describing knowledge for clinical practice and incorporating evidence into practice" (p. 288). There is no definitive evidence to support that Nursing Grand Rounds benefit patient care. At our institution, only an annual nursing continuing education credit for stroke was offered. Quarterly Multidisciplinary Stroke Grand Rounds were implemented to improve patient care through stroke awareness, promotion of enthusiasm, and highlighting best practices. Both Nursing and Medical Continuing Education credit was offered to participants. According to the American Heart Association, "stroke requires the efforts and skills of all members of the multidisciplinary team" (Summers et al., 2009, p.2911). Stroke Grand Round with multidisciplinary presenters (Physicians, Residents, Nurses, Physical therapists, Occupational therapists, Speech therapists, Dietitians, Pharmacists, and Social Service) and a multidisciplinary audience developed to address stroke patient care. Purpose To determine if Multidisciplinary Stroke Grand Rounds has an effect on Ischemic Stroke patients' lengths of hospital stay. Methods Ischemic stroke patient length of stay (LOS) prior to Multidisciplinary Stroke Grand Rounds was compared to LOS during the months that Multidisciplinary Stroke Grand were conducted. Sampling included Ischemic Stroke patients without end stage cancers and excluded patients for carotid interventions. Patients' lengths of stays were retrieved from online records in MIDAS. Multidisciplinary Stroke Grand Rounds were held in March and June 2010. Ischemic stroke average patient LOS from March and June 2010 was compared to the prior year March and May 2009. Patient confidentiality was maintained as only the Stroke Coordinator viewed patient names. Results There were 35 Ischemic patients in the months of March and May 2010 combined. The average combined LOS in March and May 2010 is 4.66 days. There were 36 Ischemic patients in the month of March and May 2009 combined. The average combined LOS in March and May 2009 is 6.64 days. **Conclusion:** Initial research indicates that Multidisciplinary Stroke Grand Rounds benefits Ischemic Stroke patients by decreasing length of stays by an average of two days. Although this data set is small, a need for Multidisciplinary Stroke Grand Rounds on a regular basis is evident. A multihospital study is needed to obtain a larger data set, with collaborative efforts to offer Multidisciplinary Stroke Grand Rounds. Future studies might explore stroke awareness and use of best practices of participants.

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Th P260

A Multidisciplinary Quality Improvement Project to Address Delays in CT Imaging and Thrombolytic Treatment in Acute Stroke Patients

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Background and Purpose: Stroke is the third major cause of death and the leading cause of long term disability in the United States. Rapid entry into the Emergency Medical System, hospital transport, and Emergency Department (ED) and neurology evaluations is essential in assessing patient eligibility for thrombolytic therapy. Difficulty in obtaining CT brain imaging frequently result in treatment delays. The purpose of this project was to measure CT scan turnaround time delays and evaluate how shortening CT turnaround times significantly decreases the overall evaluation period of the patient. **Methods:** Directed by the LEAN methodology, a multidisciplinary project team was formed to develop and measure aspects of the current procedure, analyze data, investigate and identify the causes of any delays and form action plans to improve and hardwire a new process. CT scan turnaround times were defined and measured as the total time in minutes from when the CT was ordered to when the Radiologist interpreted the scan as evidenced by the posting of the final report in the electronic medical record. We included in the analysis CT stroke brain scans ordered from the ED along with those ordered for in-house stroke codes. All door to IV rt-PA times were included as part of the review. The data was collected and analyzed to identify delays and quantify their causes. **Results:** Upon reviewing and analyzing the four months of data, the project team members noted that the median CT brain stroke turnaround times for 16 patients was 28 minutes with 64% of patients receiving IV rt-PA within 60 minutes of arrival. CT delay variances included patient registration delays, a variation in the language used when requesting a CT stroke brain, a lack of uniform notification of CT personal of a stroke code, and in-house transportation delays. Action plans were developed to address rapid imaging in unregistered patients, differentiating stroke protocol stat CTs from non stroke stat CTs and accelerating transportation. This multidisciplinary quality improvement project resulted in a decrease in the median CT brain stroke turnaround time for 20 patients to 21 minutes with 86% of the patients receiving IV rt-PA within 60 minutes after triage. **Conclusions:** The project team was able to identify barriers, recommend process changes and ensure the implementation of change within the institution. Data collection and process revision is ongoing.

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Th P261

National Institutes of Health Stroke Scale (NIHSS) Use in the Northeastern United States

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Introduction: The Northeast Cerebrovascular Consortium (NECC) was established in 2006 in eight states in the Northeast (CT, MA, ME, NH, NJ, NY, RI & VT) to address the regional disparities in stroke care. The NIHSS is widely accepted as a standard clinical measure of stroke severity. We sought to analyze patterns of use and barriers to hospital based implementation of the NIHSS. **Methods:** The NECC surveyed all GWTG-Stroke hospitals in NECC region. Online surveys were sent to 240 stroke coordinators in June 2010. The surveys assessed use of the NIHSS and any need for additional NIHSS training. Response options allowed multi-selection of categories. Differences in responses were evaluated using Fisher's exact test. **Results:** A total of 77 stroke coordinators (32%) completed the survey, representing 7/8 NECC states (none in VT). Stroke severity assessment using the NIHSS was more common than using a modified NIHSS or other scale, 84.4% (65/77) vs. 5.1% (4/77), p=.0001. Ten percent (8/77) reported using no scale. Nurses were more frequently identified as performing the scale 41.5%, than emergency physicians (25.9%, p = .06), neurologists (20.7%, p = .009) and other staff (attending physicians, stroke program coordinators)(3.8%, p = .0001). Forty five percent (35/77) reported using on-line training; of the 35 sites, use of the American Heart Association on-line tool (77.1%)was significantly higher than use of the National Stroke Association on-line tool (17.1%), p=0.0001, and use of alternative tools or methods (5.7%),p=0.0001. Only 51% of all hospitals felt their hospital's present plan for NIHSS training met their needs, regardless of whether they currently use the NIHSS scale, and 70% expressed interest in assistance with formal training on the NIHSS by the NECC. Only 53.2% (41/77) indicated adequate administrative buy-in for NIHSS training, with the remainder reporting none (15.6%) or uncertain (31.1%) buy-in. **Conclusions:** A majority of hospitals in the Northeast are using the NIHSS to assess stroke severity, and the NIHSS is most often performed by nurses. Although hospitals are providing some NIHSS training, stroke coordinators identify a need for more staff training. Further research is required to determine the prevalence and causes of variations in administrative support for training in stroke assessment.

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Th P262

No Association Between Post Stroke Emotional Dysfunction And A Tryptophan Hydroxylase 1 Gene A218C Polymorphism In a Korean Population

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Background and purposes: Emotional dysfunction is common in patients with stroke. There has been a body of literatures suggesting that serotonergic system dysfunction plays a role in the development of post stroke emotional dysfunction (PSED). There also has been some evidence which points to the involvement of tryptophan hydroxylase 1 (TPH1) gene in depression and anger-related traits in various psychiatric conditions. However, the role of a TPH1 gene A218C polymorphism responsible for 5-HT synthesis remains unclear in patients with PSED. **Methods:** A total of 539 patients with acute ischemic stroke admitted at Asan Medical Center were screened consecutively for post stroke depression (PSD), post stroke emotional incontinence (PSEI), and post stroke anger proneness (PSAP) at admission and 3 months after stroke. Blood samples were collected and genotyped from all participants for a TPH 1 A218C polymorphism. PSD was evaluated by Beck Depression Inventory, PSEI by Kim's criteria, and PSAP by modifications of Spielberg trait anger scale. **Results:** PSD was developed in 13.7 % and 16.0% whereas PSEI in 8.2% and 10.1%, and PSAP in 15.5 % and 23.6 % at admission and 3 months post-stroke, respectively. The distributions of the TPH1 A218C genotypes were in Hardy-Weinberg equilibrium. At admission, there were no significant differences in the TPH1 A218Cgenotype or allele frequencies between the patients with PSD, PSEI, PSAP (vs., those without), respectively. No differences were found between the patients who newly developed PSD, PSEI, PSAP at post-stroke 3 months and those who did not. No differences were also found between the patients who recovered from PSD, PSEI, or PSAP at 3 months and those who did not. **Conclusions:**Our data suggest that the A218C polymorphism of the TPH1 gene is not associated with PSD, PSEI, or PSAP at acute and sub acute stages.

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Th P263

A Quality Initiative To Improve Stroke Education Compliance

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Patient education is a key component of optimal stroke care. Stroke survivors and their care givers benefit from education related to the diagnosis of stroke and secondary stroke prevention. Get With The Guidelines-Stroke (GWTG) identifies stroke education as a primary quality indicator. An analysis of data for the GWTG indicator for Stroke Education at Mayo Clinic Hospital showed an opportunity for improvement with a compliance rate of 28%. Initially, a workgroup was formed to develop an education packet containing stroke education that would meet the Joint Commission/GWTG required elements and allow for individualization to meet the patient's specific needs. These included education on stroke risk factors, understanding newly prescribed medications, the need for follow-up post hospital discharge, stroke signs and symptom identification and why the patient should access emergency assistance immediately. This resulted in a compliance improvement from 28% to 60% but it was evident that more work was needed. Over the course of the next year there was increased focus on staff education related to use of the stroke packets and documentation of education provided. This was accomplished through Team Days, educational flyers and mandatory online education. Additionally, nurses from the stroke workgroup audited charts daily to ensure patients received stroke education and reinforced the need for education with the nurse. Compliance increased from 60% to 81%. It was determined that education was being provided and stroke packets utilized, but consistent documentation was lacking. To facilitate an improvement in documentation, the workgroup created a reminder sticker which was placed on the front of the stroke packet to prompt the nurse to document stroke education provided. Recognizing the provider's role in stroke education, an admission/discharge dictation template was created to remind the team to document the core measures as well. As a result of these efforts, compliance increased to 92%. These improvements demonstrate the importance of focused interventions to address deficiencies that could potentially impact stroke outcomes. By employing different strategies and utilizing the multidisciplinary team, patient care improvements can be achieved and maintained over time.

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Th P264

Salt and High Blood Pressure- Is Motivation Enough?

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Objective: High blood pressure is the most important risk factor for cardiovascular disease yet only 20% of patients with high blood pressure are aware of the diagnosis and only 35% of patients with known high blood pressure report good control. We set out to raise public awareness about the effects of dietary sodium on blood pressure, heart attack, stroke and kidney disease and to develop an easily accessible curriculum for communities that discusses sodium content, concomitant lifestyle changes and nutritional strategies to reduce stroke risk factors. **Methods:** We developed a community education module of salt intake, dietary information, and blood pressure education in conjunction with blood pressure screenings at four local community centers in Cleveland, Ohio. Educational materials used included a short PowerPoint presentation, handouts, an illustrative poster identifying sodium content in popular foods, and a question and answer session. Participants completed short, anonymous and confidential questionnaires both pre- and post- education surveying their risk factors, willingness to change and knowledge of the topics. **Results:** A total of thirty-three participants completed all the activities. The frequency of hypertension was 33%. Willingness to change, assessed by a reported desire to cut back on their daily salt intake was reported by 63% of the participants; 82% of those with high blood pressure versus 50% in those with normal blood pressure (P= 0.08). The majority (74%) reported reading food labels but the actual sodium content in their favorite foods were quite a surprise. Mastery of the key messages of the daily maximum of sodium equivalent to a teaspoon significantly improved following education from 24% (n=8) on the pre-test to 54% (n=18) on the post-test (P= 0.016). **Conclusions:** Our study demonstrates that an interested and self- motivated group of participants who reported reading food labels had limited knowledge of the basic information on the sodium content of foods. Although there was substantial willingness to change, particularly among those with hypertension and significant improvement with the focused education, the mastery of simple key messages was still only achieved in half the participants. These findings support the April 2010 recommendations from the Institute of Medicine to reduce sodium content in foods to assist individuals in reducing their daily sodium intake.

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Th P265

Short-Term Compliance with a Stroke Prevention Education Program and Distribution of Sphygmomanometer in Hospitalized Patients

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Background: Hypertension is the most prevalent and one of the most potent modifiable risk factors for stroke. Underserved populations, including minorities, are less likely to achieve reductions of blood pressure to nationally recommended goals after stroke. Enhanced stroke prevention education prior to hospital discharge including education on how to monitor of blood pressure (BP) at home may help patients with awareness and control of hypertension. **Objective:** To report short-term results of a stroke prevention educational program highlighting the importance of monitoring BP at home combined with distribution of a sphygmomanometer. **Methods:** All patients participated in SUSTAIN (Systemic Use of STroke Averting Interventions), a novel stroke prevention care program, which incorporated features of the chronic care model, group clinics and care coordination by a physician assistant (Care Manager). The program emphasizes education on the importance of vascular risk factor reduction for secondary stroke prevention and instruction on using a home sphygmomanometer prior to discharge from acute stroke hospitalization. All patients were discharged home on antihypertensive therapy according to recommendations of the Joint National Committee 7th edition (JNC7), with a goal of normotension (BP $\leq$ 120/80). Patients were asked to record their blood pressure twice a day and to report their BP readings to the Care Manager at a one week post-discharge follow-up telephone call. **Results:** A total of 13 patients (8 male, 5 female) participated in the educational

program prior to discharge from transient ischemic attack/acute ischemic stroke hospitalization and were given a sphygmomanometer for use at home. Mean age was 57 (standard deviation 8, range 49-77) years old, 11 were Latino, 7 were diabetic and all 13 were dyslipidemic (defined as LDL $\geq$ 100). Four individuals were pre-hypertensive and nine were hypertensive (5 stage 1, 4 stage 2). All patients made contact following discharge and 11 (85%) were within the desired BP range. The 13 patients recorded and reported a mean of 12 (range 7-13) individual BP readings. There were no reports of difficulty using the sphygmomanometer or recording BP readings at home. **Conclusions:** A hospital-based program of stroke prevention education and distribution of sphygmomanometers in hospitalized patients yielded high rates of short term compliance. The SUSTAIN clinical trial will be testing the long-term effects of this intervention on BP control.

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Th P266

Risk Factor Profiles Differ in Very Elderly Stroke Patients

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Background: Risk factor screening and counseling are generally applied in a non-specific fashion. We sought to determine if the prevalence of stroke risk factors in a high risk population of stroke patients, in fact, varied by age. **Methods:** This is a cross-sectional study of consecutive acute stroke patients enrolled in a multicenter acute ischemic stroke biomarker project. Clinical and demographic data including NIHSS scores at baseline and 3 month mRS were collected. Patients were divided into quintiles based on age. Those in the highest quintile were compared to all other quintiles on baseline clinical, demographic, treatment, and outcome variables. Data analysis employed basic descriptive statistics. Hypothesis tests were performed using 2-tailed tests and the level of significance was set at a$<$ 0.05. **Results:** We analyzed data on 464 subjects. There were 93 subjects in the highest age quintile (mean age 88.5, s.d. 3.1) and 371 in the remaining quintiles (mean age 66.6, s.d. 14.8). There were more women in the highest quintile, compared to the younger group (62% vs. 40%, p$=$0.0002) Compared to younger patients, those in the highest quintile had a higher prevalence of HTN (86% vs. 67%, p$=$0.0006), atrial fibrillation (59% vs. 24%, P$<$.0001) and a lower prevalence of smoking (52% vs. 35%, P$<$0.0001). Subjects in the highest quintile had a lower BMI (mean 22.7 vs. 27.7, P$<$.0001), more severe strokes (mean NIHSS 9.5 vs. 7.2, p$=$.0001) and higher 3-month mRS scores (p$<$.0001).There was no significant difference in the prevalence of prior stroke, prior TIA, DM, hyperlipidemia, carotid stenosis, CAD, or the use of tPA across the quintiles. **Conclusions:** Very elderly ($\geq$85 years) stroke patients have a higher prevalence of atrial fibrillation and hypertension compared with younger stroke patients. They are less likely to have a history of smoking or be obese. These very elderly patients have more severe strokes and poorer outcomes.

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Th P267

Lack of Knowledge of the Risk of Stroke in Women using Hormonal Contraceptives

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Lack of Knowledge of the Risks of Stroke in Women using Hormonal Contraceptives**Introduction:** Since the early 1960s, links between womens' use of oral contraceptives and increased risk for stroke have been established. With 100 million women worldwide using oral contraceptives, education and ongoing clinical monitoring of women's use of oral contraceptive users is essential (Gillum and Johnston 2004). Generally, risk-awareness originates from physican/nurse education during medical contact, package inserts and the popular media. The present study evaluated whether women who use of oral contraceptives who suffered stroke had been educated on the risk due to oral contraceptives. **Methods:** A retrospective chart review of twenty female patients with stroke aged 30-45 with a final primary diagnosis of ischemic or hemorrhagic stroke from 2008 to 2010. During post stroke education patients' were interviewed concerning their experiences of warnings on the risk of stroke due to oral contraceptives. Each chart was also reviewed for the correlation between the patient history of taking hormone components whether via oral contraceptives, IUD, or deprovera and if the patients had experienced a stroke. **Results:** 9/20 (45%) were diagnosed with ischemic stroke and 11/20 (55%) were diagnosed with either subarachnoid or intracerebral hemorrhagic stroke. None of the patients recall being educated specifically concerning increased risk of stroke related to women's use of oral contraceptive use. Of these twenty patients 5/20 (25%) were sent home without needing outpatient services, 3/20 (15%) were sent home needing outpatient services, and the remaining 12/20 (60%) needed to be referred to an inpatient rehabilitation setting. **Conclusions:** Stroke education in young women has routinely focused on hypertension, diet and obesity, hypercholesteremia, family history, irregular heartbeat, smoking and diabetes. The lack of specific understanding of the increased risk of stroke related to women's use of oral contraceptive use strongly indicates that better strategies to educate women at risk are needed. By being aware of the combination of risk factors may facilitate better preventative care and reduce the incidence of stroke.

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Th P269

A Descriptive Study of Cognitive Status Three Years Following Motor Stroke

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Stroke is the third leading cause of death in the United States and a leading cause of disability in the rapidly aging population. In the post-stroke period, intact cognition is needed to form new memories, devise problem solving strategies, or recognize dangerous situations. This is especially true for patients who have had a motor stroke, who most often have a short hospital stay and then return home to devise new strategies, cope with deficits, and attempt to make a good functional recovery. Furthermore, advanced age and decline in cognitive status are key factors in institutionalization following stroke yet cognitive status 3 years after one particular type of ischemic stroke, motor stroke, has received minimal attention. The purpose of this study, part of a larger 3 year follow-up study following patients after stroke, was to describe cognitive status 3 years following motor stroke. At 3 years of the 60 patients available, 11 had died, 30 consented to a home visit and 19 were interviewed by telephone. The mean age of patients at the time of follow-up was 64 years and cognitive status was measured using three instruments. The mean Mini-Mental State Examination (MMSE) score for the group was 27.53 ($\pm$ 2.74); there were no statistically significant differences in men with a mean score of 27.29 ($\pm$ 3.26) and women with mean scores of 27.75 ($\pm$ 2.26). Mean scores on the Neurobehavioral Cognitive Status Examination (Cognistat) for the group were 69.67 ($\pm$ 15.62); there were no statistically significant differences between men with a mean score of 69.50 ($\pm$ 19.36) and women with mean scores of 69.81 ($\pm$12.10). The mean cognitive subscore of the Functional Independence Measure (FIM^{TM}) was 26.5($\pm$ 13.25); there were no statistically significant differences between men with a mean score of 25.87 ($\pm$ 13.79) and women with mean scores of 27.13 ($\pm$ 12.89). This study provides a rich description of the cognitive status of a group of individuals 3 years after motor stroke. Although limited by a small sample size health care professionals need to be aware that cognitive status may not decline in all subtypes of stroke patients.

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Th P270

Improving Door to Needle Times in a State-Wide Publically Funded Tele-stroke Program

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Background: AR SAVES (Arkansas Stroke Assistance through Virtual Emergency Support) is a dedicated system of providing education, diagnosis and treatment for acute ischemic strokes through technology launched in July 2008. A team of highly trained technology and stroke professionals have designed a streamlined system for the treatment of stroke in rural Arkansas. Through a contract with the Department of Human Services, Division of Medical Services and the University of Arkansas for Medical Services. This program is currently serving 23 hospitals (20 spoke, 3 hubs) in an effort to improve Arkansas' ranking of 1st in Morbidity and Mortality from stroke. Aim: To create an efficient program, through quality improvement measures and assessment of all calls and consults. Through an integrated call center all aspects of the program are linked and data is tracked from time of call to the administration of t-PA. Method: A standardized checklist and performance review, that has provided hub trainer's and spoke site staff with step by step instructions on how to reach and maintain that crucial door to needle time line. This practice utilizes interactive video and on-site demonstrations providing discussions for continuous improvement. **Result:** A review of the first year indicated an average door to needle time of 115 minutes. With ongoing training of the new performance review the door to needle times were improved to 105.6 minutes. **Conclusions:** An efficient program, through quality improvement measures and assessment of all calls and consults using an integrated call center, all aspects of the AR SAVES program are linked and data is tracked from time of call to the administration of t-PA. The strategic area for review is the door to needle times of all AR SAVES consults. The evaluation team reviewed the pilot data and the aforementioned recommendations for improvement of the door to needle times.

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Th P271

Building A Financial Case For Stroke Coordinator Resources

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Background Primary Stroke Center development spurred the creation of the "stroke coordinator" role in hospitals. While certification has outlined clear expectations for certain components of stroke care, it leaves the role of stroke coordinators undefined. Currently myriad "stroke coordinator" models exist with coordinator responsibility ranging from stroke clinical measure performance to stroke program oversight to facilitation of patient care. Hospitals struggle to determine the best approach to stroke center development, and the cost of dedicated resources is often at the root of debate on how to best deliver stroke care. Purpose To compare four different "stroke coordinator" models in Primary and Comprehensive Stroke Centers and to identify the incremental inpatient and outpatient stroke-related volume and/or inpatient length-of-stay improvements needed to rationalize the direct cost incurred for each model. Methods Four stroke coordinator models were identified. In each model the primary responsibility was noted as stroke measure data coordination, stroke center standards compliance or varying degrees of stroke care facilitation - partial (8 hrs/day, 5 days/wk) or full

(24 hrs/day, 7 days/wk). Full-time equivalents, qualifications, roles and responsibilities were outlined and direct costs (recruitment, salaries, benefits, equipment, support staff, etc.) were identified. Payer mix and current payer reimbursement scenarios for inpatient and outpatient services were developed, and cost-per-inpatient-day was estimated using a proprietary database. Results Incremental inpatient stroke volume needed to financially justify investment in dedicated stroke coordinator resources varies with the cost of coordinator resources and the estimated mix of new patients receiving stroke interventions, outpatient services and the estimated length-of-stay improvements. **Conclusion:** While a financial case alone is notably short-sided when considering the benefits of dedicated stroke coordinator resources, the need for one is admittedly more important in the midst of today's healthcare realities. Projecting new, incremental patient volume and/or operational improvements that are achievable can help rationalize the financial return on investment of new, dedicated coordinator resources. This type of future return should be realistic and presented in addition to the less quantifiable, yet equally important benefits associated with stroke care coordination.

