Long-term mortality after ST-elevation myocardial infarction in the reperfusion and modern secondary prevention therapy era according to coronary artery disease extent: The FAST-MI registries

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Mortalité à long terme après un infarctus du myocarde avec sus décalage ST à l'ère des traitements de reperfusion et de prévention secondaire modernes, selon l'étendu de la maladie coronaire : d'après les registres FAST-MI

Abbreviated title: STEMI prognosis according to coronary status

Abbreviated title: Pronostic des infarctus selon l'étendu de l'atteinte coronaire

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Summary

Background. – Historical cohorts have shown extent of coronary artery disease to be a predictor of poorer outcomes in ST-segment elevation myocardial infarction. However, contemporary data in the era of reperfusion and modern secondary prevention therapy are lacking.

Aim. – To compare 3-year survival in patients with ST-segment elevation myocardial infarction with multivessel disease versus those with single-vessel disease.

Methods. – Using data from the FAST-MI 2005, 2010 and 2015 registries, three nationwide French surveys, we included all patients with ST-segment elevation myocardial infarction who underwent primary percutaneous coronary intervention within 24 hours of symptom onset. Baseline characteristics, management and 3-year all-cause mortality were analysed according to coronary status (single-, two- and three-vessel disease).

Results. – Among 3907 patients (mean age 62.4 ±13.7 years; 75.9% male), patients with multivessel disease (two- or three-vessel disease) accounted for 47.9%; overall, they were older, with higher cardiovascular risk profiles. In a multivariable adjusted Cox proportional hazard regression model, only patients with three-vessel disease had a higher rate of mortality at 3 years compared with those with single-vessel disease (hazard ratio 1.52, 95% confidence interval 1.68–2.26; $P < 0.001$). Finally, patients with multivessel disease with complete myocardial revascularization before discharge had a similar prognosis to patients with single-vessel disease (hazard ratio 1.17, 95% confidence interval 0.84–1.64; $P = 0.35$).

Conclusions. – Multivessel disease still represents an important proportion of patients with ST-segment elevation myocardial infarction. Although three-vessel disease is associated with higher 3-year mortality, patients with multivessel disease and complete myocardial revascularization in the contemporary era have a 3-year risk of death similar to that in patients with single-vessel disease.

Résumé

Contexte. – Plusieurs cohortes historiques ont montré que l'étendu de la maladie coronaire était un facteur prédictif péjoratif du devenir des patients avec infarctus du myocarde avec sus décalage ST (SCA ST+). Peu de données récentes sont toutefois disponibles avec les traitements de reperfusion et de prévention secondaire actuels.

Objectif. – Evaluer la survie à 3 ans des patients avec un SCA ST+ pluri tronculaire comparé à ceux mono tronculaires.

Méthodes. – A partir des registres FAST-MI 2005, 2010 et 2015, 3 enquêtes nationales, nous avons inclus tous les patients avec un SCA ST+ traités par angioplastie primaire dans les 24 heures après l'apparition des symptômes. Les principales caractéristiques, la prise en charge et la survie à 3 ans de ces patients ont été analysées selon le statu coronaire (1, 2 ou 3 vaisseau[x] atteint[s]).

Résultats. – Parmi les 3907 patients inclus (âge moyen 62,4 ± 13,7 ans; 75,9 % d'homme), les patients pluri tronculaires représentaient 47,9 %. Globalement, ils étaient plus âgés avec un profil de risque plus sévère. En analyse multi variée, seuls les patients tri tronculaires avaient un sur risque de mortalité à 3 ans par rapport aux patients mono tronculaires (HR 1,52, IC95 % 1,68–2,26 ; $P < 0,001$). Les patients pluri tronculaires revascularisés complétement (avant la sortie) avaient un pronostic similaire à ceux mono tronculaires (HR 1,17, IC95 % 0,84–1,64 ; $P = 0,35$).

Conclusions. – Les patients pluri tronculaires représentent encore une proportion importante des SCA ST+. Si l'atteinte tri tronculaire reste associée à une surmortalité à 3 ans, les patients pluri tronculaires complétement revascularisés semblent toutefois avoir un pronostic similaire à ceux mono tronculaires avec les traitements de reperfusion et de prévention secondaire modernes.