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Th P272

A Non-Teaching, Magnet Hospitals' Emergency Room Process Improvements Which Led to Stroke Center Accreditation

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The hospital goal was to achieve stroke center accreditation while improving stroke care. We created a collaborative team consisting of administrators, physicians, nursing departments, the laboratory department, and the radiology department; who worked towards a common goal of ensuring quality care relating to stroke patients. Our plan first encompassed ensuring all quality stroke measures: lab work, EKG, plain CAT scan of the Brain, and Chest X-ray (when medically necessary) were resulted within 45 minutes, 80% of the time. The Baptist Emergency Stroke Team (B.E.S.T.) was developed to help meet these goals. The team consists of a stroke certified nurse that responds to all suspected brain attacks, an emergency room physician, an emergency department triage and/or primary nurse, a neurologist, and a pharmacist. Emergency department nurses were required to activate the stroke team within 10 minutes of patient arrival. Other initiatives were put into action which helped us meet our objective. The emergency department collaborative established advanced nursing interventions and created an electronic computerized stroke order set. The emergency department worked in partnership with the lab creating specially labeled blood tubes and blood bags in conjunction with requiring blood to be hand delivered to laboratory personnel in order to improve turn around times. Later in the process we improved electrocardiogram (EKG) turn around times by ensuring the initiation of two IV's and an EKG upon patient arrival to the emergency department prior to going to CAT scan. CAT scans of the brain are also expedited by the radiology department and a Neuro-radiologist interprets the CAT scan immediately after completion with results being called to B.E.S.T. nurse and neurologist. Patients who are candidates for thrombolytic therapy are treated with pre-set doctor's orders to ensure administration of TPA (Tissue Plasminogen Activator) within 60 minutes of arrival. The order set includes consent for Alteplase administration and a medication dosing chart. The Stroke B.E.S.T. Call Review Committee started reviewing 100% of stroke calls in October 2009. The committee continued to monitor all B.E.S.T calls through June of 2010 with continued focus on improving stroke quality measures and turn around times. On June 10, 2010, Joint Commission surveyor for Stroke Accreditation conducted a site visit with full accreditation being recommended.

Measurements	Benchmark	Oct	Preliminary May
Time from patient arrival to assessment by Baptist Emergency Stroke Team (B.E.S.T.) member	15 min	85% Avg 7 min	100% Avg 3 min
Time from notification of B.E.S.T. Responder RN to arrival at bedside	10 min	90% Avg 5 min	96% Avg 4 min
Time from order of labs to reported to B.E.S.T. member	45 min	60% Avg 53 min	88% Avg 34 min
Time from order of a diagnostic brain image to results reported to a B.E.S.T. member	45 min	70% Avg 41 min	96% Avg 27 min
Time from order of chest x-ray, if clinically indicated, to results reported to a B.E.S.T. member	45 min	45% Avg 60 min	50% Avg 56 min
Time from order of ECG to results reviewed by a B.E.S.T. member	45 min	80% Avg 20 min	92% Avg 5 min
Time of patient arrival to administration of IV thrombolytic (t-PA) treatment (Door to needle time)	60 min	N/A	1hr 34 min
Time of neurosurgical consult ordered to time evaluation by phone	2 hours	100% Avg 0 min	100% Avg 0 min
Time of neurosurgical consult ordered to time evaluation at patient bedside	2 hours	100% Avg 65 min	100% Avg 47 min

GREEN - At or above goal of 80% compliance
RED - Below 80% compliance
Highlighted in Yellow - Turn Around Times (TAT) Benchmark required for TJC Stroke Certification with 80% compliance

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Th P273

Dysphagia Screening in the ER, How We Increased Compliance From 30 To 90+%

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Background: White Plains Hospital Center has been a designated stroke center since July 2005.According to the *Get with the Guidelines* database one of the important core measures was the dysphagia screening, a tool to identify patients at risk for aspiration due to swallowing impairment post stroke. The data collection showed that at best we were accomplishing screening no better than 60% of the time, sometimes as low as 30%. PURPOSE: We needed to improve our compliance with the screening. It was recognized that most screening needed to take place in the ER before oral meds and nutrition were initiated. **Methods:** A team from both our stroke floor & ER met to tackle the problem. Two issues were identified. The first dilemma was to identify who needed the screening. The team developed a master list of diagnoses that may be related to stroke. They then linked this to a list of chief complaints (a statement about why a patient presents to the ER seeking treatment). Finally, our IT rep was able to attach the dysphagia screening to the appropriate CC, which caused it to automatically appear on our documentation screen. The second issue was documentation. Initially, the dysphagia screen was on paper, and the actual implementation was long and cumbersome. When this screen was computerized charting became a major effort, and compliance, which was erratic, fell. The prevailing philosophy was feed no one, and let the nurses upstairs do the screening. The team streamlined the actual screening to be more user-friendly while remaining in compliance with national guidelines. Through one-to-one interactions with ED managers, staff meetings and email/printed material, the ED staff was in-serviced to expect that the dysphagia screen would be appearing on documentation screens more frequently. The rationale for its addition as a required assessment for certain Chief Complaints, was also communicated. **Results:** We have over 90% compliance consistently & many months have even reached 100% perfection!**Conclusions:** In 2009, WPHC received the Gold Performance Achievement in Stroke Care for the 3rd year in a row!

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Th P274

Dysphagia Screening: A Nurse Driven Process

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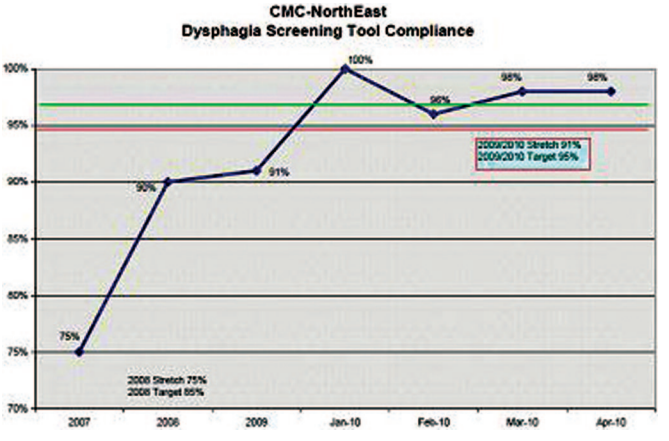
Project Selection: Stroke continues to be the third leading cause of death in the United States and the number one cause of adult disability. North Carolina is one of three states that make up the "Stroke Buckle" where the stroke death rates are two times greater than the rest of the nation (Rosamond et al., 2008). According to the North Carolina Stroke Care Collaborative, Cabarrus county stroke death rates fall slightly below that of the US at 48.9% per 100,000 populations. A frequent, yet preventable complication of stroke is aspiration pneumonia. In order to help prevent this, patients must receive nothing by mouth until they are determined to be safe to take food or liquid without signs and symptoms of aspiration. This determination is completed by performing a dysphagia screen. With a shared passion and goal for improving stroke care and outcomes, the Stroke Program and the Neuroscience Department at Carolinas Medical Center-NorthEast were committed to exploring potential solutions to this problem. Goal: The American Stroke Association had set goals for core measures associated with stroke. Our immediate goal was the 85th percentile with a stretch goal of the 95th percentile. Our goal was not only to improve performance in this area but provide quality care to our patients based on evidenced base practice. Improvement Process: After review of current policies, baseline data, and future external regulations, the team performed a literature review of published evidence and networked with other national health agencies and facilities to consider established approaches that were being utilized. Criteria for screening this population was established and the team began constructing a tool for utilization by the bedside nurse for dysphagia screenings. Compliance monitoring of the tool occurred concurrent and recommendations were reported back to the team. Results/Outcomes: The dysphagia screen compliance rate in the stroke population for year to date 2010 is 98%. Innovation, Sharing Knowledge: Staff ownership paved the way to improving this measure and ultimately ensuring better patient outcomes. By sharing ownership in the process and providing input it remained on the dashboard of bedside nurses. The patient and family/caregiver were included in the process to increase education and understanding of dysphagia and steps to prevent development of pneumonia.



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Th P275

Beating Back the Brain Attack: Improving Stroke Patients' Door to Lytic Time

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Background: The diagnosis and treatment of stroke is time-sensitive. Patient outcomes are directly affected by the amount of time that the healthcare team uses to make the stroke diagnosis and start treatment. Appropriately administering the clot-busting drug alteplase (tissue plasminogen activator) (t-PA) (thrombolytic) (lytic) during the "golden hour" following stroke diagnosis greatly increases the chance of a positive outcome. The stimulus for stroke system re-design is apparent with stroke as the third leading cause of death in the United States and this healthcare organization's location in the heart of the stroke buckle. **Purpose:** Eligible patients treated with t-PA have shorter lengths of stay, more discharges to home, decreased rehabilitation and nursing home costs, and improved quality-adjusted life-years (QALY) saved (NINDS, 1995). Given the time urgency of stroke care and deficits when stroke is untreated (Saver JL Stroke 2005), our stroke team established a goal to decrease the average emergency department door to lytic time by 15%. **Methods:** Administrative support, strong leadership, collaboration, clinical champions and continuing education are important elements of success for stroke centers. An algorithmic approach, standardization, process improvement, and high reliability principles were used for implementation of evidenced based interventions, including thrombolytic administration. Concurrent and retrospective analysis of the *Code Stroke* process and regional thrombolytic utilization and referral was performed. Staff interviews, flowcharting, and concurrent quality clinician feedback and analysis were used and a Stroke Clinical Efficiency Group was developed with diverse membership. This enhanced our stroke continued readiness and to obtain input for an integrated approach. Post thrombolytic administration team analysis was employed to "drill-down" on the barriers and challenges to meeting door to lytic benchmarks. **Results:** Improvements have positively impacted code stroke response targets. Augmentation of code stroke processes has resulted in improved door to lytic times, improved quality of life for patients and families, and reduced costs. Response time data has indicated that we are below the benchmark for several response times. The average door to lytic time decreased per data point 20% from 95 (July-December 2009) to 76 (January-May 2010), and by 30% per monthly comparison, from 97.6 to 68, respectively. **Conclusions:** Collaboration, use of best practice guidelines, and high reliability principles resulted in improvements in the rapid assessment and treatment of stroke patients. Next steps are to establish stretch goals for all code stroke response times and promote best practice in stroke care throughout the region.

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Th P276

Hospital Participation in a Voluntary Stroke Quality Improvement (QI) Collaborative in Massachusetts

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Background: Funded by the Centers for Disease Control and Prevention as a Coverdell Registry state, SCORE is a MA Department of Public Health/American Stroke Association QI collaborative. Since 2005, SCORE has assisted designated stroke service hospitals in MA in monitoring and improving the quality of care for acute stroke patients. **Objective:** To evaluate the sustainability of hospital participation in a QI initiative. **Methods:** Start up funding was provided to hospitals in the initial phase but decreased overtime from $10,000 to $1,000 per site from 2005 to 2008 respectively. No direct funding was provided to sites after 2008. Coverdell Registry and SCORE programmatic data from 2005 through 2009 were analyzed. Hospital assistance included 3 main types of training. Quarterly Learning Sessions began in 2005 and are full-day meetings with didactic sessions on clinical stroke care, QI, and data abstraction topics. Data training calls began in 2006 and are 1-hour calls held multiple times per year focused on data abstraction to improve data quality. Quarterly Regional Meetings began in 2008 and are half-day, discussion-based, small group meetings focused on clinical QI strategies. Participation was measured using: number of participating hospitals, hospitals' training attendance, and registry case entry. Joinpoint regression analysis was used to test for trend. The overall trends for attendance were computed and statistical significance set at $P<.05$. **Results:** Currently 83% of eligible hospitals (57/69) participate in SCORE. Hospitals joined in 3 cohorts: 36 in July 2005, 16 in February 2006, and 5 in March 2007. Since 2007, 1 additional hospital joined and 1 withdrew. Hospital enrollment increased over time despite a decrease in funding. High rates of stable attendance and case entry has also been sustained. Average attendance at 18 Learning Sessions was 78%, exceeding 75% at 12 of the meetings and has neither increased nor decreased significantly over time. Mean attendance at the 13 data quality training calls was 53% and has decreased slightly (ns) over time. Regional Meeting attendance has improved over time (ns) from 38% in 2008 to 52% in 2009. Mean attendance at the 6 regional meetings was 46%. The average number of quarterly cases entered into the registry from 2007 (after all sites had joined) to 2009 was 2,433 and has remained stable over time. **Conclusions:** MA hospitals demonstrated sustained participation in a voluntary stroke QI collaborative without direct funding. These data suggest this may be a sustainable model. Further analysis to explore the relationship between participation and performance measure improvement is warranted.

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Th P277

Hospital Patient Volume Correlates with the Likelihood, but not the Promptness or Risk of tPA for Ischemic Stroke

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Introduction/Hypothesis: A positive relationship between hospital patient-volume (HV) and outcomes is widely acknowledged. We asked whether this relationship holds between the HV for ischemic stroke and variables such as the likelihood, promptness, and risks of IV tissue plasminogen activator treatment (tPA). **Methods:** We used the Colorado Stroke Registry, a prospective database shared by 38 hospitals, to identify patients meeting these criteria: ischemic stroke with onset in a community setting *and* arrival to hospital from the scene by EMS or private means within 180 minutes. Transfers between hospitals were excluded. We explored the relationship of HV (the # of included records from each hospital) with the hospital-specific relative risks for: receiving tPA, receiving tPA within one hour, having a listed contraindication to tPA, and having symptomatic intracerebral hemorrhage (SICH) after tPA. We also compared HV to median arrival-to-CT and median arrival-to-tPA times. Statistical comparisons were made by linear regression, Chi-Square, t-test, and Kruskal-Wallis, as appropriate. **Results:** From >8,700 ischemic strokes we identified 2,136 patients meeting inclusion criteria. HV ranged from 1 to 289 patients across 32 hospitals with data. The median HV was 31, with an interquartile range of 4.5-127. HV was *not significantly correlated with*: median age, gender, median NIHSS, median onset-to-arrival-time, or mode of arrival. HV was *strongly correlated with* the likelihood of receiving tPA, which was 3 times more likely in hospitals above the HV median as compared to those below (24% vs. 8%, $p = 0.0002$). HV was *not correlated* with: tPA-in-1-hour, median arrival-to-CT-time, median arrival-to-tPA-time, listed contraindications to tPA, or SICH. **Conclusions:**Our data show that the number of ischemic strokes recorded by hospitals correlates positively with the likelihood of receiving tPA. It does not, however, correlate with the promptness of either CT scanning or tPA administration. Neither does it correlate with the risk of SICH following tPA. As a caveat, we acknowledge limitations in our**Conclusions:** our data are observational in nature and based on self-reporting from hospitals. Nevertheless, this analysis suggests that "practice does not make perfect" for tPA use in ischemic stroke. This is surprising since a positive correlation between volume and outcome is seen in skill-dependent procedures such as heart surgery. In comparison, administration of tPA is a relatively low skill procedure (although one requiring considerable clinical judgment). Lower volume hospitals appear to be capable of giving tPA as quickly and as safely as higher volume hospitals, but they are significantly less likely to use tPA at all. These findings, if confirmed by other investigators, may have relevance in planning and improving stroke systems of care.

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Th P278

The impact of the European Cooperative Acute Stroke Study (ECASS) III on clinical practice

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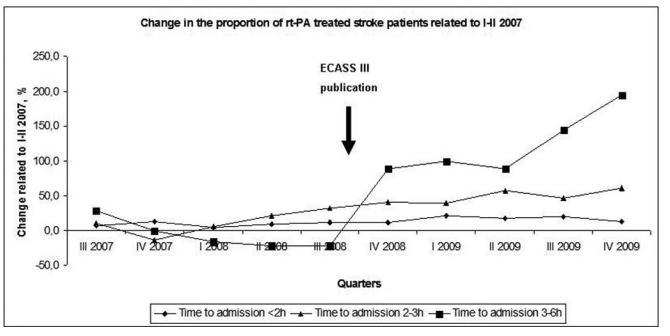
Introduction: ECASS III extended the thrombolysis time window for stroke patients from 3 to 4.5 hours after symptom onset. Since a large proportion of stroke patients arrive at hospital later than 3 hours ECASS III raised hope that more patients will be treated with rt-PA. To investigate the effect of the extended thrombolysis time window on routine stroke care we studied the proportion of stroke patients that received thrombolysis before and after the publication of ECASS III in September 2008. Additionally we determined whether the time window extension led to delay of treatment initiation. **Methods:** Data were collected prospectively within the regional Stroke Register of Northwestern Germany between January 2007 and December 2009. The onset-to-door (OTD) time was categorized into 6 hours. The door-to-needle (DTN) time was categorized into 180 minutes. To compare thrombolysis rates before and after publication of ECASS III we used a logistic regression analysis. **Results:** A total of 91805 ischemic stroke patients were included in the analysis. Overall, 9262 patients (10.1 %) were treated with rt-PA. The proportion of patients treated with rt-PA significantly increased over time. The strongest increase was observed for patients admitted between 3 and 6 hours after symptom onset between the third and the fourth quarter of 2008 (88.9% relative increase in IV 2008 compared to the first half year of 2007, $P<0.05$, Figure). During the study period the proportion of patients with a DTN time < 30 minutes continuously increased and the proportion of patients with DTN times of > 60 minutes decreased. **Conclusions:** The results of ECASS III were rapidly incorporated in clinical practice. The overall proportion of rt-PA treated stroke patients and in particular those with OTD times of 3 to 6 hours increased after ECASS III publication. Previous concerns regarding an increase in DTN time were not confirmed.



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Th P279

Physicians Delay Thrombolysis if There Is More Time to The End of The Thrombolytic Window

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Background: The earlier that thrombolysis is initiated, the greater the benefits of the treatment. We assess the hypothesis that the initiation of thrombolytic treatment is delayed if physicians have more time before the end of the thrombolytic time window. **Methods:** Prospectively collected data from the SITS register on all patients treated with thrombolysis between Jan/2004 and Feb/2010 in the Czech Republic were analyzed. A multiple regression analysis was used to assess the correlation between onset-to-door time and door-to-needle time. Also, patients were stratified according to onset-to-door time into 3 groups (0-60, 61-120, and 121-180 minutes), and inter-group differences were assessed with ANOVA and Chi-square tests. **Results:** Altogether, 2958 patients arrived within 3 hours of symptom onset in 51 stroke centers in the Czech Republic (78% of all hospital-based neurology departments). Of these, 2644 (89%) were treated with thrombolysis within 3 hours, and 314 (11%) after 3 hours. The number of patients arriving at 0-60, 61-120, and 121-180 minutes after symptom onset was 1453 (49%), 1206 (41%), and 299 (10%), respectively. Door-to-needle time was negatively correlated with onset-to-door time ($r = -0.32$, $P<0.001$) and significance did not change after adjustments for age, sex, baseline NIHSS, and year of treatment($r = -0.32$, $P<0.001$). Door-to-needle time was 85 ± 42, 70 ± 31, and 48 ± 23 min ($p<0.001$) in patients arriving 0-60, 61-120, and 121-180 minutes after symptom onset, respectively. Also, door-to-needle time $\leq$60 minutes was achieved in 31, 45, and 79% ($p<0.001$) of patients arriving 0-60, 61-120, and 121-180 minutes after symptom onset, respectively. **Conclusions:** Although half of thrombolytic candidates arrive at the hospital within 60 minutes of symptom onset, the benefit of thrombolysis is diminished for these patients because physicians delay the treatment. It is necessary to improve adherence to guidelines and to treat patients within 60 minutes of arrival at the hospital regardless of the amount of time left to the end of thrombolytic window. This study was supported by a grant from IGA MH CR NS10106-4/2008.

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Th P280

Patient Refusal of Tissue Plasminogen Activator for Acute Stroke

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Introduction: Intravenous t-PA (IV t-PA/t-PA) has been established as a cornerstone therapy for eligible patients with acute ischemic stroke (AIS). There is paucity of data on AIS patients who refuse IV t-PA. We characterized the incidence, demographics, severity, and outcome of AIS patients who were eligible yet refused IV t-PA. We hypothesized that demographic markers, clinical presentation, and outcome of AIS patients who refuse t-PA would differ from those patients who receive it. Methods A retrospective analysis of our stroke registry was conducted from July 1, 2004 to June 30, 2010. Patients presenting after the 3-hour window were excluded. We collected demographics, baseline NIH Stroke Scale (NIHSS) scores and discharge outcomes on patients who refused IV t-PA, and those who were treated with IV t-PA within 3 hours of symptom onset. A written consent for t-PA administration is usually not obtained from patients presenting within the 3-hour window. Results A total of 687 patients were treated with t-PA. Twenty six (3.7%) patients refused, translating into an incidence of one t-PA refusal for every 26 eligible patients. There has been a gradual decline in refusal with maximum number of cases (24/26 - 92.3%) occurring from 2004 to 2007. A small fraction (11.5%) of patients also refused other treatments and diagnostic work-up. The mean onset to arrival time for t-PA refusals was not statistically different from those who received t-PA. Most refusals (61.5%) were either completely or in part insured via Medicare while 15.3% were uninsured. There were a significantly higher percentage (73%) of female patients who refused t-PA as compared to 49.3% who got treated ($p=0.018$). Age and ethnicity were not significantly different between the two groups. Admission NIHSS score, discharge mRS and the length of hospital stay were all significantly lower for t-PA refusals. After controlling for baseline NIHSS, refusal patients had a 2.5 times odds of improved outcome compared to t-PA treated patients ($p=0.02$). **Conclusion:** Over the period of investigation, there has been a low and gradually declining incidence of t-PA refusal. Female gender stood out as a significant indicator for refusal. No additional clear-cut demographic characteristics came forth as refusal predictors. The refusal patients had milder strokes, shorter hospital stays, and consequently better outcomes compared with treated patients. Further research would benefit understanding of patient refusal of standard of care treatment for acute stroke.

	Refused IV t-PA	Received IV t-PA	Significance
Gender			
Female	19 (73%)	339 (49.34%)	p = 0.018
Male	7 (26.9%)	348 (50.65%)	
Race			
White	14 (53.8%)	343 (49.9%)	p = 0.7 for 2 x 2 table
Black	10 (38.5%)	218 (31.7%)	
Hispanic	1 (3.8%)	105 (15.3%)	
Asian	1 (3.8%)	18 (2.6%)	
Others	0 (0.0%)	3 (0.4%)	
Mean Age in years			
	64.04	65.76	p = 0.5
Mean ± SD Onset to Treatment Time in hours			
	1.49 ± 0.82	1.29 ± 0.57	p = 0.08
Clinical Presentation and Outcome Comparison			
Median Arrival NIHSS	7	12	p = 0.000
Median Discharge mRS	2	3	p = 0.001
Median LOS in days	4	5	p = 0.008
Improved outcome (mRS 0-2) for t-PA refusal patients			
mRS (0-2)	15 (57.7%)	241 (35.3%)	p = 0.02
mRS (3-5)	11 (42.3%)	442 (64.7%)	

Odds Ratio	95% CI Limits	p
2.5	1.13 – 5.62	0.02

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Th P281

Prognostic Modeling For An Efficacy And A Safety Of Thrombolysis In Acute Ischemic Stroke Patients

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Background: Thrombolysis is the only proven treatment against acute ischemic stroke till now, but has limitations such as uncertainty of recanalization and risk of hemorrhagic complication. In order to overcome these, new approaches are emerging such as combination therapies, development of new thrombolytic drugs, and use of prognostic models to identify patients who can benefit from thrombolysis. This study aimed at developing and validating a prognostic model on efficacy and safety for Korean patients who are eligible for thrombolysis. Method: Data from a consecutive series of patients with acute ischemic stroke, who were hospitalized to Seoul National University Bundang Hospital within 12 hours from onset between 2004/1 and 2008/3, were used to develop the prognostic model. For external validation, data collected from 6 hospitals between April 2008 and September 2009 were used. The prognostic models for efficacy (modified Rankin scale (mRS) at 3 month $\leq$2) and safety (symptomatic hemorrhagic transformation) outcomes were constructed with multivariable logistic regression models, and bootstrap procedures were used for internal validation. External validation was evaluated for applicability of the developed model. Model performance was assessed for discrimination with receiver operator characteristic (ROC) curves and for calibration with calibration plot. To improve the prediction, recalibration was conducted by updating intercept and calibration slope. **Results:** In the efficacy model, age, history of diabetes, history of stroke, prior use of antiplatelets, initial NIHSS, thrombolysis, previous mRS, and stroke subtypes were included. Internal and external validation showed excellent discrimination (AUC=0.87 and 0.84, respectively). But the calibration for the external dataset was not so good. Therefore, updating of models through recalibration method was performed with evident improvement in calibration. The safety model considered predictors of age, gender, history of diabetes, stroke, hypertension, and hyperlipidemia, prior use of antiplatelets, statin, and anticoagulants, initial NIHSS, thrombolysis, interval from onset to arrival, initial systolic BP, initial glucose, and stroke subtypes. External validation showed excellent discrimination (AUC=0.82) and its calibration using the external dataset was satisfactory. Updated models through recalibration method showed good calibration towards the external dataset. **Conclusion:** This study demonstrated the successful development of the externally validated prognostic models for thrombolysis candidates using basic clinical predictors. We hope these models are used by clinicians in emergency settings in identifying patients that would be more benefited and less harmed from thrombolysis.

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Th P282

The Risk of Thrombolysis in Demented Population: A Case Control Study

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Background: Thrombolysis for acute ischemic stroke (AIS) in elderly population is associated with higher mortality and intracerebral hemorrhage (ICH) rates. In this study, we assess impact of dementia on these outcomes. **Methods:** A cohort of patients with AIS was identified from the National Inpatient Sample database for the years 2000 to 2007. We selected patients with dementia that was identified by the ICD-9-CM codes including Alzheimer disease, senile, presenile, vascular, fronto-temporal, and Lewy body dementia. In addition, we compared the outcomes of demented patients treated with thrombolysis with a matched random sample of non-demented individuals that was selected from a pool of those with AIS and treated with thrombolysis (3 controls per case). Multivariate logistic regression analyses were used to assess covariates associated with hospital mortality and ICH. **Results:** In this analysis, 35557 patients were admitted with the diagnosis of AIS and superimposed dementia; only 207 (0.56%) had received thrombolysis treatment. In-hospital mortality (17.48% vs. 8.63%) and ICH (5.80% vs. 0.38%) were higher in the thrombolysis group ($P < 0.0001$) compared to those who did not receive thrombolysis. Multivariate analysis for hospital mortality showed association with thrombolysis (odds ratio 'OR' 16.15; 95% confidence interval 'CI' 8.54, 30.53) and ICH (OR 2.80; 95% CI, 1.82, 4.32). Compared to a matched population (non-demented and treated with thrombolysis, n= 621), those demented and treated had a slight but insignificant increase in ICH (5.80% vs. 4.51%; $P = 0.45$) and mortality (17.39% vs. 14.49%; $P = 0.31$) rates. Among all treated patients, ICH remained predictor of mortality (OR 2.25; 95% CI 1.02, 4.99). **Conclusion:** The use of thrombolysis in elderly demented population harbor the same risks compared to the non-demented counterparts. The presence of ICH remains predictor of a higher mortality rate in elderly demented patients.

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Th P283

Symptomatic Intracerebral Hemorrhage Following Stroke Thrombolysis. What Is The Impact Of Different Criteria On Patient Long-term Outcome?

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Objectives Symptomatic intracerebral hemorrhage (sICH) worsens outcome of ischemic stroke patients following thrombolysis. Dissimilar definitions of sICH were used in randomized trials and registries. We studied the magnitude of impact of sICH according to various definitions on patients' long-term outcome. Methods Our study cohort included 985 ischemic stroke patients treated with intravenous thrombolysis within 4.5 hours from the symptom onset according to the institutional guidelines at the Helsinki University Central Hospital between 1995 and 2008. Using univariate methods we analyzed differences in baseline demographic, clinical, and radiological characteristics of patients with versus without sICH (according to SITS, ECASS, and NINDS/Cochrane definitions). For each definition, we assessed association with 3-month outcome (modified Rankin Scale, mRS) in a multivariate model adjusted for possible confounders. Implementing receiver operating characteristic (ROC) curve and integrated discrimination improvement (IDI), we further studied impact of each definition on outcome. IDI analysis is, very briefly, a measure of improvement in model performance (increase in sensitivity and specificity) after adding a new parameter into the model (model M2 vs. M1). For both AUC-ROC and IDI analyses, two models were used. Patients' outcome (3-month mRS 3-6, 4-6, 5-6, or mortality) was used as a dependent variable in both models. As independent variables, model 1 (M1) included age, baseline NIHSS score, baseline glucose level, OTT, and presence of hyperdense artery sign or artery occlusion in any cerebral artery on baseline imaging. Model 2 (M2) included the same variables as M1 plus information on presence/lack of sICH (separately for each definition). Findings The frequency of sICH was 2.1% (SITS), 7.0% (ECASS), 9.4% (NINDS/Cochrane), whereas 19.8% of patients had any ICH. Of all sICH cases, 96% occurred within 36 hours after thrombolysis. Multivariate analysis showed independent association of sICH according to all definitions with poor outcome and mortality. Based on prediction modeling with AUC-ROC curve and IDI analyses, unwanted outcomes were largely explained by such parameters as age, baseline NIHSS and blood glucose, OTT, and signs of artery occlusion on baseline imaging. Compared with these parameters, the presence or lack of sICH had smaller additional predictive effect. This was especially true for minor impact of SITS-defined sICH, whereas ECASS- and NINDS/Cochrane-defined sICH had 2 to 3 times larger impact on outcome prediction. ECASS-defined sICH had somewhat bigger impact on predicting mRS 5 to 6 and mortality than NINDS/Cochrane. **Conclusions:** sICH according to the ECASS definition had largest impact on patients' outcome.

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Th P284

Graduating Neurology Residents' Experience with Intravenous tPA for Acute Stroke: a 10 Year Comparison

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Background: Intravenous tPA was approved as a treatment for acute ischemic stroke (AIS) in 1996. One potential barrier to increased use of tPA has been lack of experience and training among neurologists in the community. A survey of graduating neurology residents conducted in 2000 showed that many residents had limited experience and were not comfortable treating with tPA. We examined if graduating residents' experience using tPA has changed over the past decade. **Methods:** A 12 item survey was sent in March 2010 to all neurology residents in their final year of training as identified by AMA-GME files. Follow-up surveys were sent in April, May, and June to non-responders. Survey items established residents' experience and confidence with assessment of the acute stroke patient and treatment with tPA. Responses were assessed using a 5 point Likert scale. Questions were worded identically in the 2000 and 2010 surveys, and responses were compared between the two. **Results:** Of 493 residents for whom current addresses were available, 286 (58%) responded. There was a significant increase over the past 10 years in the percentage of residents who felt comfortable independently treating with tPA (73% to 94%, $P<0.001$), had observed the administration of tPA (88% to 99%, $P<0.001$), had personally treated with tPA (80% to 95%, $P<0.001$), and were involved in post-tPA care (89% to 98%, $P<0.001$). There was a substantial increase in the percentage of residents who were formally trained in the NIH stroke scale (65% to 93%, $P<0.001$) and who had dedicated stroke teams at their institution (84% to 93%, $P<0.001$). As in 2000, the vast majority of residents were confident in their ability to identify hemorrhage (99% to 100%, p=NS) or early infarct signs (94% to 98%, $p=0.03$) on CT. While 94% of residents somewhat or strongly agreed they felt comfortable independently treating with tPA, only 65% strongly agreed. Personal experience treating a patient with tPA was associated with strongly agreeing (68% with vs. 20% without experience, $P<0.001$). In those residents with prior experience, treating a patient without direct faculty supervision was associated with strongly agreeing (78% without direct supervision vs. 52% only with direct supervision, $P<0.001$). There was no association between career plans (i.e. academics versus private practice) and any of the items assessed. **Conclusion:** Neurology residents' experience and comfort treating acute ischemic stroke with tPA increased significantly between 2000 and 2010. Resident exposure to stroke teams and formal training in the NIHSS has also increased substantially during this time period.

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Th P285

Requirement for Emergent Neurosurgical Procedures Following Neuro-endovascular Procedures in Contemporary Practice

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Background: Provision to provide an emergent neurosurgical procedure has been considered a mandatory component for centers that perform neuroendovascular procedures. We sought to determine the need for emergent neurosurgical procedures following neuroendovascular procedures in two comprehensive stroke centers in settings with such provision. **Methods:** Prospectively collected data supplemented by chart review, was reviewed to identify any patients who may have required immediate (before the termination of the procedure) or adjunctive (within 24 hours of the procedure) neurosurgical procedures related to neuroendovascular procedure complication. The types of neurosurgical procedures and in-hospital outcomes of identified patients are reported as aggregate and per endovascular -procedure type analyses. **Results:** We reviewed 2474 procedures (1359 diagnostic angiograms and 1115 interventional procedures, see Table) performed over 3.5 years (2006- 2010). There was a need for neurosurgical procedures in 9 (0.4%) patients (mean age 46 years, 7 were women); the procedures were categorized as 6 emergent and 3 adjunctive procedures. There were 5 in-hospital deaths (55%) in these 9 patients. Major procedures performed were external ventricular drainage placement in 6 (67%) patients and decompression hemicraniectomy in 3(33%) patients. **Conclusions:** The need for emergent neurosurgical procedures is low among patients undergoing neuroendovascular procedures. Mortality in such patients is quite high.

Table: Emergent Neurosurgical Procedures following Neuro-endovascular procedures according to procedure type

Endovascular procedure	Emergent neurosurgical procedure			
Procedures (N)	Immediate (%)	Adjunctive (%)	Indications	Interventions
Unruptured aneurysms embolization (98)	1 (1%)	0	Intraprocedure rupture	DC
Ruptured aneurysm embolization (134)	3 (2.2%)	1 (0.75%)	Intraprocedure rupture	3 EVD, 1 DC
Intra-arterial treatment of AIS (165)	1 (0.6%)	1(0.6%)	1 vessel rupture during angioplasty, 1 SAH after lytics	2 EVD
AVM embolization (34)	1 (3%)	0	IPH	DC
Intracranial angioplasty/stenting (92)	0	1 (1.09%)	vessel perforation by microwire	EVD

AIS: Acute ischemic stroke, AVM: Arteriovenous malformation, SAH: Subarachnoid hemorrhage, IPH: Intraparenchymal hematoma, EVD: External ventricular drainage, DC: Decompression craniectomy

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Th P286

Quality of Life After Intra-Arterial Therapy for Ischemic Stroke

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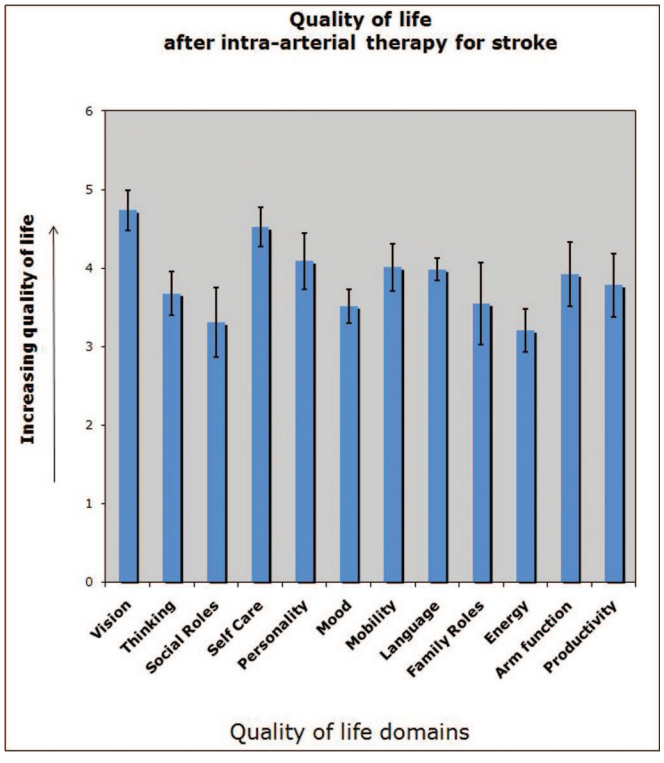
Quality of Life after Intra-Arterial Therapy for Acute Ischemic Stroke **Objective:** To determine quality of life (QOL) after intra-arterial (IA) therapy for acute ischemic stroke. **Methods:** Patients undergoing IA therapy for acute ischemic stroke from March 2005 to April 2010 were identified through a single-center, stroke database and surveyed by mail, using multiple, overlapping contact methods (the Dillman method). Outcomes were QOL, measured via the Stroke-Specific QOL Scale (SS-QOL) and reported as QOL domain means (standard deviation (SD)), and percent of recurrent TIA/stroke during follow-up. **Results:** Of the 83 patients identified in the database, 67 survived to hospital discharge and were sent surveys; there were 40 responses (response rate 60%), 11 of which represented interim deaths. Of the 29 surviving respondents, 31% were female, mean age was 59.8 (SD=13.1), and follow-up length was a median of 26.3 months (IQR 17.5, 41.2). Initial median NIHSS for all 83 patients was 15 (IQR 9, 20); for responders was 11 (6, 18). Site of vessel occlusion in all patients was left ICA/M1 in 44%, right ICA/M1 in 40%, and basilar in 10% (in respondents, 41%, 48%, and 7%, respectively). Median time from symptom onset to angiogram was 4 hrs 19 min for all patients (4 hrs 3 min for respondents); mean procedure duration was 1 hr 54 min for both groups. Treatment consisted of IA tPA in 97% of all patients (96.5% in respondents) with 12 patients receiving adjunctive IV tPA (3 of the respondents). Mechanical thrombectomy was used in 94% of patients (97% of respondents). In-hospital mortality was 19%, overall mortality was 32.5%, and the percent of recurrent TIA/stroke during follow-up was 2.4%. The overall, aggregate SS-QOL score was 3.86 (SD=0.45) on a scale of 1 to 5 with 5 being the best. The results are graphed by domain. **Conclusions:** : In this single center study, survivors of ischemic stroke who have undergone intra-arterial therapy over a 5 year period report good QOL. The domains with the lowest perceived QOL are in energy levels and social roles; the highest are in vision and self care. Patient-centered outcomes, such as QOL, should be included in all acute stroke trials, including interventional trials, since patient experience is a critical measure of success.



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Th P287

Stroke Care and Outcomes in Patients With Pre-existing Dementia

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Background: Stroke can be a devastating medical condition for patients and their families. With an aging population, patients are increasingly likely to present with stroke and pre-existing dementia. Little is known about how pre-existing dementia influences care processes and outcomes after stroke. **Objective:** To compare processes of care and short and long-term outcomes in patients with an acute ischemic stroke with and without pre-existing dementia. **Methods:** We conducted a retrospective cohort study using the Registry of the Canadian Stroke Network (RCSN) to identify patients presenting to 12 participating institutions with an acute first ischemic stroke between 2003-2008. Pre-existing dementia was defined as any type of dementia that was present prior to the stroke case index. Palliative patients were excluded. Logistic regression analysis and Cox-proportional Hazard models were developed to compare the outcomes of interest. Outcome Measures: 1°) Mortality at discharge, 30-days, and 1-year; 2°) Performance measures, disability at discharge (mRS ≥3), disposition. **Results:** Among 9304 eligible patients with an acute ischemic stroke, 702 (9.1%) had a history of dementia. Patients with dementia were older (mean age 81 vs. 70 years; P<0.001) and had more severe strokes (as per the Canadian Neurological Scale <4, 20.7% vs. 10.5%; P<0.001) than those without dementia. Stroke patients with dementia had also a higher prevalence of diabetes and atrial fibrillation. There was a minor difference in admission to stroke unit (63% vs 67.6%; OR 0.82, 95%CI 0.70-0.96) and those with dementia were less likely to receive thrombolysis (10.5% vs 15.7%; OR 0.63, 95%CI 0.49-0.81). There were no differences in other performance measures (glucose on admission, swallowing assessment, time from stroke onset to ER, discharge on antithrombotics or warfarin for AF). Patients with pre-existing dementia had higher disability at discharge (80.6% vs. 56.6%; OR 3.20, 95%CI 2.64-3.87) and were less likely discharged to place of residence prior to stroke (24% vs. 45%; P<0.001). Stroke fatality was dramatically higher in those with dementia, but this was explained by age, sex, stroke severity and co-morbid illness (Table). **Conclusions:** Stroke patients with pre-existing dementia have twice the mortality rates as those without, but, the increased rates may be attributable to older age, greater stroke severity and comorbid illness rather than dementia itself. Still, two-thirds survive one year with greater disability and institutionalization, representing an increasing stroke care challenge, given population aging.

Table. Main Outcome Measures

	Stroke Patients n=9304		Unadjusted Hazards Ratio (95% CI)	Partially Adjusted Hazards Ratio* (95% CI)	P-value†	Fully Adjusted Hazards Ratio** (95% CI)	P-value†
	History of Dementia	No Dementia					
Total No. of Patients (%)	702 (9.1)	8602 (90.9)	--	--	--	--	--
Mortality at Discharge	56 (8.0)	352 (4.1)	1.47 (1.11-1.96)	0.91 (0.67-1.24)	0.55	0.79 (0.57-1.10)	0.17
30 Day Mortality (%)	72 (10.3)	427 (5.0)	2.096 (1.63-2.69)	0.99 (0.75-1.3)	0.93	0.77 (0.57-1.02)	0.07
1 Year Mortality (%)	236 (33.6)	1206 (14.0)	2.68 (2.32-3.076)	1.19 (1.02-1.39)	0.025	0.91 (0.77-1.07)	0.27

* Partially adjusted model includes 4 baseline characteristics: age, gender (sex), Charlson Index, CNS score.

** Fully adjusted model includes 14 baseline characteristics: age, sex, stroke severity (Canadian Neurological Scale), hypertension, diabetes, hyperlipidemia, atrial fibrillation, stroke/TIA, premorbid functional status (=preadmission independence), stroke subtype, preadmission use of: antithrombotics, antihypertensive agents, statins, warfarin

† P-value for Adjusted Hazards Ratio

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Th P288

Urinary Incontinence is a Negative Predictor of Discharge Disposition in Patients with Acute Stroke

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Introduction: Urinary incontinence (UI) is the leading cause of post-stroke disability. Early treatment of UI has been shown to improve patient morale and self esteem, having an indirect effect on the speed of overall stroke recovery. Treatment of UI requires increased acuity of hospital care for bladder training and medical management. This care is provided at all levels, including Inpatient Rehabilitation (IR), Skilled Nursing Facility (SNF) and Subacute Care (Sub). Although UI has been used to predict functional outcome, there is limited data on the direct role of UI as an independent predictor of post-stroke disposition. Hypothesis: Low NIHSS is an established predictor of higher functional status. We assessed the hypothesis that absence of UI predicts post-stroke disposition to a functional level similar to low NIHSS. **Methods:** We

conducted a retrospective analysis of all patients admitted to the UTHMS Stroke Service from January 2004 to October 2009 with discharge disposition of home, IR, SNF or Sub. Baseline demographics including age, gender, race and NIHSS were collected. Cerebrovascular disease risk factors [Age > 65, Cardiovascular Disease (CV), Diabetes Mellitus (DM), Hypertension (HTN), Hyperlipidemia (HLD) History of Stroke (CVA)] were used for independent risk assessment and risk stratification. Using multivariate logistic regression, the data was analyzed for differences in post-stroke disposition among patients with UI. **Results:** *Home vs. Other Level of Care:* Of 3744 patients, a total of 3260 were included in the analysis. Approximately 1593 were discharged home, 1667 to another level of care. Patients with UI are 4.44 times less likely to be discharged home. *IR vs. SNF:* Of 1497 patients, 953 patients were discharged to IR, 544 to SNF. Patients with UI are 3.65 times less likely to be discharged to IR. **Conclusions:** Acute stroke patients with UI are more 4.44 times less likely to be discharged home. If post-stroke care is necessary, rehabilitation is 3.65 times more likely to occur at a level reflective of worse functional status (SNF). This study is limited by its retrospective nature and the undetermined role of psychosocial factors related to discharge. Prospective studies addressing problems with urinary incontinence while the person is acutely hospitalized may augment long-term complications.

Table 1. Demographic Data

	Urinary Incontinence (UI)	No Urinary Incontinence	Significance
Gender			
Female	120	1680	P = .2306
Male	149	1791	
Mean Age			
	67.74	62.74	P = <0.0001
Median Stroke Scale on Arrival (IQR)			
	17 (10 to 22)	5 (2 to 11)	P = <0.0001
Ethnicity %			
African-American	43	35	P = .0202
Hispanic	11	15	
Caucasian	43	47	
Other	3	3	
Diagnosis			
ICH	109	643	P = <0.0001
IVH	0	9	
Infarct	151	2323	
Infarct-Other	0	10	
SAH	0	8	
SAH/EDH/SDH	0	7	
SDH	0	3	
TIA	9	469	

Table 2. Discharge Disposition to Home vs. Other Level of Care

	P	Odds Ratio	95% CI - Lower	95% CI - Upper
UI	<0.0001	0.225	0.136	0.372
Age > 65	<0.0001	0.534	0.452	0.630
CV	0.735	1.031	0.864	1.230
DM	0.004	0.776	0.652	0.923
HTN	0.005	0.757	0.625	0.918
HLD	0.007	0.792	0.668	0.938
CVA	0.0006	1.400	1.156	1.694
NIHSS < 8	<0.0001	14.459	10.497	19.916

Table 3. Discharge Disposition to Inpatient Rehabilitation vs. Skilled Nursing Facility

	P	Odds Ratio	95% CI - Lower	95% CI - Upper
UI	<0.0001	0.215	0.142	0.326
Age > 65	<0.0001	0.348	0.269	0.450
CV	0.004	0.691	0.538	0.888
DM	0.082	0.797	0.617	1.030
HTN	0.523	1.099	0.820	1.473
HLD	0.364	1.126	0.871	1.455
CVA	<0.0001	3.255	2.491	4.254
NIHSS < 8	<0.0001	3.366	2.471	4.585

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Th P289

Urinary Tract Infections in Hospitalized Ischemic Stroke Patients: Source and Impact on Outcome

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Introduction: Recent initiatives have focused on eliminating infections, such as urinary tract infections (UTI), in hospitalized ischemic stroke patients. However, many UTI may in fact be present on admission and little is known about the different factors that lead ischemic stroke patients to develop UTI and what affect the presence of UTI may have on overall outcome. **Methods:** We searched our prospective Stroke Center database for the 2 year period July 2008 - June 2010 for patients admitted with a diagnosis of ischemic stroke. Data obtained included, demographics, admission source, medical history, smoking status, BMI, admission HbA1c and serum creatinine, admission NIHSS, ambulatory status by day 2, UTI occurrence, and clinical outcome. For clinical outcome we used a combination of discharge location and ambulatory status at discharge, whereby any ambulatory patient discharged to home or to a rehabilitation hospital was considered to have had a good outcome. **Results:** A total of 842 patients were analyzed. 541 patients (64%) were admitted from the community, while the remainder were transfered from another healthcare facility. The overall rate of UTI was 12% (103 patients). Of these, 67 patients (8% of total and 65% of UTI) had a UTI present on admission, with the vast majority of these coming from community settings (61 patients). Female gender (OR 3.6 95%CI2.3-5.7, P<0.0001) and smoking (OR 0.3 95%CI0.1-0.6, P=0.0013) were significantly associated with UTI. Increasing age (p<0.001) and higher admission NIHSS (P=0.004) were also significantly associated with UTI. BMI, HbA1c and admission serum creatinine were not associated with UTI. When comparing community acquired UTI (cUTI) to hospital acquired UTI (hUTI), those who were not ambulatory by day 2 (OR 3.3 95%CI1.0-10.5, P=0.0463) and those that were not ambulatory at discharge (OR 4.8 95%CI1.3-17.4, P=0.0172) were more likely suffer a hUTI. Increasing age (p=0.013) and higher admission NIHSS (P=0.01) were also associated with the presence of a hUTI as compared to a cUTI. In univariate outcome analysis, UTI showed a significant association with poor outcome (OR 3.0 95%CI1.8-5.0, P<0.0001) and cUTI patients were more likely to have a good outcome when compared to hUTI patients (OR 3.5 95%CI1.1-11.2, P=0.0376). However, in the multivariate models, UTI variables did not remain as significant independent predictors of outcome. **Conclusions:** Our results suggest that UTI is a common problem among ischemic stroke patients, but that the majority of UTI seen in these patients are actually community acquired and present on admission. In addition, it appears that UTI is not independently associated with a poor outcome after ischemic stroke. These results have implications for hospital infection recording and tracking.