Abbreviations: 1-VD, single-vessel disease; 2-VD, two-vessel disease; 3-VD, three-vessel disease; AMI, acute myocardial infarction; CAD, coronary artery disease; CI, confidence interval; CK-MB, creatine kinase myocardial band; CPP, Committee for the Protection of Persons; FAST-MI, French registry of Acute ST-elevation or non-ST-elevation Myocardial Infarction; HR, hazard ratio; MVD, multivessel disease; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction; TIMI, Thrombolysis In Myocardial Infarction.

Background

In 40–65% of patients presenting with acute ST-segment elevation myocardial infarction (STEMI), additional angiographic significant lesions (i.e. > 50% diameter stenosis) may exist in non-culprit vessels [1-5]. The presence of multivessel disease (MVD) in these patients is an important predictor of short-term as well as long-term mortality after primary percutaneous coronary intervention (PCI) compared with patients with single-vessel disease (1-VD) [1-5].

Several sources, including registries specific to acute myocardial infarction (AMI) and large administrative or billing databases, have shown a decrease in mortality in patients with STEMI over the last 20 years [6-15]. The decline in short- and long-term mortality in these patients is explained by several factors, including: increased use and improved delivery of reperfusion therapy, particularly primary PCI; temporal changes in patient population characteristics; and increased use and improved delivery of recommended secondary prevention [6-15]. To our knowledge, the prognosis of patients with STEMI according to coronary status has not been recently assessed after these changes.

The aim of the present study was to evaluate characteristics, management and survival at 3 years in patients with STEMI undergoing primary PCI within the recommended delay (i.e. within 24 hours of symptoms onset) according to coronary status, in the modern reperfusion era and with optimized secondary prevention medication.

Methods

FAST-MI registries

Three nationwide French registries were conducted 5 years apart over a 10-year period (2005–2015): French registry of Acute ST-elevation or non-ST-elevation Myocardial Infarction (FAST-MI) 2005 (ClinicalTrials.gov identifier: NCT00673036) [16], FAST-MI 2010 (ClinicalTrials.gov identifier: NCT01237418) [17] and FAST-MI 2015 (ClinicalTrials.gov identifier: NCT02566200) [18] (Appendix). The methods used for these registries have been detailed previously [16-18]; briefly, their primary objectives were to evaluate the characteristics, management and outcomes of patients with AMI, as seen in routine clinical practice, on a countrywide scale.

All registries consecutively included patients with STEMI or non-ST-segment elevation myocardial infarction admitted to cardiac intensive care units within 48 hours of symptom onset, during a specified 1-month period (October to December 2005, 2010, and 2015). AMI was defined by increased levels of

cardiac biomarkers (troponins, creatine kinase or creatine kinase myocardial band [CK-MB]), together with either compatible symptoms or electrocardiogram changes. Patients who died soon after admission and for whom cardiac markers were not measured were included if they had signs or symptoms associated with typical ST-segment changes. Exclusion criteria were: (1) refusal to participate; (2) iatrogenic myocardial infarction, defined as occurring within 48 hours of any therapeutic procedure; and (3) AMI diagnosis invalidated in favour of another diagnosis. STEMI was diagnosed when ST-segment elevation ≥ 1 mm was seen in at least two contiguous leads in any location on the index or qualifying electrocardiogram, or when presumed new left bundle branch block or documented new Q waves were observed.

Participation in the study was offered to all institutions that received AMI emergencies (including university teaching hospitals, general and regional hospitals and private clinics). Physicians were instructed that the study should not affect clinical care or management. The study was conducted in accordance with the guidelines on good clinical practice and French law. The study protocol for the 2005 registry was reviewed by the Committee for the Protection of Persons (CPP) in Biomedical Research of Saint Antoine University Hospital, Paris; the 2010 registry was reviewed and approved by the CPP of Saint Louis University Hospital, Paris; and the protocol of 2015 registry was reviewed and approved by the CPP of Saint Louis University Hospital, Paris, France. Data file collection and storage were approved by the Commission Nationale Informatique et Liberté. All patients were informed of the nature and aims of the surveys, and could request to be excluded; in addition, written consent was obtained for all three surveys.