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Th P290

Effect of Coronary Artery Disease on the Outcomes of the Patients with Ischemic Stroke in Taiwan

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Background Patients with cerebral infarction may have an increased risk of death. Previous reports in Western countries showed their death were more often due to coronary artery disease (CAD) than recurrent cerebral infarction or other neurological diseases. However, there is no such evidence of data for Taiwanese patients. The present study would investigate CAD and the relevant outcomes for the patients with ischemic stroke in Taiwan. Methods and Results We conducted a prospective study of consecutive 615 hospitalized patients of the neurology service with a diagnosis of TIA or ischemic stroke from Sep. 2006 to Dec. 2008. All patients underwent brain CT on the day of admission, and repeated brain CT or MRI within one week. Carotid and transcranial ultrasonography with systemic evaluation were done. The baseline data, including BMI, cholesterol, and triglyceride levels, were collected. We defined extracranial or intracranial stenosis as the area stenosis over 50%. There were 174 patients (28.3%) who had CAD. Male gender, hypertension, diabetes mellitus, atrial fibrillation, and other non-ischemic heart disease were significantly more prevalent in the patients with CAD than those without CAD (65.5% vs 54.7%, P=0.015; 81% vs 70.5%, P=0.008; 52.3% vs 37.0%, P=0.001; 22.4% vs 14.5%, P=0.022; 32.2% vs 20.2%, P=0.002, respectively). The prevalence rate of extracranial carotid stenosis was also significantly higher in the CAD than the non-CAD groups (14.7 vs 6.58%, P=0.005). During the 12-months follow-up period, the incidence rate (by Kaplan-Meier method) of cardiovascular death, non-fatal ischemic heart event, major adverse cardiac event (MACE), and major adverse cardiac and cerebral event (MACCE) were significantly higher in the patients with CAD than those without CAD (4.02% vs 1.13%, P=0.045; 4.6% vs 0.45%, P=0.001; 8.62% vs 1.59%, P<0.0001; 14.94% vs 5.58%, P=0.002, respectively). **Conclusion:** The study showed a higher incidence rate of cardiovascular death, non-fatal ischemic heart event, MACE, and MACCE during the 12-month follow-up in the ischemic stroke patients with CAD than those without CAD in Taiwan. It is implied that the workup for CAD may be useful to identify the group of higher risk of recurrent cardiovascular events in the patients with ischemic stroke in Asian population.

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Th P291

Albumin-Corrected Calcium Level is Associated with Mortality after Acute Ischemic Stroke

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Background: Influx of calcium ion into intracellular component is known to initiate ischemic cell death pathway. However, the association between serum calcium level and consequences of acute ischemic stroke has not been reported in detail. We aimed to investigate whether acute ischemic stroke patients with elevated serum calcium are at increased risk of mortality. **Methods:** Among a total of 1,957 patients screened between October 2002 and September 2008, 1,921 subjects were included in the final analysis after excluding 36 patients whose calcium level, height or NIH Stroke Scale (NIHSS) was not documented. Demographic and clinical information including cardiovascular risk factors, laboratory informations and NIHSS at admission were collected during hospitalization. Mortality status of each patient was ascertained from the Korean National Death Certificates on December 31, 2008. As calcium level is alleged to be affected by serum albumin and albumin-bound calcium is considered as physiologically inactive, we used albumin-corrected calcium calculated by the following

formula: [0.8 X (average albumin - patient's albumin(g/dL)) + measured calcium(mg/dL)]. Cox proportional hazard models were constructed to investigate the effect of serum calcium level on the post-stroke mortality, adjusted for relevant covariates that were significant on univariate analyses. **Results:** Among a total of 1,921 acute ischemic stroke patients, the mean (±SD) of albumin-corrected calcium was 9.07 (±0.49) mg/dl. The mean follow-up period was 918.4±609.8 days and 334 (17.4%) patients died until December 2008. Albumin-corrected calcium level was associated with increased risk of mortality (HR, 1.49 per 1-mg/dL increase; 95% CI, 1.18-1.88) after adjusting for age (HR, 1.05; 95% CI, 1.04-1.06), body-mass index (HR, 0.95 per 1-Kg/m^2 increase); 95% CI, 0.92-0.99), previous stroke history (HR, 1.23; 95% CI, 0.97-1.56), hyperlipidemia (HR, 0.75; 95% CI, 0.54-1.04), cardiogenic embolism risks (HR, 1.28; 95% CI, 1.02-1.61), serum glucose (HR, 1.03 per 10-mg/dL increase; 95% CI, 1.002-1.05), total cholesterol (HR, 0.96 per 10-mg/dL increase; 95% CI, 0.94-0.995), total protein (HR, 0.94 per 1-mg/dL increase; 95% CI, 0.80-1.10), systolic blood pressure (HR, 0.93 per 10-mm Hg increase; 95% CI, 0.90-0.97), and NIHSS at admission (HR, 1.07 per 1-point increase; 95% CI, 1.06-1.09). **Conclusions:** Elevated albumin-corrected calcium is associated with an increased risk for mortality after acute ischemic stroke, when adjusted for relevant covariates including serum total protein and cholesterol levels. Further prospective studies with a direct measurement of ionized calcium are warranted.

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Th P292

The Relationship Between Blood Glucose Fluctuation And Neurological Outcome In Acute Ischemic Stroke Patients

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Objective: Hyperglycemia in acute stroke is associated with a poor prognosis. We previously investigated whether poor prognosis of stroke was related to not only hyperglycemia but also variation of blood glucose levels among patients with severe cerebral hemorrhage. In the present study, we report the relationships between the mean and variation of blood glucose levels and outcome in acute ischemic stroke patients. **Methods:** Subjects were a total of 360 patients (mean age, 71.3±9.6 years; median age, 71 years) who were either already undergoing treatment for diabetes or had a hemoglobin A1c level of ≥5.8% at the time of admission among 2,597 acute stroke patients admitted within seven days of onset to our hospital between April 2006 and March 2009. In addition to patient attributes, the following items were measured: NIHSS score at admission and discharge, mean morning fasting blood glucose level (mean BG), and as an indicator of variation of blood glucose levels, successive variation (SV) = $(BGi+1-BGi)^2/(n-1)$. Mean BG and SV were calculated from the seven consecutive morning measurements. Patients in whom the NIHSS score increased by ≥4 points from admission to discharge were classified into the exacerbation group, while other patients were classified into the non-exacerbation group. Logistic regression analysis was performed using the exacerbation and non-exacerbation groups as dependent variables, and factors related to exacerbation were investigated. **Results:** The exacerbation and non-exacerbation groups included 18 (5%) and 342 (95%) patients, respectively. The non-exacerbation group had a higher proportion of men but no intergroup differences were observed for age, hypertension, hyperlipidemia, smoking history, or drinking history. Logistic regression analysis performed by including the above factors showed no relationship between mean BG and symptom exacerbation (OR=1.00, 95%CI:0.98-1.01, p=0.87), but a large SV was related to exacerbation (OR=1.03, 95%CI:1.00-1.05, p=0.02). **Conclusion:** Large variation of morning fasting blood glucose level, rather than its absolute value, was an independent risk factor correlated with exacerbation of neurological symptoms in patients with stroke complicated by diabetes. These findings suggest that variation of blood glucose levels worsens prognosis or induces impaired glucose tolerance in patients with symptom progression.

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Th P293

Patient and Facility Characteristics Associated with Discharge to Inpatient Rehabilitation Post-stroke

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Background: Most stroke survivors require rehabilitation (rehab) to maximize recovery, and studies have shown that patient outcomes vary depending on the structure and quality of post-stroke rehab provided. The aim of this study was to investigate the relationship of patient and facility characteristics to inpatient rehab discharge for veterans with ischemic stroke. **Methods:** We used the national OQP Stroke database, which includes veterans hospitalized for ischemic stroke at any VA medical center in FY2007. Patient and facility level data were collected via chart abstraction and were merged with other VA administrative data. For this analysis, we excluded subjects that were admitted from a nursing home, those with in-hospital death, and those that had comfort care measures or hospice discharge. We also excluded facilities with < 20 stroke admissions. Independent patient variables included: demographics, admission NIH Stroke Scale (NIHSS) score, and Charlson comorbidity score. Facility variables included: complexity score, stroke volume, and presence of a co-located inpatient rehab unit. Discharge destination was categorized as home, inpatient rehab, or extended care facility (ECF). We used ANOVA and Chi-square tests to assess relationships of candidate variables to discharge destination. We developed a multinomial hierarchical regression model to assess the independent relationship of patient and facility variables to the three discharge categories. **Results:** Of the 2655 subjects from 70 facilities, 2107 (79%) were discharged home, 432 (16%) to ECF, and 116 (4%) to inpatient rehab. Subjects discharged to inpatient rehab had similar age and comorbidity scores as those discharged home (mean age 64.9 and 65.8 years, mean Charlson 4.4 and 4.5); those discharged to ECF were older (mean age 72.8) and had greater comorbidity (mean Charlson 5.5). Stroke severity was similar in the inpatient rehab and ECF groups (mean NIHSS 5.9 and 6.2) but was less severe in those discharged home (mean NIHSS 2.8). Facility characteristics that differed in the inpatient rehab group included greater prevalence of a co-located inpatient rehab facility, increased hospital complexity, and moderate stroke admission volume (60-79 cases annually). In the hierarchical multinomial model, patient variables of age, NIHSS, race, marital status, and receipt of speech consult, and facility variables of complexity and stroke volume, remained significantly associated with discharge destination. **Conclusions:** Among veterans admitted to a VA facility for ischemic stroke, both patient and facility characteristics are associated with discharge destination. Since ideally patient factors would drive decisions about discharge, further work to explore the process of decision-making around stroke discharge is needed to ensure veterans have access to post-stroke care that will maximize their stroke recovery..

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Th P294

Are Stroke Suvivors Getting the Rehabilitation Services they Need?

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Objective: To determine the proportion of all stroke survivors who are appropriate candidates for inpatient rehabilitation and what services they actually receive within a universal healthcare system. Design: Descriptive study consisting of a retrospective chart audit using objective criteria to identify appropriate candidates for inpatient rehabilitation from all acute stroke admissions. Participants: All persons hospitalized with acute stroke (ICD10 codes 161-169) and discharged alive from eight community and rural hospitals over two calendar years; a sample of convenience. Main Outcome Measures: Modified Rankin Scale (mRS), Stroke Rehabilitation Candidacy Screening Tool (criteria include stroke severity, ability to follow commands, identified rehabilitation goals, demonstration of change over time and willingness to participate), Discharge Disposition. **Results:** Data were collected on a total of 788 subjects, 51.1% male, with a mean age of 73.7 +/- 12.4 years. The mean and median lengths of stay in acute care were 12.4 and 7 days respectively. Proportions of all stroke by mRS severity category were: mild or resolved (mRS 0-2) 29.4%; moderate (mRS 3) 15.6%; moderately severe (mRS 4) 37.8% and severe (mRS 5) 15.0%. Three hundred and one (38%) of the 788 met the criteria for inpatient rehabilitation while 9% of all charts audited had insufficient information to determine candidacy. From the 9%, if we assume that 23 patients with moderately severe stroke (mRS 4) were candidates, then 41% met the criteria for inpatient rehabilitation. One third of severe, two thirds of moderately severe, and half of moderate clients were identified as appropriate candidates for rehabilitation, as well as 5.6% from the mild category. For actual services received on discharge from acute care, only 75% of those who met the criteria for inpatient rehabilitation received it. The most frequently cited reason for not receiving inpatient rehabilitation was lack of access to an available bed. **Conclusions:** Of all acute stroke survivors, approximately 40% are appropriate candidates for inpatient rehabilitation when objective criteria are applied. Persons who met the candidacy criteria for inpatient rehabilitation were identified in all categories (mild to severe) of stroke severity. At the participating facilities, one in four stroke survivors who should receive inpatient rehabilitation did not receive it.

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Th P295

Patterns of Rehabilitation Service use following Acute Stroke and its Association With Rehospitalization: The AVAIL Registry

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Background: While the important role of rehabilitation (rehab) services following stroke is well established, prior studies have suggested that these services are often underutilized. We investigated the factors associated with stroke rehab service use, and whether use of rehab was associated with lower 12-month rehospitalization rates. **Methods:** The Adherence eValuation After Ischemic stroke - Longitudinal (AVAIL) was a multi-center registry of 101 U.S. hospitals participating in the AHA's Get With The Guidelines - Stroke program. We evaluated 2,035 ischemic stroke patients who were living independently prior to their stroke and survived >3 months post stroke. Participants were contacted at 3 and 12 months to determine use of rehab services, service type (inpatient, outpatient, or home), duration and follow-up hospitalizations, if any. A Generalized Estimating Equation (GEE) logistic model identified factors associated with rehab utilization. The association of rehab services with 12 month rehospitalization was also determined using GEE logistic regression after adjusting for clinical confounders. **Results:** Overall, 62.4% (n=1271) of stroke patients received rehab services within 3 months of their event: 32.2% (n=409) inpatient, 57.1% (n=726) outpatient, 31.7% (n=403) home; 248 patients (19.5%) received rehab services in more than one location. In the multivariate model, more severe strokes (modified Rankin Score (mRS) of 3, 4, or 5 vs. 2) and

failure to ambulate at discharge and increasing number of discharge medications were independently associated with rehab services use (Table). Of the patients who received rehab services, 298 patients (23.4%) were rehospitalized at least once by 12 months. After adjustment, overall use of rehab services was not associated with rehospitalization (OR 1.098, 95% CI 0.843-1.428, p=0.488). **Conclusions:** In the AVAIL registry, nearly two-thirds of ischemic stroke patients received some form of rehab services, and the important predictors at baseline were number of medications and failure to ambulate. We were unable to demonstrate that rehab use reduced the odds for rehospitalization following stroke.

Table

Multivariate model of rehab utilization by 3-months post-discharge (C = 0.7721)*

Variable	*OR (95% CI)*	*P value*
Number of Discharge Medications (per 1 increase)	1.058 (1.016-1.102)	0.006
Failure to ambulate independently at discharge	5.650 (4.274-7.519)	<.001
mRS = 3 (vs. ≤ 2)	2.460 (1.941-3.119)	<.001
mRS = 4 (vs. ≤ 2)	4.485 (2.154-9.339)	<.001
mRS = 5 (vs. ≤ 2)	8.409 (3.811-18.557)	<.001

*The model also adjusted for age, medical history of stroke/TIA, medical history of CAD/prior MI, marital status (married/living as married vs. other), living situation (living with someone vs. other), education level (at least college vs. other), household income meeting needs, perceived burden of medication cost, work status, insurance status, geographic region of the site, hospital type, and number of stroke discharges.

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Th P296

Patients with Stroke in Northeastern Brazil are Infrequently Treated with Thrombolysis and Evaluated for Stroke Etiology

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Introduction: Little information exists on the epidemiology of patients admitted to Brazilian emergency departments (EDs) with stroke. Fortaleza is the state capital of Ceará (Northeastern Brazil), has a population of over 2.5 million, and is the 5th largest city in Brazil. Hypothesis: We hypothesized that patients admitted with stroke in Fortaleza are infrequently treated with thrombolysis and that investigation of stroke etiology is not routinely performed. **Methods:** Data were prospectively collected from patients admitted to the EDs of 19 hospitals in Fortaleza with a diagnosis of stroke or transient ischemic attack (TIA) by trained research coordinators from June-2009 to May-2010. In 2008, 90% of the patients admitted with stroke in Fortaleza were evaluated in either one of the 19 hospitals studied. Daily visits to EDs of the selected hospital were performed and all patients admitted with a diagnosis of stroke or TIA were prospectively evaluated. A dedicated nurse coordinator reviewed all the patients. Controversies were discussed with two stroke neurologists. **Results:** We evaluated 1510 patients. Mean age was 67.9 ± 14.5 yo (50.2% males). Ischemic stroke was the most frequent subtype (71.8%), followed by parenchymal hemorrhage (20%), subarachnoid hemorrhage (5.4%) and TIA (2.7%). The prevalence of stroke risk factors was: hypertension (81.8%), diabetes (39.1%), hyperlipidemia (22.6%), obesity (10.1%), smoking (22%), alcohol use (18.8%), previous stroke (32.4%) and previous myocardial infarction (8.4%). Head computerized tomography was performed in 90.3% of the patients, carotid-ultrasonography in 18.5%, cerebral angiography in 4.7%, electrocardiogram in 68.6% and echocardiogram in 24.8%. One hundred thirty seven patients (9.1%) were admitted to stroke units. Mortality in patients admitted to stroke units was lower when compared to patients admitted to regular wards (11.8% versus 24.7%, P<0.01). Eleven patients (1% of the patients with ischemic stroke) were treated with thrombolysis. Twenty three percent of the patients died during hospital admission. Age, history of hypertension, diabetes and having depressed level of consciousness (p<0.01) were univariate predictors of in hospital mortality. After multivariate logistic regression analysis, admission to regular wards was an independent predictor of in hospital mortality. **Conclusion:** The prevalence of stroke risk factors and clinical presentation in our cohort was similar to previously reported series. Evaluation of stroke etiology and treatment with thrombolysis were infrequent. Less of 25% of the patients with ischemic stroke were properly evaluated to exclude cardioembolic or large artery atherosclerotic sources. Although less than 10% of the patients were treated in specialized stroke units, a difference in in hospital mortality favoring stroke unit care could be observed.

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Th P297

Representativeness of Get with the Guidelines-Stroke among Fee-for-Service Medicare Beneficiaries with Ischemic Stroke

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Background: Get with the Guidelines (GWTG)-Stroke is a widely used quality improvement registry but questions remain about its representativeness. We used national fee-for-service Medicare (FFS CMS) claims data to compare patient characteristics of ischemic stroke cases enrolled in GWTG-Stroke to those not enrolled in the registry. **Methods:** All 926,756 FFS CMS claims for ischemic stroke (primary ICD-9 discharge code 434 or 436) for the period 4/2003 and 12/2007 were matched to 228,815 subjects who had a clinical diagnosis of ischemic stroke in the GWTG-Stroke registry during the same time period. Data on patient characteristics were obtained from CMS claims. Comparisons between the FFS CMS cases that were matched to GWTG-Stroke registry and the remaining unmatched FFS CMS cases were performed using unadjusted analyses. Because of the sample size, all differences, regardless of magnitude, were statistically significant. **Results:** Among 926,756 FFS CMS claims, 144,344 were successfully matched to the GWTG-Stroke registry, leaving 782,412 unmatched FFS CMS claims. Demographic differences between the two groups were relatively minor (Table). GWTG-Stroke cases had a higher prevalence of a past medical history of carotid stenosis. Patients enrolled in GWTG-Stroke were more likely to be admitted to larger, teaching hospitals in urban areas. The geographic distribution was similar, except for modestly fewer patients in the Midwest. (Table) **Discussion:** Despite differences in hospital characteristics, FFS CMS ischemic stroke cases entered into GWTG-Stroke were largely similar to other FFS CMS cases with respect to demographics and other clinical characteristics. These data suggest that the Medicare-aged GWTG-Stroke population may be broadly representative of the national Medicare ischemic stroke population.

Table. Comparison between Medicare-aged ischemic stroke cases enrolled in GWTG-Stroke and those not enrolled in GWTG-Stroke (N, %)

Characteristic	Level	Medicare Cases Enrolled in GWTG-Stroke	%	Medicare Cases Not Enrolled in GWTG-Stroke	%
Patient Demographics					
Age	Mean	144344	79.4	782412	79.7
Gender	Male	60772	42.1	312307	39.9
Race	White	124165	86.0	649877	83.1
	Black	14723	10.2	95868	12.3
	Other	5456	3.8	36667	4.6
Past Medical History					
Hypertension	Yes	113948	78.9	609721	77.9
AMI	Yes	16718	11.6	78606	10.1
Stroke	Yes	15667	10.9	67982	8.7
Diabetes	Yes	41196	28.5	233390	29.8
Renal disease	Yes	18432	12.8	76296	9.8
COPD	Yes	27302	18.9	152421	19.5
Carotid Stenosis	Yes	23531	16.3	64751	8.3
Complications					
Pneumonia	Yes	11703	8.1	71071	9.1
Hospital Characteristics		144344		782412	
Bed size	Median		362		258
Ischemic stroke discharges/year	Median		155		103
Teaching hospital	Yes		27.0		13.7
Urban area hospital	Yes		99.6		93.9

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Th P298

Trends in Acute Ischemic Stroke Presentation in the GWTG Stroke Database 2004-2009: Opportunities for Improvement and Implications of Longer Treatment Time Windows

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Background: There are few data on temporal trends in the time from ischemic stroke symptom onset to hospital presentation. Recent trials have expanded the time window for acute treatment but there are few data on the number of patients arriving in later time windows. **Methods:** Characteristics of ischemic stroke patients enrolled in GWTG-Stroke between 2004-2009 were determined across different epochs of symptom onset to arrival time. Patients were divided into specific time epochs ranging from 24h. Logistic regression was used to identify independent predictors of early arrival, defined as
2h, among all patients with documented time of onset
24h. **Results:** Of 414,540 ischemic stroke patients, 182,691 (44%) had a recorded time of onset 24 hours, and 49,986 (11.3%) were missing both onset time and date. There was a small but significant decrease in the percentage of patients presenting
2h (20.9% in 2004 vs. 18.5% in 2009), and a small but significant increase in those arriving between 2-3.5h after onset (6.61% vs. 5.83%), and 3.5-8h (10.6% vs. 7.9%). Independent factors associated with presentation
2h after symptom onset included younger age, arrival by EMS and stroke onset during weekday regular hours (9 am -5 pm) (Table). Factors associated with lower likelihood of presentation
2h included increasing calendar year, diabetes, and smoking. Similar results, including the same relationship between increasing calendar year and lower likelihood of
2h presentation, were seen when the model was re-run in all patients including those with missing onset times; the sole exception was that previous stroke or TIA was no longer associated with <=2h presentation. **Conclusions:** Arrival times of acute ischemic stroke showed no improvement from 2004 to 2009, and may have slightly lengthened. Further efforts are needed to improve stroke recognition and response. Nevertheless, around 20% of ischemic stroke patients arrive <=2h , 25% <=3.5h, and 35% <=8h, suggesting that a substantial proportion of patients could potentially be eligible for acute stroke interventional therapies.

TABLE: Independent Predictors of Arrival ≤2 Hours after Symptom Onset, Among Patients With Documented Time of Arrival ≤24 hrs after Symptom Onset

Variable	OR	95% Confidence Limits		P-value
		Lower	Upper	
Calendar Year (per 1 year increase)	0.92	0.91	0.94	<.001
Age (per 10 year increase)	0.93	0.92	0.94	<.001
Female gender	0.97	0.95	0.99	0.002
Race (White vs. Non-white)	1.11	1.08	1.14	<.001
Arrival by ambulance	2.31	2.24	2.37	<.001
Onset weekday regular hrs (9a-5p)	1.30	1.27	1.33	<.001
Atrial Fibrillation	1.29	1.26	1.33	<.001
Previous Stroke/TIA	1.03	1.01	1.06	0.004
CAD/Prior MI	1.09	1.07	1.12	<.001
Diabetes Mellitus	0.77	0.75	0.79	<.001
PVD	0.95	0.90	0.99	0.028
Hypertension	0.91	0.89	0.93	<.001
Smoking	0.79	0.77	0.81	<.001
Dyslipidemia	1.03	1.01	1.05	0.004
Academic hospital	0.90	0.86	0.94	<.001
Region				
Northeast (reference)	1.00	--	--	--
Midwest	0.93	0.88	0.99	0.03
South	1.02	0.96	1.08	
West	0.99	0.93	1.05	
Number of Beds (per 100 increase)	0.98	0.97	0.99	<.001

Legend: Independent predictors of early arrival determined by logistic regression, using the generalized estimating equation method to account for patient clustering by hospital.

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Th P299

Growth of Regional Stroke Systems of Care in the United States in the First Decade of the 21st Century

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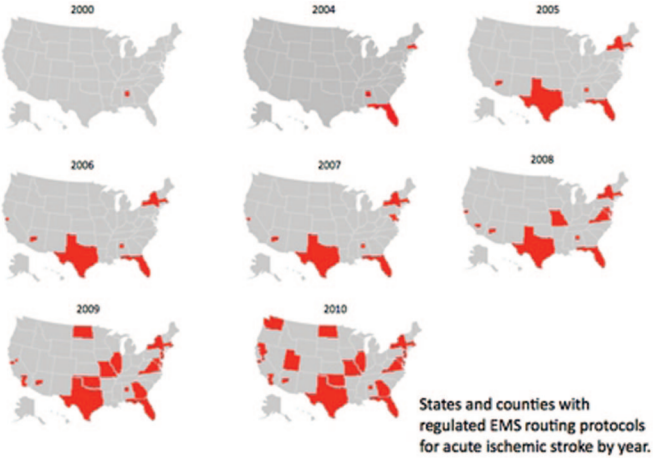
Background: With the advent of effective treatment for acute stroke, including thrombolytic therapy and organized supportive care in certified stroke centers, states and counties through the US medical system began implementing regional systems of acute stroke care in the first decade of the 21st century. In these systems, laws or regulations direct that emergency medical services (EMS) systems preferentially route acute stroke patients directly to Primary Stroke Centers (PSCs) certified as capable of reliably delivering proven therapies. The pace, geographic range, and population reach of regional stroke system implementation has not previously been delineated. **Methods:** We identified the occurrence and year of implementation of regional stroke systems of care by review of legislative archives, internet and media reports, consultation with the American Heart Association/American Stroke Association and the Centers for Disease Control, and phone interviews with state public health and emergency medical service officials from each of the fifty states. U.S. census population databases were researched. **Results:** The first counties to pass regional stroke system of care regulations were in Alabama in 2000 and the first states to pass laws for EMS to route patients directly to PSCs were Florida and Massachusetts in 2004. By 2010, a total of 16 states had state-level legislation or regulations requiring EMS routing to PSCs, as did individual counties in an additional 3 states. The geographic spread of systems is shown in the figure below. The US population covered residing in jurisdictions with regional stroke systems of care increased substantially in the latter half of the decade, from 0.4% in 2000; through 9% in 2004; 24% in 2005; 25% in 2006; 27% in 2007; 32% in 2008; and 50% in 2009. By mid-2010, 52% of the U.S. population was being serviced by EMS preferential PSC routing protocols. **Conclusions:** The first decade of the 21st century witnessed a remarkable structural transformation in acute stroke care, with over half of all Americans now living in states/counties that ensure patients are brought to stroke-capable facilities. However, additional efforts are needed to extend regional stroke systems of care to more states and counties and the nearly half of US citizens currently not assured of emergency access to best care practices.



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Th P300

Stroke care in England, Wales and Northern Ireland. Results from the National Sentinel Organisation of Care Audit of Stroke 2010

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Introduction: The National Sentinel Audit has been monitoring the quality of stroke care in England, Wales and Northern Ireland across all hospitals providing stroke services since 1998. We report the results of the 2010 survey on stroke service structures. **Methods:** All participating hospitals completed a web based form providing information on the structure of stroke services as of 1st April 2010 providing data on number of patients managed, staffing levels and expertise, imaging resources, thrombolysis services treatment rates**Results:** 100% of hospitals providing acute stroke care participated in the audit (159 hospital organisations with 201 sites. The proportion of hospitals offering thrombolysis on site has increased from 42% in 2008 to 74% with the median number of patients treated over the previous year increasing from 6 (IQR 2-14) to 14 (IQR 6-27). Nationally 3.8% of unselected stroke admissions were thrombolysed and 37% of centres treated more than 20 patients over the previous year. 10.7% of hospitals thrombolysed more than 10% of their stroke admissions. The quality of thrombolysis services appears to be high with all services under the supervision of specialist stroke physicians. All sites now have a stroke unit and the number of stroke beds has increased from a national ratio of 1 bed per patient to 1.07. TIA services have improved with the proportion of hospitals with a neurovascular clinic increasing from 95% to 98% and with reduced waiting times for an appointment from 7 days (IQR 5-12) to 3 days (IQR 2-7) over the last two years. **Conclusions:** Hyperacute stroke care and access to thrombolysis in the UK have improved substantially in the last two years with treatment rates matching those of other European and North American health care systems.

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Th P301

Acute Stroke Care: Telestroke vs. On-site Stroke Specialist Care. Results from the Ontario Telestroke Experience

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Background Ontario's population is over 13 million with 15% living in rural areas. The Ontario Telestroke Program was launched in 2003 to increase access to thrombolytic therapy (tPA) for stroke patients living in remote areas. Currently, the program is supported by 15 neurologists who provide consultations for patients presenting to 13 hospitals with videoconferencing and imaging provided by the Ontario Telemedicine Network. Emergency physicians in participating hospitals call a provincial 1-800 service (Criticall) to be connected with the Telestroke stroke neurologist on-call. Methods We performed a chart audit of patients managed by Telestroke between April 1, 2006 and March 31, 2009 and compared the results with data from the 2008/09 provincial stroke audit from our Registry of the Canadian Stroke Network. Telestroke patients at seven referring sites were identified through a probabilistic match between the Criticall database and the Canadian Institute of Health Information (CIHI) emergency department and inpatient databases and using one Telestroke site's consultation log. Ethics approval was obtained from each participating hospital and identified charts were abstracted using the same methodology and case record form used in the provincial stroke audit. Results Over the study period, the number of Telestroke activations increased from 182 in 2007 to 241 in 2009. Our total sample consisted of 498 patient charts. Of the patients who received a Telestroke consultation 65% had an ischemic stroke, 4% a hemorrhagic stroke and in 13% the stroke type was undetermined. The mean patient age was 71 years. Amongst those with ischemic stroke 51% were treated with tPA. The median NIHSS of the tPA treated patients was 12 and the median door to needle time was 74 minutes. The rate of symptomatic secondary hemorrhage was 8.3%, median length of stay 6 days, and in-hospital mortality was 18.9%. In comparison, 137 patients that received tPA at a designated stroke centre with an on-site stroke specialist in our 2008/09 provincial stroke audit similar quality of stroke care and outcomes were observed (door to needle 72 minutes, median length of stay 8 days, symptomatic secondary hemorrhage 8.0% ($P=0.94$) and in-hospital mortality 15.3% ($P = 0.41$)). **Conclusions:** The Ontario Telestroke Program demonstrates that advanced stroke care and access to thrombolysis can be effectively provided for patients in remote areas by having one neurologist on-call for an entire province. Based on our experience, stroke quality indicators among patients managed with the assistance of Telestroke are comparable to patients treated by on-site stroke specialists.

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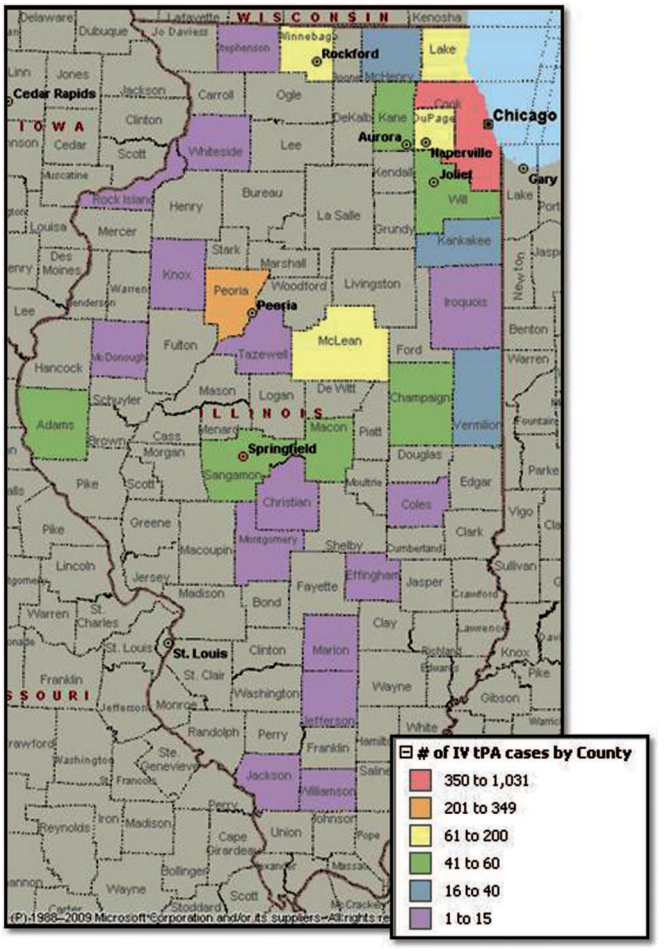

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Th P302

Primary Stroke Center Designation is Associated with Increased Utilization of Intravenous Tissue Plasminogen Activator and Mechanical Embolectomy for Acute Ischemic Stroke in Illinois

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Objective: To assess the use of revascularization therapies for acute ischemic stroke (AIS) in Illinois from 2003 to 2009. Background: Prior studies have estimated that only 1.8-3.0% of AIS patients receive tissue plasminogen activator (tPA) while utilization of mechanical embolectomy (ME) is unknown. In August 2009, Illinois passed legislation that emphasized the importance of primary stroke centers (PSC) designation and improved access to acute stroke care in rural areas. **Methods:** A retrospective analysis of the Illinois Hospital Association CompData® was performed, specifically, identifying those patients with primary discharge diagnosis of AIS based on ICD-9 codes (433.01, 433.11, 433.21, 433.31, 433.81, 433.91, 434.01, 434.11, 434.91, or 436). We analyzed the trends for utilization of acute revascularization therapies based on their ICD-9 procedure codes (tPA: 99.10; ME: 39.74). We employed univariable and multivariable logistic regression to calculate odds ratios (ORs) and 95% confidence intervals for factors associated with use of acute revascularization therapy. **Results:** Between January 2003 and September 2009, there were 119,539 AIS discharges (mean age 72 years and 55.2% women) from Illinois hospitals. Over the study period, only 1.9% received treatment with tPA and 0.19% underwent ME. In 72 counties (68.7%), tPA was never used for AIS (Figure). Overall, tPA and ME utilization increased over time (tPA: 0.8% to 3.2%; ME: 0.0016% to 0.57%; $p < 0.001$ for both trends). In multivariable analysis, factors independently associated with increased tPA or ME utilization included PSC status (adj. OR 3.25, 2.96-3.56), year of study (adj. OR 1.30, 1.27-1.33), emergency department (ED) source of admission (adj. OR 1.42, 1.26-1.59), hospital bed capacity greater than 200 (adj. OR1.19, 1.04-1.36), and possessing commercial insurance adj. (adj. OR 1.17, 1.06-1.30). Location in southern Illinois (adj. OR 0.23, 0.16-0.33) and increased age (adj. OR 0.989, 0.986-0.992) were associated with decreased odds of tPA or ME use. A significant interaction was noted between ED presentation and PSC status: PSC hospitals were more likely to provide tPA or ME than non-PSC hospitals but this was greater for ED vs. non-ED presentation (OR 9.1 vs. 2.9, $p < 0.001$). **Conclusions:** Though increasing over time, acute revascularization therapies are used in less than 4% of AIS patients in Illinois. Implementation of PSCs and preferential triage of AIS patients to them, especially in key regions in the southern part of the state, will likely provide Illinois residents more access to approved acute revascularization therapies.

Th P303

Participation in a Statewide Stroke Registry is Associated with Shorter Door-to- Needle Time in Patients with Acute Ischemic Stroke Receiving Intravenous tissue-Plasminogen Activator.

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Background: The benefit of intravenous (IV) tissue-Plasminogen Activator (t-PA) in patients with acute ischemic stroke is dependent on early administration in eligible patients. It has been estimated that 2 million neurons are lost for every minute the brain is deprived of blood flow. The Georgia Coverdell Acute Stroke Registry (GCASR), funded by the Centers for Disease Control and Prevention, provides a platform for actively engaging hospitals in a continuous multi-faceted interventional strategy to improve the quality of in-hospital stroke care. Stroke registries are used to track and improve the process of care, including identifying factors that predict earlier treatment and recommending methods to shorten treatment delay. Such information would assist hospitals in improving their quality of stroke care. **Objective:** The purpose of this analysis is to determine factors associated with the time from hospital arrival to the initiation of intravenous t-PA (door-to-needle time) in patients with acute ischemic stroke. **Methods:** We examined predictors of door-to-needle time including demographic (age, gender, race, time of presentation), clinical (stroke severity, past medical history), and administrative (duration in registry, hospital size) variables. Duration of hospital participation in the registry varied depending on when hospitals were recruited. A multivariate analysis was performed using the generalized linear MIXED method. **Results:** We analyzed data collected on 798 patients admitted with acute ischemic stroke who were treated with IV t-PA at 22 hospitals over a four year period (2005 - 2009). The average door-to-needle time was 84.1 minutes. After adjusting for baseline differences, the mean door-to-needle time in patients with atrial fibrillation was 11 minutes longer than that for other patients (95% CI: 3.6-18.5, $p=0.004$). In patients admitted to hospitals participating in the registry for more than 1 year, the mean door-to-needle time was 11.6 minutes shorter (95% CI: 3.1-20.0, $p=0.0086$). **Conclusion:** Quality improvement efforts are effective in reducing delays in treatment with IV t-PA. Longer duration of participation in the GCASR shortened the time to treatment with IV t-PA by reducing the door-to-needle time. Other patient variables, such as atrial fibrillation, may be helpful in

identifying patients who need special attention to avoid delay in treatment. Delayed door-to-needle times in patients with atrial fibrillation in this analysis may reflect the additional time required to analyze coagulation parameters.

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Th P304

Quality of Acute Stroke Care Improves during Participation in a Statewide Stroke Registry

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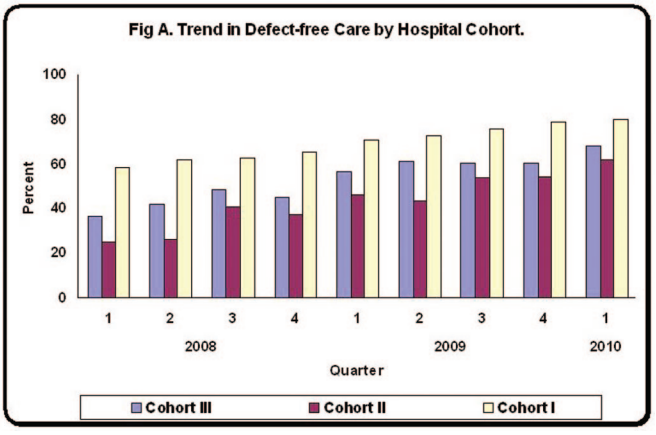
Background: The Georgia Coverdell Acute Stroke Registry (GCASR), part of the Centers for Disease Control and Prevention's Paul Coverdell National Stroke Registry, provides a platform for actively engaging hospitals in a continuous multi-faceted intervention to improve the quality of in-hospital stroke care. It is designed to track and improve the quality of in-hospital acute stroke care. Defect-free care is an accepted method for conservatively defining optimal quality care using multiple indicators for assessment. **Objective:** The purpose of this study is to assess trends in quality of care defined by defect-free care among hospitals participating in the GCASR. **Methods:** Hospitals were recruited during three phases in time. We analyzed 10 standard quality indicators of stroke care, including intravenous thrombolytic therapy within 3 hours, venous thromboembolism prophylaxis and antithrombotic therapy at discharge. We defined defect-free care at the patient level as 100% adherence to all of the indicators for which the patient was eligible, and compared the temporal relationship of participation in the registry among the three cohorts. **Results:** The three cohorts in the analysis were comprised of 23, 16, and 10 hospitals respectively. Cohort 1 started in November 2005, Cohort 2 in October 2006, and Cohort 3 in March 2008. Collectively, these hospitals represented approximately 35% of hospitals providing stroke care and 63% of stroke patients in Georgia. A positive trajectory of improving defect-free care was seen in each of the three cohorts (see Figure A). Some data elements and indicators were revised over time but analyses limited to time periods without revisions showed a similar pattern. **Conclusions:** Defect-free care improved steadily among hospitals participating in the GCASR. The consistent pattern of improvement seen within each cohort suggests that participation in a statewide registry can improve the quality of in-hospital acute stroke care.



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Th P305

What Hospital Characteristics Are Associated With Better Quality Of Care? Results from The Michigan Coverdell Stroke Registry

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Background: Primary Stroke Center (PSC) certification, involving the assessment of specific Brain Attack Coalition (BAC) criteria, is a mainstay of current stroke QI activities in the U.S. However, the degree to which these criteria are associated with better stroke care is still unclear. Our goal was to examine the relationship between hospital-level characteristics including BAC criteria and quality of stroke care in the Michigan Stroke Registry Quality Improvement Program (MiSRQIP). **Methods:** Data were collected on 4121 acute ischemic stroke and TIA admissions from 20 hospitals participating in MiSRQIP in 2008. Information on hospital-level variables, collected by questionnaire, included BAC criteria (i.e., acute stroke team, stroke unit, availability of neurology expertise, teaching status, written care orders, EMS notification) as well as stroke volume, bed size, residency programs, urban/rural, and PSC status. Information on 10 stroke performance measures (rt-PA treatment, antithrombotics within 24 hrs, DVT prophylaxis, dysphagia screening, smoking cessation, discharge antithrombotics, discharge anticoagulants, discharge lipid treatment, assessed for rehabilitation and stroke education) were summarized in a single composite measure of care defined as the percentage of all needed care opportunities given. GEE-based multivariable linear regression models were developed to identify hospital-level predictors of the composite measure of care, while adjusting for patient-level factors (i.e., age, race, sex, stroke type). **Results:** Of the 4121 admissions, the mean age was 70 years, 53% were female, and 70% were white. Almost 30% of the admissions were for TIA. Thirteen (65%) of the 20 hospitals were PSC certified. Overall performance across all 20 sites on the individual performance measures varied from 62% (rt-PA treatment) to 96% (antithrombotics at discharge). The average composite measure of care was 83%. Following adjustment for patient-level factors, only the presence of an acute stroke team was statistically associated with higher composite scores ($P = 0.08$) were both marginally significantly associated with higher composite scores. **Conclusions:** The presence of an acute stroke team was the most important hospital-level characteristic associated with better quality of care although, evidence also pointed towards the value of PSC certification and neurology expertise.

Table. Final GEE multivariable linear regression model of hospital-level predictors of composite score (%).

Hospital-level variable	Estimate	SE	P value
Acute Stroke Team	0.052	0.016	0.0001
PSC certified	0.038	0.014	0.07
Neurology expertise available	0.028	0.014	0.08

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Th P306

Does Implementation of Critical Pathway improve the Clinical Outcomes on Acute Ischemic Stroke?

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Background: Critical pathways (CP) are multidisciplinary plans of best clinical practice for specified group of patients that aid delivery of high quality care. It is not clear whether the implementation of the CP in acute ischemic stroke (AIS) improve the clinical outcomes. Methods Based on the prospective stroke registry, the consecutive series of stroke patients were selected who were hospitalized from Jan 2004 to Sep 2009 within 12 hours from stroke onset (first abnormal time, FAT) and diagnosed AIS by brain CT or MRI. Among them, the patients who were hospitalized between Sep 2006 and Mar 2007 were excluded due to incomplete implementation of CP. We also excluded the patients developed AIS during hospitalization or performed the thrombolytic therapy in another hospital. We defined the patients who entered the hospital between Jan 2004 and Aug 2006 as preCP group and the other patients as postCP group. The CP was characterized by multi-pathway (clear or unclear onset), multi-thrombolytic therapy use (intravenous (IV), intra-arterial (IA), combined) and image-based thrombolysis decision (Figure 1). We analyzed the arrival to admission time, the arrival to first image time and the arrival to IV or IA thrombolysis time as process indicators. The modified Rankin scale (mRS) at 3 months was adopted as an indicator of clinical outcome and dichotomized into 0 to 2 (favorable) and 3 to 6 (unfavorable). Results A total of 1170 patients met our eligibility criteria. Among them, 521 patients (age, 67.3±12.8; male, 61.6%) were enrolled as preCP group, and 649 patients (age, 68.0±12.7; male, 61.5%) were enrolled postCP group. Histories of TIA, atrial fibrillation, prior statin use, and prior antiplatelet use were more frequent in postCP group. However, NIHSS at hospitalization, mRS before stroke and symptom onset to hospital arrival time did not differ between two CP groups. The patients in the postCP group received thrombolysis more frequently (preCP vs. postCP, 16.7% vs. 26.0%). The arrival

to thrombolysis time was not different significantly between the two CP groups. However, the arrival to admission time was shortened in the postCP group. For analysis of clinical outcome, we removed 47 patients due to invalid outcome. The difference of independency at 3 months did not show statistical significance between two groups (59.8% vs. 61.6%, p=0.54). The difference of outcome did not change in adjusted analysis. **Conclusion:** The implementation of CP may improve the process of care but may not associate with clinical outcome. We may need a additional study about implementation of CP.

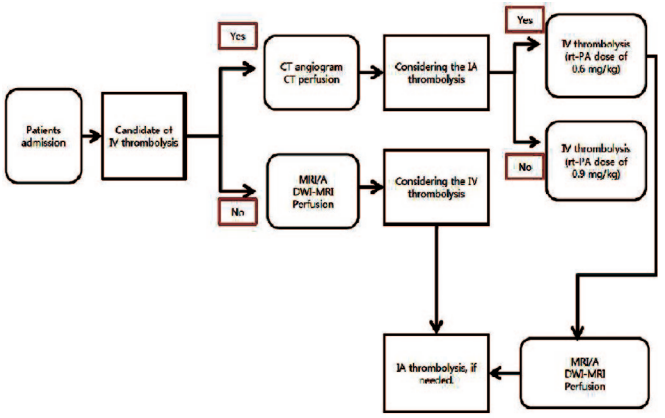

Figure 1. The Schematic algorithm of our Critical pathway for acute ischemic stroke

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Th P307

Impact of a New Neuroscience Intermediate Care Unit on Acute Stroke Care: Quality, Cost, and Nursing Productivity

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Objective: The implementation of a Neuroscience Intermediate Care Unit (NIU) offers "step-down" level of care with intensive monitoring and treatment while optimizing the hospital critical care resources. We studied quality indicators, cost and nursing productivity relative to acute stroke care both prior to and following the introduction of the NIU. **Methods:** With IRB approval, we prospectively analyzed data from all strokes (DRGs 61-69) discharged from University Hospitals Case Medical Center from January 1 through December 31, 2009 encompassing the NIU launch on June 1, 2009. Financial data obtained concurrently included total monthly direct and indirect costs. University HealthSystem Consortium© and the NDNQI® repository provided data on length of stay, readmission rates, in-hospital mortality indices, and discharge locations. Nursing productivity indices were derived from our Kronos® for Healthcare workforce management system and monthly self satisfaction surveys were submitted online by NIU nurses throughout the implementation. **Results:** Data was analyzed in periods of January to May (pre-NIU) and June to December (post-NIU). Of 723 total hospital wide stroke discharges in 2009, 314 were pre-NIU and 407 were post-NIU. Stroke discharges directly from our neuroscience ward increased from 38% (n=124) pre-NIU to 72% (n=292, P<0.001) post-NIU. For those patients spending at least one day in a critical care unit, the average direct cost per patient was $8,203.48 (SD=5874.13) pre-NIU to $4,904.33 (SD=3172.30; p<0.001) post-NIU. There were no detectable differences in stroke mortality indices (0.91, 0.90; p=0.976), readmissions at 7, 14, and 30 days (1, 1, and 2 pre-NIU vs 1.4, 1.6, 1.6 post-NIU, p=0.614; 0.571; 0.707), mean total falls (5,7; p=0.175), unadjusted average lengths of stay (ALOS) for pre-NIU critical care patients (5.64 days, n=132), post-NIU critical care (5.92, n=130), or NIU patients (5.29, n=21, p=0.768) and NIU nursing productivity indices (0.997 vs 0.987, p=0.72). **Conclusions:** The implementation of the Neuroscience Intermediate Care Unit had an immediate and significant effect in reducing critical care bed usage while enhancing geographic localization of stroke patients to the neuroscience floor . Although mortality and readmission rates were low, there was no change following NIU implementation while per patient costs were significantly reduced. Nursing productivity had a slight but non-significant decline but remained high in both environments. Further studies are needed to define optimal utilization and other downstream effects on hospital resources after initiating an NIU.