Study population

For the present analysis, we enrolled in the three surveys all consecutive patients with STEMI undergoing primary PCI within 24 hours of symptoms onset, with known coronary status (n = 4059). Patients with previous coronary artery bypass grafting were excluded (n = 115), as were patients with no significant coronary artery disease (CAD) on coronary angiography (n = 37). Finally, 3907 patients were selected for this study (Fig. A.1).

A non-culprit lesion was defined as ≥ 50% diameter stenosis by visual estimate in at least one non-infarct-related vessel. In addition, non-culprit lesions had to be located in a vessel that was not stented as part of the index culprit lesion PCI. To define CAD extent, all three coronary arteries were

assigned one point each, and two points for the left main coronary artery, whatever the status of the left anterior descending and left circumflex arteries, resulting in a maximum score of 3 (i.e. 1-VD versus two-vessel disease [2-VD] versus three-vessel disease [3-VD]). Multivessel CAD was defined as 2-VD or 3-VD. Procedural success for the culprit lesion was defined as a final Thrombolysis In Myocardial Infarction (TIMI) flow of 2 or 3 after PCI, whereas failure was defined as a final TIMI flow of 0 or 1 (data available in 3576/3907 patients). Finally, complete myocardial revascularization was defined by successful PCI of the culprit lesion and all non-culprit lesions (i.e. restoration of blood supply to the myocardium), achieved before discharge.

Patient characteristics, management and outcomes were analysed according to coronary status (i.e. 1-VD versus 2-VD versus 3-VD). The primary endpoint of the study was survival at 3 years.

Data collection

Data on baseline characteristics, including demographics, risk factors and medical history, were collected as described previously [16-18]. Information on the use of cardiac procedures, including the use of PCI and the use of medications (anticoagulants, antiplatelet agents, diuretics, beta-blockers, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers and lipid-lowering agents) in the first 48 hours and at hospital discharge, was collected. For all surveys, follow-up was centralized at the French Society of Cardiology. Three-year mortality follow-up was > 97% complete.

Statistical analysis

Continuous variables are reported as means ± standard deviations or medians (interquartile ranges), as appropriate. Discrete variables are described as counts and percentages. Groups were compared by analysis of variance for continuous variables and by the χ^2 test (or Fisher's exact test) for discrete variables. Hazard ratios (HRs) are presented with their 95% confidence intervals (CIs). Survival curves were estimated using the Kaplan-Meier estimators and were compared using log-rank tests. One-year and 3-year survival were analysed according to number of vessels involved, and the impact of MVD was compared using a multivariable backward stepwise Cox analysis, with a threshold of 0.10 for variable elimination, among the different risk groups. Variables included in the final models were selected *ad hoc*, based on their physiological relevance and potential to be associated with outcomes; they comprised age, sex, risk factors, co-morbidities, left ventricular ejection fraction, year of the study

and management (medications and interventional). Procedural success and complete myocardial revascularization were added in a second model, including four groups: 1-VD with successful PCI; MVD with complete revascularization before discharge; MVD without complete revascularization before discharge; and primary PCI failure. A sensitivity analysis was performed in the population surviving the index hospitalization. Analyses were repeated using forward stepwise analysis to check the consistency of the results. Statistical analyses were performed using IBM SPSS Statistics, version 26.0 (IBM SPSS Inc., Chicago, IL, USA). For all analyses, two-sided P values < 0.05 were considered significant.

Results

Patient characteristics

Fig. A.1 shows the patient recruitment flow chart. Briefly, out of 13,130 patients enrolled in the FAST-MI registries, 3907 patients with STEMI undergoing PCI within 24 hours of symptoms onset with available medical information were enrolled for the present analysis. The mean age of the population was 62.4 ±13.7 years (75.9% male). MVD was present in 47.9% of patients. Patient characteristics are presented in Table 1 according to coronary status (i.e. 1-VD, 2-VD, 3-VD and MVD). Overall, cardiovascular risk profile increased progressively from patients with 1-VD to patients with 3-VD. Patients with MVD were older, with more risk factors and co-morbidities (i.e. chronic kidney disease, history of stroke, peripheral artery disease and atrial fibrillation); more of these patients had a history of myocardial infarction and myocardial revascularization.