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Th P308

Hospital-Based Study of Acute Stroke Management and Outcome: Results from the Thai Stroke Registry (TSR)

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Background: There is no data concerning acute stroke care and outcome in Thailand. **Methods:** We performed a prospective multicenter countrywide study involving all level of health care providers composed of university hospitals, regional medical centers, and community hospitals. Patients' baseline characteristics including demographic data, type of public health insurance schemes, diagnosis, initial stroke severity, length of stay, and complications were recorded. Indicators of acute stroke care including acute stroke unit admission, rate of thrombolysis, aspirin initiation within 48 hours were collected. Ischemic stroke outcomes were measured at discharge and 3 months according to the modified Rankin Scale (mRS). **Results:** There were 1,512 acute stroke patients from 118 hospitals across the country enrolled between May 2008 and February 2010. Mean (±SD) age was 64.31±13.17 years. Male comprised of 55.64%. Patients were Thai nationality in 99.14%. Ischemic stroke composed of 80.89%. There were 60.91, 27.38, 2.38 and 9.33 % of patients under 4 different types of medical insurance schemes including Universal Coverage Scheme (UCS), Civil Servant Medical Benefit Scheme (CSMBS), Social Security Insurance (SSS), and Self Paid (SP) respectively. Median initial NIHSS was 7. Acute stroke treatments including intravenous thrombolysis, aspirin within 48 hours, and stroke unit/corner admission were given in 3.80, 71.18 and 23.25% respectively. Mean (±SD) length of stay was 7.17±9.17 days. Complications occurred in 14.88% and 3.71% of patients died at discharge. Factors predicting poor outcome (mRS 5,6) at discharge were as follows: age, decades (adjusted OR 1.53, 1.21-1.94), initial stroke severity (adjusted OR 1.53, 1.21-1.94), female sex (adjusted OR 1.89, 1.05-3.40), in-hospital stroke (adjusted OR 4.61, 1.07-19.9), and in-hospital complications (adjusted OR 2.74, 1.40-5.35). There was no statistically significance difference in regards to stroke outcome between different types of public health insurance schemes (p=0.13). **Conclusion:** Stroke management in centers participating in the TSR reaches standard acute stroke care in many domains but certain areas for improvement remain. Type of public health insurance schemes was not found to predict poor outcome in this stroke cohort. These findings are crucial for health care providers and policy makers to encourage improvements in stroke care delivery.

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Th P309

Predictors of the Use of Dysphagia Screening in Patients with Acute Ischemic Stroke

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Introduction: Pneumonia is a potentially devastating complication of stroke. A simple bedside dysphagia screen (DS) protocol can be used by healthcare providers to detect risk of aspiration in acute ischemic stroke (AIS) patients. Routine use of formal DS protocols has been associated with decreased rates of pneumonia and improved clinical outcomes. We sought to identify those characteristics of acute ischemic stroke (AIS) patients associated with use of DS prior to any oral intake in the Get With The Guidelines-Stroke (GWTG-S) program. **Methods:** Data from 1256 GWTG-S hospitals from 04/01/2003 to 03/30/2009 were analyzed. DS was defined as the use of a bedside swallow screen prior to any oral intake. Patients who were kept strictly without oral intake (NPO) the entire hospital stay were excluded. Univariate analyses (chi-square for categorical variables or Wilcoxon for continuous variables) and multivariate logistic regression analyses were performed to identify independent factors associated with use of DS in AIS patients, adjusting for patient and hospital characteristics. In multivariate analyses, NIHSS was not included due to high rates of missing data (55%). **Results:** Among 446,056 ischemic stroke patients, 300,874 (67.4%) had DS performance documented. When compared with patients without DS, those with DS were slightly older, had higher NIHSS (when measured) and more frequently arrived by EMS and had a history of atrial fibrillation. They were less often diabetics, and had similar rates of prior stroke/TIA, dyslipidemia, PVD, and current smoking. Among patients with mild stroke (NIHSS <=2), rates of DS were less than 11% (Table 1). In multivariate analysis, factors independently associated with DS were age (OR 1.06 [1.05-1.07] per 10 years increase), presence of multiple medical comorbidities (OR 1.08 [1.06-1.10]), admission to an academic hospital (OR 1.26 [1.12-1.43]), and geographic region (Table 2). **Discussion:** National guidelines recommend DS before any oral intake in all AIS but the overall rate remains low (67.4%). Patients with increased age,

multiple comorbidities, at academic hospitals, or in certain regions are more likely to get DS. Further studies are needed to identify barriers and propose strategies to increase the routine use of dysphagia screening among all stroke patients.

Table 1. Unadjusted Patient and Hospital Characteristics of Dysphagia Screening Prior to Oral Intake

Patient Characteristics	*Dysphagia Screen*	*No Dysphagia Screen*	*P value*
Demographics	***N=300874***	***N=145182***	
Age, median [IQR]	73 [61-82]	72 [60-81]	<0.001
Race (White) %	73.2	73.0	<0.001
Arrival by EMS %	60.3	49.4	<0.001
Initial NIHSS (median[IQR])*	5 [2-11]	3 [1-6]	<0.001
NIHSS < 2 *, %	10.9	8.0	<0.001
Past Medical History (%)			
Diabetes mellitus	31.9	33.6	<0.001
Atrial Fibrillation	19.4	15.8	<0.001
Dyslipidemia	39.7	40.3	0.002
Prior Stroke/TIA	32.7	32.2	0.002
Smoking	20.5	21.1	<0.001
Hospital Characteristics			
Number of beds (median [IQR])	380 [263-561]	358 [253-520]	<0.001
Academic %	60.9	56.5	<0.001
Region % West	68.8	31.2	<0.001
- South	69.0	31.0	
- Midwest	66.1	33.9	
- Northeast	65.3	34.7	

* NIHSS missing in 55% of patients

Table 2. Multivariate Predictors of Performance of Dysphagia Screening Prior to Oral Intake

Variable	*OR*	*95% CI*	*P value*
Age (per 10 years increase)	1.06	1.05,1.07	<0.001
Multiple (2+) Medical History	1.08	1.06, 1.10	<0.001
Hospital Type (Academic vs. Non Academic)	1.26	1.12,1.42	<0.001
Region (v. West)			
-Northeast	0.78	0.65,0.93	0.007
-Midwest	0.89	0.73,1.08	0.23
-South	1.03	0.86,1.23	0.77

Variables in the initial model: patient characteristics of age, gender, race, multiple medical history (2 or more of medical history of Afib, stroke/ TIA, CAD/prior MI, carotid stenosis, diabetes, PVD, hypertension, dyslipidemia, smoking), hospital characteristics of region, number of beds, academic vs. not. Variables with p-value > 0.1 in the full model were removed.

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Th P310

Association between Do Not Resuscitate Orders and the Quality of Acute Stroke Care in the Veterans Health Administration (VHA)

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Background: Do Not Resuscitate (DNR) orders are common in patients hospitalized with acute ischemic stroke. Our objectives were to describe factors associated with DNR orders in hospitalized ischemic stroke patients, and to assess the relationship between DNR orders and quality of stroke care in the VHA. **Methods:** To document the quality of stroke care in the VHA, a sample of 5,000 acute ischemic stroke admissions to 131 VA facilities in FY2007 underwent chart abstraction. Fourteen quality indicators were adapted from standard Joint Commission definitions and exclusions. Although patients receiving 'comfort measures only' were included in the sample, they were excluded from the calculation of most of the quality indicator measures. DNR code status was identified on the basis of specific documentation of DNR code status including "no code," "no CPR," or "no resuscitation." Quality indicator rates were compared between subjects with and without DNR code status. **Results:** Among 3965 ischemic stroke patients, 535 (13.5%) had DNR code status. In 71%, DNR orders were first documented within 1 day of admission. Of 145 patients designated as 'comfort measures only', 96% (n= 139) were also DNR. Compared to patients without DNR orders, those with DNR orders were significantly older (age 74.6 vs. 66.8 years), more likely to be white (71.8% vs. 61.8%), had more comorbidities (Charlson score 5.9 vs. 4.6), had greater stroke severity (NIHSS 9.3 vs. 3.8), were more likely to be 'comfort measures only' (26.0% vs. 0.2%), and were more likely to die or be discharged to hospice (29.7% vs.1.0%). Patients with DNR were less likely to receive recommended processes of care for 6 of the 14 quality indicators: tPA treatment, NIHSS recorded, ambulation by hospital day 2, fall risk assessment by hospital day 2, cholesterol treatment at discharge, and stroke education. (Table)**Conclusions:** Although DNR orders were a very strong risk factor for death or discharge to hospice, they were associated with relatively limited differences in the quality of inpatient stroke care.

Table. Comparison of Quality Indicator Compliance by DNR Code status

Indicator (total eligible subjects)	DNR (n = 535)		No DNR (n = 3430)		P value
	N*	%	N*	%	
Thrombolysis (tPA) given (n=308)	55	0.0	253	7.5	0.04
Dysphagia screening (n=3648)	341	20.2	3307	17.9	0.29
DVT prophylaxis (n=1052)	253	74.3	799	74.2	0.98
NIH Stroke Scale completed (n=3645)	461	20.6	3184	26.5	0.006
Pressure ulcer assessment HD 1 (n=3792)	506	91.3	3286	91.6	0.84
Anti-thrombotic therapy HD 2 (n=3533)	431	93.5	3102	95.2	0.13
Ambulatory HD 2 (n=3042)	278	72.7	2764	85.5	<0.001
Fall risk assessment HD 2 (n=3676)	493	82.2	3183	77.5	0.03
Rehab consultation (n=3531)	325	81.5	3206	79.3	0.33
Antithrombotic therapy at DC (n=3529)	313	95.6	3216	95.6	0.56
Anticoagulation therapy (A.Fib) at DC (n=447)	43	72.1	404	68.3	0.61
Cholesterol treatment at DC (n=3044)	274	71.5	2770	81.4	<0.001
Stroke education (n=2526)	156	8.1	2370	16.5	0.007
Smoking cessation (n=1272)	77	89.5	1195	94.1	0.11

N* = eligible subjects.
DC= discharge.
HD= hospital day.

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Th P311

Palliative Care in Acute Stroke and its Effects on Symptom Management and Family Satisfaction: A Systematic Review

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Background: Stroke is an abrupt and frequently devastating event. It is the third leading cause of death, but guidelines for palliative care following acute stroke are few. We undertook a literature review to evaluate the effects of palliative care following acute stroke; specifically, on the effects of palliative management on the frequency and severity of common symptoms such as pain and respiratory distress, and on how palliative management affected the satisfaction and concerns of family members following acute stroke. Data Sources: A search strategy was developed with the help of an information specialist. Records from MEDLINE, CINAHL, EMBASE and PsycINFO from 1950 to the end of April 2010 were eligible. Study Selection: We included studies in English language and which dealt with provision of palliative care in hospital for adults who died following acute stroke (ischemic, intracerebral and subarachnoid hemorrhage). We did not restrict study type, but studies had to include provision of palliative care, including discontinuation of non-palliative medications and interventions and active management of pain, respiratory secretions, and restlessness. Studies were also included if family satisfaction with palliative care was examined by direct observation, chart review, or retrospective questionnaire. **Results:** 1491 studies were screened. 10 studies ultimately met eligibility criteria, reflecting data from 905 patients. These data suggest that most patients receiving palliative care following acute stroke have similar care needs, with relatively consistent strategies for management of symptoms; however, the needs of families in these circumstances has been examined only in small studies, with family concerns regarding feeding and hydration, symptom management, and the nature of palliative care being common points of concern for family members. Satisfaction was most likely when families felt that symptoms

were appropriately managed or when they were involved in decision-making regarding the palliative care process. **Conclusions:** A limited number of studies have examined patient needs and the needs of patients and determinants of family satisfaction in the palliative care of individuals with stroke. Death due to stroke is a frequent event and more work is required regarding to ensure appropriate guidelines are developed to reduce the burden of suffering in this process.

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Th P312

Follow-up Neuroimaging in Perinatal Arterial Ischemic Stroke

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Objective: Perinatal arterial ischemic stroke (PAS) is a leading cause of childhood disability. We sought to determine if there is indication for follow-up neuroimaging (MRI) in PAS given the low rate of progression or recurrence in this population. **Methods:** We studied all newborns within our prospective cohort study (Colorado Pediatric Stroke Program) with PAS from 08/01/2000 - 04/30/2009. Radiologically confirmed PAS cases were identified in our cohort database and confirmed with chart review by a pediatric stroke neurologist. **Results:** Of the 27 cases of PAS in our cohort, 63% were male with ethnic distribution reflective of the Rocky Mountain Region. Stroke was identified within 72 hours of birth in 59%; nearly all cases presented with seizure (85%). Over one-half of newborns had initial CT imaging (56%); MRI was obtained within 72 hours of presentation for most newborns (59%). Strokes were commonly left-sided (59%) with two cases of bilateral involvement. All 27 cases involved the anterior circulation with only one case involving both the anterior and posterior circulation. The majority were in the MCA distribution (85%). Imaging follow-up ranged from 5.69 months - 15.78 years (median 11.64 months). One-third of newborns received follow-up MRI at 1 year; only one child received MRI for clinical indication (infantile spasms). There were no new MRI findings among those cases receiving follow-up neuroimaging. There was no stroke symptom progression or recurrence in the entire cohort (Table). **Conclusions:** In our cohort, there was neither radiological or clinical progression - nor stroke recurrence - in newborns who received routine follow-up MRI. Our findings suggest that there is no indication for subsequent MRI in asymptomatic children with prior perinatal arterial ischemic stroke.

Summary of Perinatal Arterial Ischemic Stroke Imaging

	N = 27	%
Male gender	17	63
Presentation		
Seizure	23	85
Encephalopathy alone	1	3
Incidental	3	11
Initial imaging		
CT	15	56
MRI	11	41
Cranial ultrasound	1	3
Time of MRI after birth		
<72 hours	16	59
72 hours to one week	8	30
>1 week	3	11
Stroke location		
Left-sided	16	59
MCA distribution	23	85
Follow-up MRI at 1 year	9	33
New finding or progression	0	--
Stroke recurrence	0	--

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Th P313

Intraventricular Hemorrhage Score Applied to Children

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Objective: In pediatric intracerebral hemorrhage (ICH), there is little data other than ICH volume to help the clinician predict outcome. In adult ICH, the presence of intraventricular hemorrhage (IVH) is an independent predictor of outcome. We hypothesized that children with the most severe IVH would do poorly. **Methods:** Children, full term to 17 years, with spontaneous ICH and/or IVH on CT or MRI were prospectively enrolled from 2007-9. Exclusion: trauma; isolated SAH; ICH due to brain tumor; hemorrhagic conversion of stroke. Outcome analysis excluded children with pre-existing neurological deficits or death due to non-ICH causes. Measurements: Volumetric analysis of total brain volume (TBV), ICH, and IVH volume was performed by 2 raters using ImageJ. An IVH score was assigned independently by 4 raters using the Hallevi scheme to quantify IVH size in the right and left lateral ventricles, 3rd and 4th ventricles: 0, no blood; 1, posterior sedimentation of blood in the ventricle; 2, partly filled ventricle; 3, completely filled for each ventricle (range 0-12). Outcome assessment: Children were assessed at follow-up by a pediatric stroke neurologist with the King's Outcome Scale for Childhood Head Injury (KOSCHI) which ranges from 1 (death) to 5 (good recovery) at 3 and 12 months post-ICH. Functionally impairing deficits were KOSCHI <5 with KOSCHI ≤ 2 as poor outcome. Linear regression assessed the correlation of IVH score with volumetric measures. IVH score was added to a logistic regression model for prediction of functional impairment and poor outcome. **Results:** We enrolled 46 children, median age 2.73 years (0-17); 26 had pure ICH, 10 had pure IVH, and 10 had both. IVH scores ranged from 0-11, IVH volumes from 0.1-63.8cm3 and ventricles from 0.3-19% of TBV. Weighted Kappa statistic for IVH score agreement among raters was 0.84 (95%CI: 0.76 - 0.91), 93.7% agreement. IVH score and manual IVH volume correlation was fair, $R2=0.52$. At a median of 10 months (1-28 months), 25 children had KOSCHI <5. There were 2 deaths, both had ICH volume $>4\%$ of TBV, IVH scores ≥ 5, and herniation. Presence of hydrocephalus showed a trend for poorer outcome ($p=0.09$). Presence of IVH, high IVH score, or high IVH volume did not predict poor outcome or functional impairment in univariable or multivariable analyses. **Conclusion:** Only large ICH volume predicted poor outcome. Despite excellent agreement between raters, the IVH score and other measures of IVH did not predict outcome in this small pediatric sample. Hydrocephalus showed a trend toward poor outcome, and therefore may be important as a marker of clinically significant IVH.

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Th P314

Diagnosis Of Moyamoya Disease Using Multidetector Row CT

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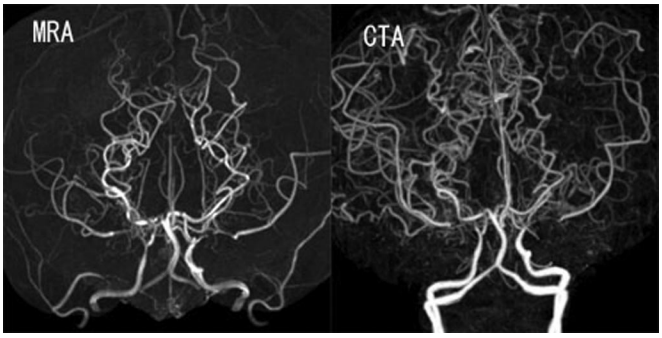
Background Due to the remarkable recent advances in magnetic resonance imaging technology, magnetic resonance angiography (MRA) is now acknowledged as a reliable diagnostic tool with high sensitivity and specificity. Moreover, MRA is a non-invasive method that can be repeated after surgery as a follow-up procedure. Occasionally, however, the extent of stenosis and that of occlusion are over-estimated when MRA is used. The purpose of this study was to establish a method of evaluating these factors using multidetector row computed tomography (MDCT). Methods Twenty-four patients (48 sides) with moyamoya disease diagnosed by MRA were evaluated by means of computed tomography angiography (CTA) using MDCT during the past 2 years. MRA and CTA scores were assigned based on the severity of occlusive changes in the internal carotid artery, the horizontal portion of the middle cerebral artery, the anterior and posterior cerebral arteries and the signals of the distal branches of these arteries. Total scores ranged from 0 (normal) to 10 (most severe). The MRA and CTA scores were classified into four grades for more convenient evaluation of the progress of the disease (MRA and CTA grades 1-4). CT examination was performed using a multidetector row CT scanner (GE LightSpeed VCT; GE Healthcare, Milwaukee, WI, U.S.A.). The following three-dimensional CT angiography (3DCTA) scanning parameters were used: tube voltage 120 kV, collimation 0.625 mm x 32, slice thickness 0.625 mm, slice interval 0.312 mm. A total of 1-1.2 mL/kg Iopamidol (Iopamiron 300; Bayer Healthcare, Leverkusen, Germany), a low-osmolar iodinated contrast material, was administered intravenously using a bolus tracking method via an 18-20 gauge catheter positioned in an antecubital vein. Results CTA scores (0-10) were significantly correlated with MRA scores ($p<0.0001$, $R2=0.796$). The detection rate of moyamoya-affected vessels at the level of the basal ganglia was significantly higher on CTA. Suzuki's stages could be evaluated in all cases. Moreover, our detailed and comprehensive analysis of the 3D images proved very helpful in establishing a good surgical strategy. **Conclusions:** CTA scores measured using an MDCT can serve as a reliable alternative to MRA scores. In the evaluation of Suzuki's stages, angiography does not necessarily relate to clinical severity or to cerebral blood flow. CTA can be performed quickly, which provides a great boon for patients with moyamoya disease, particularly pediatric patients.



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Th P315

MRI Based Measures of Cerebrovascular Reactivity Show Longterm Impact of Transient Cerebral Arteriopathy Related Steno-occlusive Disease.

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Objective: To describe the influence of chronic unilateral steno-occlusive arteriopathy on cerebrovascular reactivity (CVR) assessed by blood oxygen level dependent (BOLD) functional MRI Background: Transient cerebral arteriopathy (TCA) is one of the commonest causes of arterial ischemic stroke (AIS) in childhood. Recurrent infarction is rare beyond the acute (<3 months) phase after initial stroke despite persistence of long-term arterial stenosis. Neuropsychological sequelae have been related to the initial ischemic injury. However, the additional consequences of persistent stenosis on cerebral blood flow and cognition in this group are not well understood. MRI based CVR studies allow assessment of the ability of cerebral vasculature to increase blood flow under conditions of stress, such as hypercapnic challenge, and can provide information on tissue at increased risk of infarction or neurocognitive demise. **Methods:** We reviewed the images of 44 number of children diagnosed with transient cerebral arteriopathy (TCA) between 1990 and 2007, with moderate to severe (greater than 50%) stenosis of the middle cerebral artery (4/4) and distal internal carotid artery (2/4) on conventional angiography over two time points (range 4.33yrs - 14.5yrs). Children with subcortical or deep white matter infarcts were selected for CVR studies. Children with large cortical strokes were excluded. Follow-up clinical and educational information was obtained (mean 6.81 years; range 4.1 - 14.3 years). **Results:** Four children (7 years 5 months - 17 years 4 months age) evaluated at 4.3- 14.5 years following an acute arterial ischemic stroke had a persistent stenosis. None of the children had had further ischemic events. Four children with formal neuropsychometry had learning disability with variable attention, visuo-spatial, auditory processing and working memory difficulties. Three out of four had serial testing. All children showed reduced reactivity particularly in areas corresponding to the persistent stenosis and previous stroke. Impaired reactivity was mostly confined to the deep white matter with relative sparing of the cortex. **Conclusion:** In children with TCA and > 50% residual arterial stenosis cerebral blood flow appears to be chronically impaired even years after the acute ischemic event. Abnormal CVR does not appear to be associated with long term recurrent stroke in these children. However further studies are required to determine whether neurocognitive deficits were consistent with the initial stroke lesion or chronically impaired cerebral blood flow.

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Th P316

Inhibition Of The Sodium-Hydrogen Exchanger After Neonatal Hypoxia-Ischemia Results In Sparing Of White Matter Injury And Improved Memory And Learning

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Objective: Neonatal hypoxia ischemia is a major cause of brain injury in infants, affecting as many as 6 in 1000 live births in the US. Few treatment options are available, and survivors suffer from chronic morbidities such as cerebral palsy, learning disability, and seizure disorders. After cerebral ischemia, over-stimulation of the sodium-hydrogen ion exchanger isoform 1 (NHE1) contributes to cell swelling and ischemic injury. We have previously shown that inhibition of NHE1 is neuroprotective after focal ischemia in adult mice; however, little is known about the effect of NHE1 inhibition in neonatal hypoxia ischemia. **Methods:** Hypoxia-ischemia was induced in 9 day old C57/Black6 mice by unilateral carotid artery ligation and subsequent exposure to 8% oxygen for 55 minutes. Mice were treated with HOE 642, a potent inhibitor of NHE1, at 10 minutes following hypoxia-ischemia and again at 24 and 48 hours following the injury. Experimental groups consisted of HOE treated (n=8), vehicle treated (n=9), and sham operated (n=5) mice. Rotarod and Morris Water Maze tests were performed 2 months following the injury. T2 MRI was performed using a 4.7 Tesla Varian small animal MRI scanner. Animals were sacrificed and brains were perfusion fixed for ex-vivo Diffusion Tensor MRI scanning and immunohistochemistry. **Results:** HOE treated animals demonstrated improved performance on Rotarod ($p<0.05$) and Morris Water Maze tests (probe trial: 23.3 $\pm$ 12.8s vs. 9.1 $\pm$ 9.0s, $p=0.02$). T2 MRI demonstrated a spectrum of injury in both HOE treated and untreated mice, from large cyst formation and cerebral atrophy to mild ventriculomegaly. The degree of hemispheric volume loss on the in-vivo T2 MRI correlated well with performance on Morris Water Maze test ($r=0.713$, $p=0.004$). However, despite the improved performance on behavioral testing seen in the HOE treated animals, no significant difference in hemispheric volume loss was seen in the injured hemisphere between groups (17% vs 19%). Ex-vivo DTI demonstrated a decrease in fractional anisotropy values in the corpus callosum of the control mice compared to sham ($p=0.02$), which was not seen in the HOE treated animals. **Conclusion:** NHE1 inhibition after neonatal hypoxia-ischemia leads to improved memory and learning at 2 months following the injury. There is no significant difference in hemispheric volume loss in treated animals, indicating that improved performance cannot be explained solely by an acute effect on neuronal survival after the injury. Decreased FA in corpus callosum of vehicle treated animals suggests white matter injury which is spared in the HOE treated group. Immunohistochemistry will serve to further characterize the effect of NHE1 inhibition on white matter injury after neonatal hypoxia-ischemia.

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Th P317

Thromboprophylaxis With Antiplatelet Agents Prevents Cerebral Thromboembolism In Patients With Mechanical Aortic Prostheses

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Objective: Cerebral thromboembolism (TE) is the most serious complication of aortic mechanical prostheses (AMP). Thromboembolism is secondary to platelet activation due to shear forces and release of ADP from fractured RBC. Warfarin, the anticoagulant "of choice" does not fully prevent thromboembolism in patients with AMP because it lacks platelet inhibitory activity. If thromboembolism from AMP is a platelet mediated event; thromboprophylaxis with antiplatelet agents should prevent cerebral TE. **Methods:** Since 2001, 160 patients who underwent aortic valve replacement with AMP alone or in combination with another cardiac or thoracic aortic procedure were treated with clopidogrel and aspirin as sole thromboprophylaxis. Platelet inhibition (PI) was maintained at >40-50%, measured with Accumetrics® and thromboelastography platelet mapping (TEG-PM) since 2006 and 2007. Patients were followed with 2D echocardiograms every six months. **Results:** The total follow up was 5,809.6 months (484.3 patients years (pt yrs). The average follow up was 36.8 $\pm$ 27.8 mo. Eighteen patients (11%) died, 8 from coronary artery disease and 3 from valve related causes. Five patients bled (3.1%) (1.03%/pt yrs). From 2001 to 2007, 7 patients had strokes (4.3%) (1.45%/pt yrs). Five had stopped clopidogrel and aspirin. Of these, 3 were on warfarin. Of the remaining 2, 1 was a non responder to clopidogrel and the other occurred in a non tested, compliant patient. Two patients had TiA's, 1 in an excellent clopidogrel responder and the other is a non responder. During the last 2.5 years none of the patients has sustained a neurologic event. 20 patients demonstrated clopidogrel poor responsiveness. With reloading, stopping statins or proton pump inhibitors, use of cilostazol or ticlopidine, we were able to increase the degree of PI in most hyporesponders. Since September 2009 we converted 16 hyporesponders to prasugrel. All patients responded well to this medication. All patients were responsive to aspirin when tested by Accumetrics and TEG-PM. Patients who had any response to clopidogrel and were responsive to aspirin were protected from strokes. **Conclusion:** Platelet activation causes TE in patients with AMP. If the patient responds to the antiplatelet agents, is compliant, has normal sinus rhythm and a small left atrium, TE in patients with AMP can be prevented. Clopidogrel hyporesponders achieved excellent PI on prasugrel. Antiplatelet thrombophylaxis for patients with AMP is effective if one blocks the synthesis of thromboxane A_2 and partially blocks the P_2 $Y1_2$ receptor on the platelet.

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Th P318

The Short-term Effect of Atorvastatin on Carotid Plaque Morphology Assessed by Computer-Assisted Gray Scale Densitometry

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Background and Objective: Soft, lipid-containing carotid plaques have been associated with increased ischemic stroke risk and appear echolucent on ultrasound evaluation. Stabilization of carotid plaques by pharmacologic intervention, including statins, is a promising strategy for stroke prevention. Our objective was to assess the change in carotid plaque echolucency following short-term treatment with atorvastatin. Subjects and**Methods:** We treated 40 subjects over 45 years of age (mean age: 70$\pm$7 years, 60% women) with 80 mg atorvastatin daily for one month. High-resolution carotid ultrasound was performed to detect plaques in long axis in any segment of carotid arteries at baseline and 30 days after treatment. Computer-assisted gray scale densitometry (GSD) index, a measure of echogenicity, was calculated from the normalized images off-line. Absolute GSD index changes were compared by a paired *t*-test (one-tailed difference was considered significant at alpha$\leq$0.05). Any increase in an individual GSD index was considered a positive change or plaque stabilization effect. Logistic regression was used to assess the mediation effect of LDL cholesterol on plaque stabilization after adjusting for age, sex, and smoking. **Results:** The average median number of carotid plaques was 2 (range 0-5, 24 subjects with carotid plaque) at baseline and did not change 30 days following treatment. The maximal carotid plaque thickness did not significantly change between baseline and the follow up (1.78 mm vs. 1.69 mm). The mean GSD index was 73$\pm$16 (range 1-125) at baseline and 89$\pm$15 (range 1-137) at 30 days ($p<0.05$). Of 24 study participants, 4 (17%) showed a reduction of GSD levels and 14 (60%) showed GSD increase. The adjusted odds ratio for the positive GSD plaque index change (vs. no change or decreased GSM index) was 1.71 (95% confidence interval; 1.1, 7.6). This association was independent of the baseline levels of LDL as well as LDL reduction. **Conclusion:** We observed decreased echolucency (increased echodensity) of carotid artery plaques after short-term treatment with atorvastatin. Further studies are needed to determine whether decreased echolucency leads to plaque stabilization and reduction of risk of stroke and other vascular events.

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Th P319

Regression of Vulnerable Intracranial Plaques by Intensive Risk Factor Control: A Longitudinal Study On Plaque Morphology by 3D-Rotational Angiography

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Background: One forth of stroke patients with a high-grade intracranial stenosis had recurrence within 2 years. The morphology and progression of acute symptomatic intracranial plaques are poorly understood. **Methods:** In this on-going study, patients with acute strokes attributed to a >70% intracranial stenosis were recruited to receive an intensive control of atherosclerotic risks. Patients with non-atherosclerosis stroke etiology were excluded. In addition to aspirin (80mg/day), pre-specified therapeutic targets were low-density lipoprotein (LDL) ≤70 mg/dL, HbA1c ≤6.5%, systolic blood pressure ≤140mmHg, and abstinence from smoking. Clinical progress and risk factor profile were serially monitored. 3D-rotational and digital subtraction angiograms were obtained at baseline (within 2 weeks from the index stroke) and in 12 months. An independent radiologist masked to the sequence of the angiograms rated the plaque vulnerability based on surface irregularity, presence of ulcer and maximal luminal diameter loss. Plaque regression was defined as a diameter gain >15% and healing of ulcer, if any, in 12-month angiogram. **Results:** Of the 30 patients enrolled, 15 completed the 12-month angiogram. Mean age was 65.0 years and 11 were males. Distributed in middle cerebral arteries (n=13) and distal internal carotid artery (n=2), the baseline stenosis (mean) was (78.33±8.6%). Surface irregularity and ulcers were found in 9 (60%) lesions. Overall, mean LDL (mg/dL) was reduced from baseline 136 (IQR 117-159) to 61 (IQR 51-70) ($p<0.01$); HbA1c (%) from 6.7 (IQR 5.9-7.5) to 5.7 (IQR 5.3-6.3) ($p<0.05$); systolic blood pressure (mmHg) from 132 (IQR 120-140) to 123 (IQR 120-132) ($p<0.05$). In 12 months, no recurrence of stroke was reported. Plaque regression was evident in 9 lesions (60%). One lesion (6.7%) progressed and 5 stenoses (33.3%) remained static. **Conclusion:** Morphological evaluation of intracranial plaque is feasible with 3D-rotational angiography. Intensive control of cardiovascular risks may halt progression of symptomatic intracranial plaques. **Figure legends:** With an intensive medical therapy, ulcer healing with plaque regression was evident in the 3D-rotational angiogram (right panel) of this 66-year-old woman. Left panel showed the ulcerative, high-grade middle cerebral artery stenosis at baseline.

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Th P320

Analysis of baseline data on the Cilostazol-Aspirin Therapy Against Recurrent Stroke with Intracranial Artery Stenosis (CATHARSIS)

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Intracranial arterial stenosis (IAS) is more common in Asian than in Caucasian. Based on the results of the Warfarin-Aspirin Symptomatic Intracranial Disease (WASID), warfarin is not recommended because of the concern of safety, whereas the efficacy of aspirin is not enough for stroke prevention in these high-risk patients. Recent results of Cilostazol Stroke Prevention Study II (CSPS II) showed that ciloztazol was more effective than aspirin for stroke prevention in Japanese patients with non-cardioembolic ischemic stroke without increasing bleeding risk. The CATHARSIS (ClinicalTrials.gov Identifier; NCT00333164) was a randomized controlled trial to compare the effect of aspirin plus cilostazol with that of aspirin alone on the progression of IAS as well as ischemic and hemorrhagic events in patients with symptomatic IAS. Inclusion criteria were (1) ischemic stroke after two weeks to six months from onset, (2) responsible lesions identified on MRI, (3) IAS >50% on MRA in the territory of responsible lesion, (4) IAS in the supraclinoid internal carotid artery (ICA), M1 portion of the middle cerebral artery, or basilar artery (BA), (5) age of 45-85 years, (6) out-patients, and (7) a written informed consent from the patient or family. A total of 165 patients (109 males, average 68 years) were enrolled from 60 stroke centers across Japan. Median duration from onset of stroke to the study entry was 30 days. An infarct with more than 1.5 cm in diameter was identified in 70 (42.4%) patients. The responsible lesions in the cortex, white matter, basal ganglia, and brainstem were observed in 57 (34.5%), 57 (34.5%), 33 (20.2%), and 13 (7.9%) patients, respectively. The stenosis of M1, supraclinoid ICA, and BA was seen in 127 (77.0%), 20 (12.1%), and 18 (10.9%) patients, respectively. Hypertension, hypercholesterolemia, diabetes, obesity (BMI≥25), CKD (eGFR<60 mL/min/1.73m^2), and current cigarette smoking were associated in 72.1%, 51.5%, 35.8%, 32.1%, 26.1%, and 20.0% of the patients, respectively. Non-medication rates of diabetes, hypercholesterolemia, and hypertension were 33.9%, 21.2%, and 15.1%. In conclusion, M1 was the most predominant site of stenosis in our patients with symptomatic IAS, who had metabolic risk factors including hypercholesterolemia, diabetes, and obesity as compared with general Japanese patients with ischemic stroke, that are not well recognized or controlled.

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Th P321

Antiplatelet Resistance in Patients with Recent Cerebral Ischemic Events

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Background: Antiplatelet agents reduce the risk of vascular events by about 25% in high-risk individuals. A substantial proportion of patients continue to experience vascular events while on antiplatelet therapy. Antiplatelet resistance or non-response could partially explain this limited efficacy. Furthermore, antiplatelet resistance in patients with previous ischemic stroke or TIA could increase the risk of recurrent ischemic events. The purpose of this study, therefore, was to determine if antiplatelet responsiveness, as measured by the PFA-100, is associated with recurrent ischemic events. **Methods:** Patients with a recent TIA or ischemic stroke (IS) within the previous 3 months on antiplatelet therapy were recruited. Demographic data were collected including type and dose of antiplatelet agent (ASA, dipyridamole, clopidogrel, or combination). All subjects underwent complete neurological evaluations, routine blood tests, as well as measurement of platelet function using the PFA-100 technique (Col/Epi and Col/ADP) at baseline and every 4 months during their follow up. Patients were followed prospectively for a period of 2 years for the occurrence of ischemic events (defined as either TIA, IS, MI, angina, or vascular death). Investigators were blinded to the patients' antiplatelet response status at all times. Antiplatelet resistance was correlated with the occurrence of ischemic events. **Results:** Eighty one patients were recruited in the study from the McGill University Cerebrovascular Clinic from 2002 to 2009. The mean age is 69 years and 67% are male. Eleven patients were lost to follow up and 8 patients were followed for less than 12 months. Analysis of data was done for all patients who were followed for a minimum period of 12 months. Consequently, 19 patients were excluded from analysis leaving us with sixty two patients followed over an average of 22.8 months. Amongst these patients, a little more than 60% were taking ASA, either alone or in combination. At baseline, 42% were non-responders / resistant to antiplatelet agents (defined as PFA-100 Col/Epi ≤ 170 sec). Recurrent ischemic events were slightly more common in responders compared to non-responders (22% vs. 19%, p=NS). **Conclusions:** A significant proportion of patients with cerebrovascular disease exhibit antiplatelet resistance. Our study shows that antiplatelet resistance as determined by PFA-100 is not correlated with a higher risk of recurrent ischemic events.

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Th P323

Underuse of Antithrombotic Therapy and Clinical Outcome in Patients with Acute Ischemic Stroke and Atrial Fibrillation in a Hispanic Population

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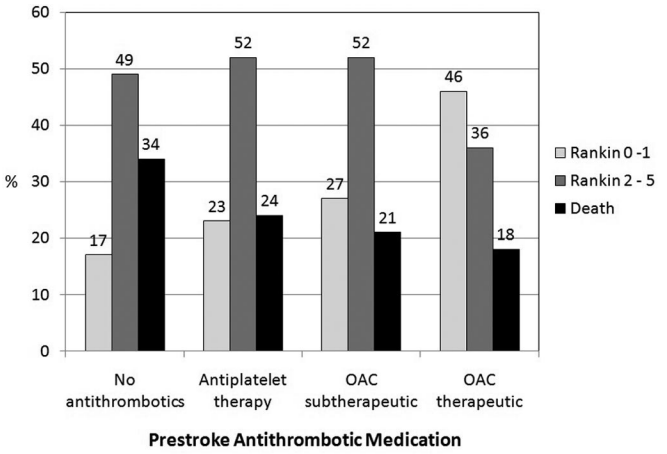
Background and Purpose: Guidelines strongly recommend oral anticoagulants (OAC) for stroke prevention for high-risk individuals with atrial fibrillation, yet it is often underused in developed countries. Moreover, stroke patients taking OAC at stroke onset have less disabling strokes than individuals taking aspirin or no antithrombotic therapy. This study examined the magnitude of this problem in a developing country using a large prospective stroke registry in a Hispanic population. **Methods:** We analyzed data from patients who presented with a recent ischemic stroke (IS) or TIA that were enrolled in three Mexican stroke registries; databases were merged into a common stroke registry (n=3194: IS=2837, TIA =357). We selected patients with a known history of atrial fibrillation (AF). Cerebrovascular events were categorized as first-ever stroke/TIA or recurrent strokes. Primary end points were (1) the use of prestroke antithrombotic medications and admission international normalized ratio (INR), and (2) short-term outcome regarding prestroke antithrombotic medication. **Results:** There were 385 patients with known AF for a prevalence of 12.5% in IS and 8.1% in TIA patients. In patients with a history of AF and a previous TIA/IS (n=145), only 13.1% were taking oral anticoagulants (OAC) with therapeutic INR at the time of stroke onset, 22.8% were taking OAC with subtherapeutic INR (<2), 32.4% were on antiplatelets, and 31.7% were on no antithrombotics. Among patients with a history of AF and a first-ever IS/TIA (n=240), preadmission medications were OAC in 24% (subtherapeutic INR<2.0 in 20%), antiplatelets in 25%, and no antithrombotics in 51%. There were significant differences in disability (Rankin 2-5) and case fatality rate regarding the use of prestroke antithrombotic medication as shown in the Figure: patients using OAC in therapeutic range at the time of ischemic stroke had a better outcome when compared with individuals taking aspirin or no antithrombotic therapy (P=0.01). **Conclusions:** In this Hispanic population most of the patients with atrial fibrillation admitted with an acute stroke, and who were candidates for oral anticoagulation, were on no antithrombotic therapy or were either not taking OAC or were subtherapeutic at the time of ischemic stroke. Patients taking OAC in therapeutic range at stroke onset had less disability and mortality on short-term outcome.



OAC, oral anticoagulant

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Th P324

PROTEGE-ACV Program: Achieving Long-term Adherence To Secondary Stroke Prevention Goals

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Background: Long-term compliance is a huge challenge in stroke secondary prevention. We assessed the effectiveness of a quality-of-care stroke program on achieving long-term adherence in a Latin American university hospital. **Methods:** ischemic stroke patients were included in PROTEGE-ACV, a multidisciplinary program adapted from UCLA PROTECT Program, aimed to meet secondary prevention goals. Patients with severe functional impairment (Rankin ≥4), severe dementia or life expectancy less than three years after stroke were excluded. **Results:** In March 2010, 171 of 413 patients (41%) included in PROTEGE-ACV had two or more years of follow-up. Mean age was 74.9±11 years, with 50.3% females. Vascular RF profile was: HT (87%), dyslipidemia (88%), metabolic syndrome (50%); obesity (50%); type 2 DBT (17%); smokers and former smokers (46%); history of stroke or TIA (26%), CHD (15%), peripheral artery disease (12%); AF (15%); and CRF (10%). There was high level of compliance to ambulatory visits to their primary care physician (10.2±7) and neurologists (6.5±6) during this period. Most patients achieved optimal vascular RF control as well as very high adherence to drug therapy after one and two years of follow-up (table). Kaplan-Meier analysis showed a two-year recurrence probability and all-cause mortality rate of 9.3% and 20%, respectively. **Conclusion:** A multidisciplinary approach, with special focus on vascular RF control and patient education, significantly improves adherence to treatment and narrows the gap between evidence-based guidelines and clinical practice. A team-work strategy, patients close supervision and electronic records follow-up with frequent reminders to primary care physicians, could be key factors to improve compliance over long follow-up, with high impact on decreasing mortality and recurrence rates.

Variable	1 year after stroke	2 years after stroke	p
SBP (mmHg)	128.5±13	127.6±13	NS
DBP (mmHg)	75.4±9	76.9±9	NS
PP (mmHg)	53.1±11	50.3±10	0.05
Fasting glucose (mg/dL)	99.9±24	100.2±23	NS
Total cholesterol (mg/dL)	161.6±35	161.4±35	NS
HDL-C (mg/dL)	47.2±13	45±13	NS
LDL-C (mg/dL)	91.6±28	92.3±27	NS
Tryglicerides (mg/dL)	111.8±61	111.6±58	NS
Drug therapy (% of patients)			
Antihypertensives	91	92	NS
Statins	88	90	NS
Antiplatelet	84	82	NS
Oral anticoagulants	21	24	NS

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Th P325

Increase of popular awareness in Argentina after World Stroke Day campaign

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Background: Stroke is considered an epidemic on the rise, which has lead to the setting of a specific date for World Stroke Day. The aim is to Inform, Educate, and Raise the Awareness of society about this disease. **Objective:** To analyze the educational impact that the World Stroke Day campaign had on a determined population. MATERIAL AND**Methods:** An analytic, observational study carried out between August 2008 through March 2009, with a total of 3950 people randomly surveyed in strategic public places in the city of Rosario, Argentina and administered by previously trained medical students. The survey was conducted in three distinct periods: 10 days before the campaign, immediately after the campaign and three months later. Pearson Chi Test, Level: 95% and Contingent Coefficiency (C=); 45 interviewees were excluded by presented exclusion criteria. **Results:** 3950 questionnaires were analyzed. We found a predominance of females (68%; n=2,647)and mean age was 45 years (18-90). When we associated level of education with awareness of the disease we found a statistically signficant positive association (Chi value 461.4 and C=0.33) previous to and after the campaign. 60% (n=2343) believed that stroke is infrequent; of the 10 risk factors mentioned in the survey, the most recognized was Arterial Hypertension. 37% (n=605) before the campaign did not recognize any of the symptoms, while this percentage fell by 10% (n=90) in the post-campaign period. 35.5% in the pre-campaign period was unaware of the appropriate actions to take during a stroke, while at the three-month post-campaign period 65.4% responded with the correct option. 40% in the pre-campagin period recognized the specific treatment, a figure that increased to 83.4% three months later. **Conclusions:** This study reveals the lack of knowledge in this population and the positive impact of education created by the campaign. We should continue to carry out population studies, as this is the appropriate tool for delineating and improving the objectives for new strategies.

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Th P326

High Factor XI Is a Common, Ubiquitous Thromobophilic Abnaormality for both Arterial and Venous Thrombosis.

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Background: We assessed associations between high factor XI and arterial and venous thrombosis.The patients with high Factor XI included a broad mixture of disorders which can lead to Deep venous thrombosis (DVT), Pulmonary embolism (PE), Idiopathic intracranial hypertension (IIH), central retinal vein occlusion and recurrent pregnancy loss. Routine measurement of Factor XI in these high risk patients may open new doors to prevent and treat the above mentioned thromboembolic complications. Methods : Of 661 patients referred for evaluation for atherothrombosis-cerebrovascular disease (ATCVD) or venous thrombosis, of whom 50 (7.6%) had high factor XI (>or=150%), we assessed associations between high factor XI and arterial and venous thrombosis. The 50 patients included 30 women, 20 men, 45 Caucasians, 2 African American and 3 others with a mean ± SD age of 50 ± 11. High Factor XI was the only coagulation disorder in 5 patients (10%), and was accompanied by 1,2,3,4, and >or = 5 other thrombophilic-hypofibrinolytic disorders in 13(26%), 9(18%), 11(22%), 6(12%) and 6(12%) patients, respectively. The patients with high Factor XI included a broad mixture of disorders where arterial and venous thrombi are a major pathoetiology. Results : Of the 50 patients, 16 (32%) had ATCVD, 12(25%) deep venous thrombosis/pulmonary embolism (DVT/PE), 7(14%) idiopathic intracranial hypertension (IIH), 5(10%) osteonecrosis of the hip, 3 (6%) central retinal vein thrombosis, 3 (6%) amourosis fugax, 3 (6%) recurrent pregnancy loss and 1 (2%) ischemic stroke. Mean± SD age in the 16 patients with high Factor XI and ATCVD was 51 ± 10 years (range 32-74), with mean total cholesterol 212 ± 66 mg/dl, triglycerides 399 ± 40 mg/dl, and HDL cholesterol 39 ± 11 mg/dl. Triglycerides levels were > 150 mg/dl in 11 of the 16 patients with ATCVD and high Factor XI. In the 661 patients in our center having Factor XI and triglycerides measures, Factor XI correlated with triglycerides (r= .19), P<.0001). We have found high Factor XI (>or =150%) in 12 of 20 (60%) patients with DVT/PE, 5/25 (20%) with osteonecrosis of the hip, 3/16 (18%) recurrent pregnancy loss, 16/102 (16%) premature ATCVD, 3/24 (13%) amaurosis fugax, 3/32 (9%) central retinal vein thrombosis, 7/190 (3.7%) IIH, and 6/29 (21%) ischemic stroke (5 of these 6 also had premature ATCVD. **Conclusion:** High Factor XI is a common, Ubiquitous thrombophilic abnormality for both venous and arterial thrombosis, and should be included in the panel of coagulation measurements made in arterial and venous thrombosis.

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Th P327

Subclinical Disorders Of Thyroid Function And Risk Of Cardiovascular Events Following Suspected Transient Ischemic Attack; A Cohort Study.