Clinical presentation and management

Median time from symptom onset to first call (patient delay) was longer in patients with MVD, whereas no difference was observed in delay from call to primary PCI (system delay) (Table 2).

Clinical presentation on admission was different according to coronary status (Table 2). The proportion of anterior myocardial infarction was higher in patients with 1-VD. Symptoms of heart failure (Killip class ≥ II) were more frequent in patients with MVD (1-VD, 8.7%; 2-VD, 11.5%; 3-VD, 17%; $P < 0.001$). The Global Registry of Acute Coronary Events (GRACE) score increased gradually from patients with 1-VD to patients with 3-VD (1-VD, 139 ± 32; 2-VD, 145 ± 31; 3-VD, 150 ± 33; $P < 0.001$).

The rates of TIMI score 0/1 for the culprit lesion before primary PCI were similar in all groups. Procedural characteristics are detailed in Table 2. Thrombus aspiration was mainly used in patients with 1-VD. Drug-eluting stents were used similarly in all study groups. Proportion of PCI success (i.e. TIMI score 2/3 after PCI) was higher in patients with 1-VD (95.7% in the overall population). In patients with MVD, 41% had complete myocardial revascularization before discharge. The rate of patients with MVD and complete revascularization before discharge increased from 29.9% to 58.9% between 2005 and 2015.

Medications used during the first 48 hours are listed in Table A.1. Ticagrelor and prasugrel were prescribed more frequently in patients with 1-VD, as were glycoprotein IIb/IIIa inhibitors. Finally, no difference was observed for anticoagulant therapies, statins and beta-blockers according to number of vessels involved. Diuretics were mainly used in patients with MVD.

In-hospital complications and mortality at 1 and 3 years

In-hospital complications were more frequent in patients with MVD (Table A.2). The in-hospital death rates were 2.0%, 3.5% and 4.5%, according to coronary status (1-VD, 2-VD and 3-VD, respectively; P < 0.001). Medications at discharge are listed in Table A.3. Overall, the use of recommended medications (beta-blockers, antiplatelet therapy, statins and angiotensin-converting enzyme inhibitors or angiotensin receptor blockers) was lower in patients with 3-VD.

At 1 year, only patients with 3-VD had significantly higher mortality compared with patients with 1-VD (for 2-VD: HR 1.22, 95% CI 0.87–1.72 [P = 0.25]; for 3-VD: HR 1.52, 95% CI 1.04–2.22 [P = 0.03]; for all MVD: HR 1.33, 95% CI 0.97–1.81 [P = 0.07]) (Table A.4).

At 3 years, the mortality rate was higher in patients with MVD and in those with 3-VD only compared with patients with 1-VD (for 2-VD: HR 1.22, 95% CI 0.92–1.58 [P = 0.18]; for 3-VD: HR 1.52, 95% CI 1.68–2.26 [P < 0.001]; for all MVD: HR 1.34, 95% CI 1.05–1.71 [P = 0.02]) (Fig. 1, Table 3). Similar results were found after excluding patients who died during the index hospital stay (data not shown).

Finally, in patients with MVD, the prognosis at 3 years did not differ compared with patients with 1-VD in those with successful complete myocardial revascularization before discharge (HR 1.17, 95% CI 0.84–1.64 [P = 0.35] in all patients with MVD; HR 1.19, 95% CI 0.83–1.73 [P = 0.35] in patients with 2-VD; HR 1.23, 95% CI 0.70–2.18 [P = 0.47] in patients with 3-VD). In contrast, patients

with MVD without complete myocardial revascularization had higher mortality rates than patients with 1-VD (HR 1.54, 95% CI 1.16–2.04 [P = 0.003] in all patients with MVD; HR 1.34, 95% CI 0.96–1.86 [P = 0.09] in patients with 2-VD; HR 1.84, 95% CI 1.29–2.63 [P < 0.001] in patients with 3-VD), as did patients with failed PCI of the culprit lesion (HR 1.88, 95% CI 1.19–2.98 [P = 0.007] in all patients with MVD; HR 1.60, 95% CI 0.92–2.79 [P = 0.097] in patients with 2-VD; HR 2.46, 95% CI 1.47–4.11 [P < 0.001] in patients with 3-VD) (Table A.5, Table A.6, Fig. 2). Similar results were found after excluding patients who died during the index hospitalization (data not shown).

Discussion

Multivessel disease is currently found in approximately 50% of patients with STEMI undergoing primary PCI within the recommended delay. Patients with MVD have a more severe cardiovascular risk profile and, even in the current era, they receive fewer recommended secondary prevention medications compared with patients with 1-VD. The independent deleterious impact of CAD extent on mortality is mostly found in patients with 3-VD, but is no longer present in patients with MVD who get complete revascularization during the initial hospital stay.

Improvement in survival among patients with STEMI

Over the last 25 years, several registries specific to AMI and large administrative or billing databases have shown a decrease in mortality in patients with STEMI [6-15]. Most benefits in short- and long-term outcomes in patients with STEMI were related to the uptake and increased use of new and, in time, established interventional and medical treatments [5]. Improvement in hospital survival was mainly related to the increased use of reperfusion treatment, including primary PCI, although the reduction in mortality was also associated with a substantial change in the patient risk profile [10].

Improved survival among patients with STEMI has been reported in all categories of patients over the last 25 years [6-15]. To our knowledge, there is no recent comparison focused on patients with MVD compared with those with 1-VD. Using clinical trial data from patients with STEMI with myocardial revascularization and MVD from 2008, it is possible to estimate the trends in all-cause mortality over the last 10-year period [19-23]. In the Preventive Angioplasty in Acute Myocardial Infarction (PRAMI) trial, the rate of all-cause death (mean follow-up of 23 months) was 5.1% (12/234) in patients with preventive PCI and 6.9% (16/231) in those without preventive PCI [23]. In contrast, in

the most recent study (Complete versus Culprit-Only Revascularization Strategies to Treat Multivessel Disease after Early PCI for STEMI [COMPLETE] trial), the rate of all-cause death (median follow-up of 3 years) was 2.6% in patients who had a complete revascularization strategy and 2.7% in those with culprit lesion-only PCI, which represents a decrease of 56% in terms of mortality over a 6-year period between the two trials [21]. Similar trends have been reported for major cardiovascular events, although it is difficult to compare all these studies because primary outcomes and follow-up durations were not similar [19-23]. These data suggest that the prognosis of patients with STEMI has changed, whatever the extent of CAD, and the difference in mortality according to coronary status has narrowed. In our analyses, the adjusted difference in mortality between 1-VD and MVD was observed only in patients with 3-VD.

Management of STEMI with MVD

Primary PCI is the preferred reperfusion strategy in patients with STEMI within 12 hours of symptom onset. MVD is commonly reported in this population (in approximately 50%), as observed in our study. A series of clinical trials has proven the improved survival and lower morbidity with complete myocardial revascularization compared with culprit lesion-only PCI in patients with STEMI with MVD [19-23]. This has led to very consistent global treatment recommendations. Therefore, the use of complete myocardial revascularization has increased over the last 10 years, even if the optimal timing of complete revascularization is a matter of debate [24].

In the COMPLETE trial, the benefit of complete revascularization was consistently observed, regardless of whether non-culprit-lesion PCI was performed during the index hospitalization or several weeks after discharge from hospital [21]. Our observational data suggest that complete revascularization performed before discharge is probably preferable to subsequent scheduled PCI of significantly narrowed non-culprit lesions.

On the other hand, the International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA) did not find evidence that the initial invasive strategy reduced the risk of ischaemic cardiovascular events or death from any cause [25]. These data were obtained in patients with coronary chronic syndrome and moderate or severe ischaemia (i.e. not in patients with recent myocardial infarction).