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Introduction: Subclinical disorders of thyroid function may be associated with increased vascular risk. We explored the relationship between biochemical thyroid status and subsequent cardiovascular events in a cohort of patients referred with suspected TIA. Methods - Data from consecutive referrals attending our clinic from August 1992 onwards were used. Subjects were followed up by record linkage to death and hospital discharge records. The primary endpoint was the occurrence of a cardiovascular (CV) event defined as death or hospital discharge following stroke, myocardial infarction or other vascular cause. Patients had serum thyroid stimulating hormone (TSH) and thyroxine (T4) measured at first clinic attendance. Based on these results, patients were classed as: euthyroid (TSH 0.45 to 4.5mU/L); treated hypothyroidism (taking thyroid replacement); overt hypothyroidism; overt hyperthyroidism; subclinical hypothyroidism or subclinical hyperthyroidism. Those with untreated overt disease were excluded from the main analysis. A Cox proportional hazard model was generated to compare the CV event rate between the thyroid groups. **Results:** Thyroid function tests were available for 2306 of 3522 (65%) individuals; 1023 (44.4%) were male and mean age was 65.4 years (SD 13.2). The majority of individuals (1924, 83.4%) were euthyroid, 173 (7.5%) had treated hypothyroidism, 128 (5.6%) had subclinical hypothyroidism, 56 (2.4%) had subclinical hyperthyroidism, leaving 3 (0.1%) individuals with overt hyperthyroidism and 22 (1%) with overt hypothyroidism. Of the total, 817 (35.4%) experienced a primary endpoint event and 400 (17.3%) died from vascular causes. Following exclusion of overt thyroid disorders, those with subclinical hyperthyroidism had lowest serum total cholesterol ($p=<0.001$, one-way ANOVA), while euthyroid subjects were youngest ($p=0.003$, one-way ANOVA) and had the lowest proportion of females. On univariate analysis, greater age, male gender, previous hypertension, previous stroke, diabetes, cerebrovascular disease and greater serum creatinine linked with the primary outcome. There was no relationship between thyroid status and occurrence of the primary outcome. This remained after adjustment for the above variables (HR for CV event on multivariate analysis (relative to euthyroid individuals) for treated hypothyroidism 0.89 (95% CI 0.66 to 1.2), subclinical hypothyroidism 1.16 (95% CI 0.86 to 1.56) and subclinical hyperthyroidism 1.10, (95% CI 0.72 to 1.69)). **Conclusion:** We found no evidence of a relationship between subclinical disorders of thyroid function and occurrence of subsequent cardiovascular events in those referred to a cerebrovascular clinic.

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Th P328

Antihypertensive Class And Stroke Recurrence: An Analysis Of The VISP Trial

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Background: Hypertension is a major modifiable risk in stroke recurrence, but the optimal antihypertensive class for reducing future risk is uncertain. Agents that increase levels of angiotensin II (e.g. thiazide diuretics) may be more effective at reducing recurrent stroke compared to agents that lower angiotensin II levels (e.g. ACE inhibitors (ACE-I)) independent of antihypertensive effects. The Vitamin In Stroke Prevention Study (VISP) was a multi-center trial of high- versus low-dose vitamin therapy in individuals with non-disabling ischemic stroke and elevated homocysteine. We investigated recurrent stroke among those taking thiazides vs. ACE-I in the VISP study and hypothesized a lower risk of recurrent stroke in patients taking thiazides compared to those on ACE-I. **Methods:** Retrospective analysis of stroke recurrence in participants enrolled in VISP. To reduce potential confounding due to medication changes over the course of the two year trial or any effect due to the interaction between vitamins and antihypertensive agents, we used medication status at the randomization visit. We classified participants as; 1) thiazides but not ACE-I; 2) ACE-I but not thiazides and 3) neither agent. We excluded 242 individuals on both thiazides and ACE-I. Because of low recurrent stroke rates in the entire population, analysis by other antihypertensive classes was not possible. **Results:** Demographic data are summarized in the table. More of those taking only ACE-I at randomization had recurrent stroke compared to those taking only thiazides (OR = 1.92, 95% CI = 1.09, 3.40). Fewer recurrent strokes occurred in those taking thiazides compared to patients on antihypertensives other than ACE-I or thiazides (OR = 0.49, 95% = CI 0.28-0.85). Excluding the 1,258 not on any antihypertensive agent, the association between reduced stroke recurrence in patients taking thiazides vs. any other agent remained (OR= 0.39, 95% CI = 0.22-0.69). **Conclusion:** Based on this *post hoc* analysis, thiazides are associated with a lower risk of recurrent stroke compared to the use of ACE-I in patients with hyperhomocystenemia. Conversely, ACE- I use is associated with a higher risk of stroke recurrence when compared to the use of thiazides. In future studies, we plan to explore possible genetic determinants of these associations through the use of genomic techniques.

TABLE

	ACE I (n = 1,041)	Thiazide (n = 285)	Neither (n = 2,112)
Age (mean)	66	67	66
Sex male (%)	663 (63)	148 (52)	1351 (63)
Race White (%)	791 (76)	202 (71)	1753 (83)
African American (%)	179 (17)	62 (22)	258 (12)
Other (%)	71 (6.8)	21(7.4)	101(4.8)
Current Smoker [1](%)	150 (1.44)	42 (15)	389 (18.4)
Hypertension[1] (%)	955 (92)	275 (96)	1254 (59)
Diabetes Mellitus[1] (%)	475 (46)	55 (20)	454 (21)
Prior stroke [1] (%)	187 (18)	50 (18)	324 (15)
#Antihypertensives (mean)	1.55	1.42	0.5[2]
Stroke recurrence [1] (%)	94 (9)	14 (4.9)	202 (9.5)

[1] The values are expressed as the number of participants responding "yes" followed by a percent.
[2] Note that this value excludes those individuals not on any antihypertensive agent (n = 1,258).

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Th P329

The Unawareness of Patients' Own Individual Risk Factors in Korean Patients with Acute Ischemic Stroke: Reports of Multicenter Observational Study

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Background: Control of the stroke risk factors is essential to prevent first stroke and its recurrence. Regular assessment of blood pressure, pulse rate, and the measurement of blood sugar and lipid level are recommended. The awareness and recognition of their individual risk factors are the first step for control and prevention for stroke. Patients are often unaware of having their own risk factors before hospital admission. Relatively, a little research has examined patients' self-perception and awareness of stroke risk factor and the related socio-demographic factors in stroke population. The information on which population goes unaware of the risk factors is crucial in the development of health policies for prevention, control, and early diagnosis of this condition. **Methods:** In a prospectively maintained hospital registry, consecutive 4290 patients were enrolled who were diagnosed as acute ischemic stroke or TIA within 7 days after the onset of symptoms at 9 hospitals from 2008 to 2009. We assessed data on unawareness of patients' individual risk factors before hospital admission. The unaware risk factors were defined as newly-diagnosed hypertension, diabetes, hyperlipidemia, and atrial fibrillation. We also analyzed socio-demographic data such as an age, sex, region, education level. **Results:** At the time of stroke/TIA, individual unawareness regarding hypertension, diabetes, hyperlipidemia, and atrial fibrillation was 7.8%, 15.3%, 36.5%, and 47.3% respectively. Global unawareness, if any unawareness of 4 risk factors above, was observed in 26.5% of patients ($n=1136$). The global unawareness was not related with age and gender in the univariate analysis. The unaware risk factors were more often found in metropolitan residents compared with the residents at small cities and rural areas (31.4% vs. 22.3, $p=0.01$). Level of education was associated with the unawareness (education years: >6 vs. ≤ 6; 33.9% vs. 28.8%, $p=0.002$). In multivariate analysis, including other confounders such as history of stroke or coronary artery disease, smoking, and obesity, the global unawareness were associated with education years (OR 0.86; 95%CI, 0.78-0.95) and living in the metropolitan area (OR 1.74; 95% CI 1.49-2.04). **Conclusion:** A considerable portion of stroke patients is unaware of their own risk factors, especially hyperlipidemia and atrial fibrillation, before the stroke. The difference in living region and education level may influence the awareness which is the first step for prevention and control of stroke.

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Th P330

Soluble Endoglin and Vasospasm in Subarachnoid Hemorrhage.

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Cerebral vasospasm (VS) is a frequently encountered complication of SAH that is associated with delayed brain ischemia and poor neurological outcome. Approximately 60-70% of SAH patients have angiographic evidence of VS, half of them being symptomatic (sVS). The pathogenesis of VS is multifactorial and not completely understood. Soluble endoglin (sEng) is an antiangiogenic protein that has been associated with pre-eclampsia which, as is the case of SAH, is characterized by endothelial dysfunction and VS. Here we examined whether the

cerebrospinal fluid (CSF) and serum levels of sEng in patients with SAH are associated with VS in SAH patients. This study included adult controls (n=5) and Fisher-3 SAH patients (n=16). Controls were individuals with no prior history of neurological disorders but who underwent lumbar puncture for headache workup and had normal CSF studies. Demographics, medical history, and history of exposure to elicit drugs were documented. Patients were followed prospectively and samples of CSF and serum were obtained between days 5 and 7 post-bleed. sEng levels were determined using commercially available ELISA test (R&D). Protein levels in the CSF and serum were measured and utilized to calculate CSF sEng index. SAH subjects were subcategorized into those with sVS and those who did not develop symptomatic VS (noVS). sVS was defined as a neurological deterioration in the setting of angiographically proven VS and in the absence of other active conditions that could explain the occurrence of neurological decline. The levels of sEng in both groups were compared using the nonparametric Mann-Whitney U test. Age, history of hypertension, exposure to elicit drugs, RBC count in the CSF and proteinorrachia were not statistically different within sVS and noVS. The mean CSF level of sEng was (0.031±0.006) pg/mL in the control group, (0.1410±0.069) pg/mL in the noVS group, and (0.547±0.233) pg/mL in the sVS group ($p<0.021$). CSF sEng in the sVS and in the noVS groups was >2 indicating this mediator was produced intrathecally. Elevated levels of intrathecally synthesized sEng are observed in SAH patients, particularly in those with sVS. These results suggest sEng may participate in the pathogenesis of VS.

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Th P331

Hemodynamics are Altered in Patients with Aneurysm-related Vasospasm pre- & post-therapy: Serial Evaluation with Whole-brain CT Perfusion

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Background & Purpose: Cerebral vasospasm from aneurysm-related SAH(aSAH) is a major cause of morbidity. Diagnosis & monitoring of vasospasm remains a challenge with limitations using TCD, cerebral angiography & CTA. In most settings decreased cerebral perfusion is inferred from changes in arterial diameter rather than by simultaneous measurement. Recent generation of 320-slice CT scanners now give whole brain CT perfusion(CTP) & CTA information with a single contrast bolus. When performed in suspected aSAH, simultaneous CTA/CTP allows simultaneous assessment of the arterial tree as well as cerebral perfusion. The purpose of our pilot study was to determine: 1. if changes in arterial diameter on CTA are associated with altered perfusion 2. if there is decreased perfusion when pts develop symptomatic vasospasm 3. if the use of intra-arterial milrinone & hemodynamic augmentation for vasospasm improves perfusion. **Materials & Methods:** Pts with aSAH who had whole-brain baseline CTA/CTP were included . Followup CTA/CTP was performed if pts clinically deteriorated, had TCD evidence of vasospasm(vasospasm group) or at d 7-14 if asymptomatic(without vasospasm). All individuals with TCD evidence of vasospasm were treated with hemodynamic augmentation & intra-arterial milrinone(per institutional protocol). A total of 31 automated ROIs/hemisphere placed at 6 standard levels covering the entire brain measured serial perfusion parameters: CBF, CBV, MTT, TTP. Individual ROIs were then grouped to evaluate perfusion in the MCA, ACA, PCA territories. Arterial diameters were measured in the terminal ICA, MCA(M1,M2) & PCA(P1,P2). A Pearson-correlation coefficient was used to evaluate the relationship between artery diameter & perfusion. To evaluate the effect of treatment, a t-test was used to compare perfusion pre- & post-vasospasm therapy. Because of the exploratory nature of the analysis, no correction was performed for multiple comparisons. **Results:** There 10 pts without(total 20 CTP/CTA) and 6 pts with vasospasm(total 17 CTP/CTA) who had perfusion studies for comparison. Changes in arterial diameter were significantly correlated with changes in MTT($r=-0.58$, $p=0.02$) & TTP($r=-0.54$, $p=0.01$)i.e. pts who developed angiographic vasospasm had prolongation of MTT & TTP. Pts who developed vasospasm had decreased CBF from baseline in MCA & ACA territories ($p<0.05$). For vasospasm pts treated with milrinone, there was a significant improvement in MTT($p=0.02$) & trends towards improved CBF(0.07) & TTP($p=0.07$) **Conclusion:** : Changes in perfusion are seen with changes in arterial diameter from vasospasm. Pts who develop vasospasm had significant changes from baseline CBF in the MCA and ACA territories. There was improvement in perfusion seen with intra-arterial treatment. This pilot study suggests a larger prospective study is required to determine the most appropriate perfusion parameter to follow.

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Correlation between Anemia and Delayed Cerebral Ischemia (DCI) in aneurysmal subarachnoid haemorrhage.

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Title Correlation between Anemia and incidence of Delayed Cerebral Ischemia(DCI) in aneurysmal subarachnoid haemorrhage. **Introduction:** Delayed cerebral ischemia(DCI) is the most important determinant of the morbidity associated with aneurysmal subarchnoid hemorrhage after aneurysm is secured. Higher clinical grades (fisher or WFNS) are associated with higher incidence of cerebral vasospasm and DCI. Conventional treatment to prevent DCI consists of hypertension, hypervolemia and hemodilution (HHH therapy). Changes in hematocrit can potentially affect the brain tissue oxygenation in two ways: higher hematocrit increases oxygen carrying capacity and lower hematocrit decreases viscosity and hence facilitate cerebral blood flow. This optimal hematocrit is unknown. Recent studies have shown that blood transfusion increases cerebral blood flow and decreases O2 extraction ratio in subarachnoid patients. We analyzed relationship of hematocrit with incidence of stroke in our subarachnoid population. Methods Retrospective chart review. Results 86 patient with aneurysmal subarachnoid hemorrhage were identified from July 2009-June 2010. 19 delayed cerebral ischemic events occurred in 19 patients. One was periprocedural and was therefore excluded. DCI were diagnosed clinically and were confirmed by either CT head or MRI brain. Patients were divided among three groups based on their lowest hematocrit during the first 21 days: group A Hematocrit 30%(n=60). Incidence of delayed cerebral ischemia in group A =9/15(60%), group B= 3/12(25%) and group C= 7/60(11.6%). All patients had higher fisher grades (II, III and IV). **Conclusions:** Although lower hematocrit decreases blood viscosity and theoretically should increase cerebral blood flow, at lower levels it significantly decreases the oxygen carrying capacity of blood and therefore could result in ischemia of brain tissue. In our cohort of patients, the highest incidence of DCI. while keeping the clinical grade constant, was observed in patients with a hematocrit of <26%. This suggest that severe anemia predisposes patients with aneurysmal subarachnoid to DCI. Since blood transfusion is also related with morbidities, the best approach is to avoid blood loss in these patients by limiting the surgical blood loss and daily blood draws for unnecessary routine labs.

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Identification of Predictors Differentiating Reversible Cerebral Vasoconstriction Syndrome with Subarachnoid Hemorrhage from Aneurysmal Subarachnoid Hemorrhage

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Introduction: Reversible Cerebral Vasoconstriction Syndrome (RCVS) mimics aneurysmal subarachnoid hemorrhage (aSAH) with thunderclap headache at onset in nearly 90% and SAH in up to 42%. RCVS with SAH (RCVS-SAH) is often initially misinterpreted as aSAH, subjecting patients to unnecessary imaging, invasive procedures and prolonged ICU stay. Our objective was to identify predictors that can reliably differentiate RCVS-SAH from aSAH. **Methods:** Clinical and imaging features were compared between 515 consecutive aSAH and 35 consecutive RCVS-SAH patients at Massachusetts General Hospital. Data were analyzed using student's T-test, Chi-Square or Fisher's Exact test, as appropriate. To avoid overfitting due to the small number of events, we limited our logistic regression models to four predictors each. We compared the fit to multivariable logistic models using exact estimation methods containing the same variables with age dichotomized at the mean to predict RCVS-SAH. **Results:** Univariate analysis: RCVS-SAH patients were younger (43±12 vs. 55±14 years; $P<0.001$), with a higher proportion of women (87% vs. 71%; $p=0.04$), prior self-reported migraine (47% vs. 8%), depression (45% vs. 8%), alcohol abuse (34% vs. 9%), COPD (32% vs. 43%) and drug abuse (21% vs. 5%; all $p < 0.001$). RCVS-SAH had lower Hunt & Hess (HH) and Fisher scale (median 2 (IQR 2;2) vs. 3 (1;3); $P<0.001$ and 2(2;2) vs. 3(2;3); $P<0.001$). No difference in smoking status was present (37% vs. 36%; $p=0.99$). Imaging analysis showed that RCVS-SAH had a higher proportion of hypodensities on admission CT (63% vs. 35%; $P<0.001$) and angiographic vasospasm (100% vs. 62%; $P<0.001$); more arteries affected by vasospasm (6 (6;9) vs. 2 (0;4); $P<0.001$), bilateral vasoconstriction (89% vs. 36%, $P<0.001$), and earlier occurrence of vasospasm (day 1 (1;1) vs. 6 (5;8); $P<0.001$). After ruling out colinearity between migraine and depression, multiple logistic regression showed the following predictors of RCVS-SAH: model 1: age (OR 0.93 [95% CI 0.9-0.97]), prior migraine (OR 9.1 [95% CI 3.8-21.7]), depression (OR 10.1 [95% CI 4.2-24.1], COPD (OR 7.1 [95% CI 2.7-18.4]); model 2: HH grade (OR 0.4 [95% CI 0.2-0.7, Fisher scale (OR 0.1 [95% CI 0.05-0.296], bilateral vasoconstriction (OR 5.7 [95% CI 2.2-15]), number of affected arteries (OR 1.4 [95% CI 1.2-1.6]). The EXACT logistic model did not improve the model fit. After controlling for prior antidepressant use, migraine and depression remained significant. **Conclusion:** : We identified important clinical and imaging differences between RCVS-SAH and aSAH, which may improve correct diagnosis, treatment and resource utilization with a potential to decrease length of stay.

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Th P334

Systemic Hemodynamics Is Different Between Clipping And Coiling After Aneurismal Subarachnoid Hemorrhage -SAH Picco Multicenter Study-

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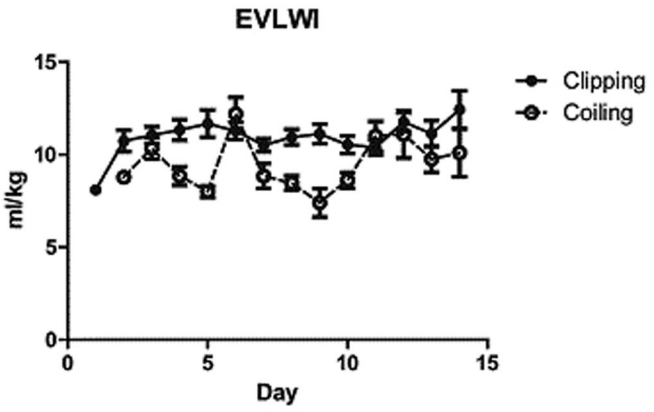
Background and Purpose: Volume management is critical for the assessment of the vasospasm after aneurismal subarachnoid hemorrhage (SAH). We have registered 62 patients in SAH Picco multicenter study, and prospectively analyzed the hemodynamic parameters postoperatively until Day 14. Here, we investigate the difference of the systemic hemodynamics between surgical clipping and endovascular coiling after the treatment. **Methods:** Multiple parameters were calculated by single indicator transpulmonary thermodilution (Picco, PULSION medical systems) system in real time. This modality enables us to evaluate multiple parameters including global end diastolic volume (GEDI) and intrathoratic blood pressure (ITBI) as an indicator of preload, cardiac index (CI), systemic vascular resistance index (SVRI) and mean arterial pressure (MAP) as an indicator of afterload, and extravascular lung water index (ELWI). These parameters were analyzed

from days 3 to 14 in the patients with SAH. **Results:** Clipping was performed in 52 patients and coiling was performed in 10 patients. The patient characteristics were similar in both groups. Preload was similar (GEDI 853 ±96.1 ml/m2, ITBI 1076 ±119.0ml/m2) in clipping and coiling. Coiling group has significantly less CI (3.98 l/min/m2) compared with clipping (4.49 l/min/m2) suggesting that coiling was preferably selected for severe cases. Interestingly, ELWI was significantly higher in clipping group (10.9 ml/kg) than coiling group (9.4 ml/kg). In terms of the afterload, coiling has higher SVRI and MAP than clipping group (SVRI: coiling 2166 vs. clipping 1848, MAP coiling 108 mmHg vs. clipping 101 mmHg). **Conclusions:** We first show that systemic hemodynamics is different between clipping and coiling after the treatment following aneurismal subarachnoid hemorrhage. This result indicates volume management should be different between clipping and coiling. Bedside monitoring with Picco system is a powerful tool for the volume management of patients with SAH.



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Subclinical Lacunar Infarction And Chronic Kidney Disease Are Independently Associated With Frontal Lobe Dysfunction In Community-dwelling Elderly Subjects - The Sefuri Brain MRI Study

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Background and Purpose: Although recent studies have found that chronic kidney disease (CKD) is an independent risk factor for cognitive impairment and dementia in population-based cohorts, the cause of cognitive impairment in CKD subjects is unclear. In the present study, we conducted a population-based, cross-sectional analysis of brain magnetic resonance imaging (MRI) findings and vascular risk factors including CKD in relation to cognition particularly frontal lobe function. **Methods:** We examined 506 elderly subjects (192 men and 314 women) aged 60 years or older, who were living independently at home without apparent dementia. Frontal lobe dysfunction was defined as the most prolonged fifth quintile of the modified Stroop test for each given decade. Glomerular filtration rate (GFR) was estimated with the new Japanese equation modified from the Modification of Diet in Renal Disease Study equation. Subclinical lacunar infarction was shown as low signal intensities on T1-weighted images, and their size was 5-15 mm. Deep white matter lesions (DWMLs) and periventricular hyperintensities (PVHs) were defined as isointense with normal brain parenchyma on T1-weighted images, and high signal intensity areas on T2-weighted images. The data were analyzed with the SPSS Statistics 18.0. **Results:** The frequency of CKD was 16.4%. Subclinical lacunar infarction, DWMLs and PVHs were detected in 79 (15.6%), 217 (42.9%) and 150 (29.6%) of 506 subjects, respectively. The frontal lobe dysfunction group tended to have higher blood pressure (BP) (146.0/80.0 vs. 140.0/78.0 mmHg), less education (8.0 vs. 9.0 years), more history of minor stroke (6.8% vs. 1.7%), higher creatinine (61.9 vs.59.2 μmol/L), and lower GFR (72.8 vs. 75.3 mL/min/1.73 m2). When possible confounders were entered into the multivariate logistic regression model (the forward stepwise method), the independent predictors of frontal lobe dysfunction were diastolic BP (odds ratio 1.023; 95% CI 1.001 to 1.045 per 1 mmHg), GFR (odds ratio 0.848; 95% CI 0.737 to 0.975 per 10 mL/min/1.73 m2), and number of lacune(s) (odds ratio 1.471; 95% CI 1.135 to 1.908). The score of Stroop test was compared according to the GFR category with ANCOVA adjusted for age and diastolic BP. The mean of logarithmic-transformed scores of Stroop test in the GFR<60 mL/min/1.73 m2 group was 1.376 (95%CI 1.301-1.451), which was significantly higher (worse) than 1.250 (95%CI 1.214-1.285) in the GFR 60-89 mL/min/1.73 m2 group ($p=0.009$). CKD was not related to global cognition defined by Mini-Mental State Examination. **Conclusions:** The present study showed that CKD, high blood pressure, and subclinical lacunar infarction might contribute to frontal lobe dysfunction. The intervention directed at treatment and prevention of CKD, and silent ischemic brain lesions particularly lacune(s) would be beneficial to attenuate the frontal cognitive decline in healthy elderly subjects.

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