Study limitations

Our study suffers from the same limitations as all observational studies: namely, no causality can be asserted between variables that are correlated. Comparisons between patients with 1-VD and those with MVD with complete revascularization before discharge were not randomized and, despite careful adjustments on a large number of potentially confounding variables, the results can only be considered indicative. Only patients with STEMI of ≤ 24 hours' duration admitted to a cardiac catheterization laboratory were included, which represents a selection bias. Details of myocardial revascularization after discharge were not available, especially the rate of late complete revascularization. Patients with cardiogenic shock accounted for fewer than 5% of patients in the present study, and complete revascularization in this population needs to be confirmed. Finally, the fact that patients with complete revascularization had a long-term mortality rate similar to that of patients with 1-VD should not be viewed as an incentive to perform complete revascularization "at any cost". Indeed, it is expected that a substantial proportion of patients with incomplete revascularization had long-standing total coronary occlusions of arteries supplying a myocardial scar; in such patients, with permanently impaired left ventricular function, reopening the corresponding artery would be unlikely to improve long-term outcome.

Conclusions

Patients with STEMI with MVD still represent half of patients with STEMI, and maintain a more severe cardiovascular risk profile, with a higher rate of mortality at 3 years of follow-up. However, in the contemporary era, patients with MVD and complete revascularization before discharge have a long-term mortality that no longer differs substantially from that of patients with 1-VD.

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Disclosure of interest

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Figure legends

Figure 1. Three-year survival according to coronary status. 1-VD: single-vessel disease; 2-VD: two-vessel disease; 3-VD: three-vessel disease; CI: confidence interval; HR: hazard ratio.

Figure 2. Three-year survival according to coronary status and myocardial revascularization. MVD: multivessel disease; PCI: percutaneous coronary intervention; VD: vessel disease.

Table 1 Baseline characteristics.

	All patients	1-VD	2-VD	3-VD	MVD[a]	P[b]
	(n = 3907)	(n = 2034)	(n = 1247)	(n = 626)	(n = 1873)	
Age (years)	62.4 ± 13.7	60.3 ± 13.7	64.2 ± 13.2	65.9 ± 13.4	64.8 ± 13.4	< 0.001
Age ≥ 75 years	827 (21.2)	352 (17.3)	299 (24.0)	176 (28.1)	475 (25.4)	< 0.001
Men	2964 (75.9)	1536 (75.5)	927 (74.3)	501 (80.0)	1428 (76.2)	0.002
Risk factors						
Hypertension	1736 (44.4)	803 (39.5)	595 (47.7)	338 (54.0)	933 (49.8)	< 0.001
Diabetes	655 (16.8)	253 (12.4)	263 (21.1)	139 (22.2)	402 (21.5)	< 0.001
Hypercholesterolaemia	1530 (39.2)	713 (35.1)	557 (44.7)	260 (41.5)	817 (43.6)	< 0.001
Current smoking	1695 (43.4)	985 (48.4)	482 (38.7)	228 (36.4)	710 (37.9)	< 0.001
Family history	997 (25.5)	531 (26.1)	317 (25.4)	149 (23.8)	466 (24.9)	0.51
BMI ≥ 30 kg/m²	764 (20.6)	399 (20.6)	233 (19.7)	132 (22.3)	365 (20.6)	0.45
Medical history						
Previous MI	410 (10.5)	163 (8.0)	166 (13.3)	81 (12.9)	247 (13.2)	< 0.001
Previous PCI	430 (11.0)	179 (8.8)	175 (14.0)	76 (12.1)	251 (13.4)	< 0.001
History of stroke	159 (4.1)	69 (3.4)	51 (4.1)	39 (6.2)	90 (4.8)	< 0.001
Peripheral artery disease	171 (4.4)	69 (3.4)	55 (4.4)	47 (7.5)	102 (5.4)	< 0.001

Chronic kidney disease	91 (2.3)	36 (1.8)	27 (2.2)	28 (4.5)	55 (2.9)	< 0.001
Chronic heart failure	77 (2.0)	30 (1.5)	35 (2.8)	12 (1.9)	47 (2.5)	0.06
Atrial fibrillation	105 (3.2)	42 (2.5)	38 (3.7)	25 (4.7)	63 (4.0)	0.03
Cancer	297 (7.6)	142 (7.0)	103 (8.3)	52 (8.3)	155 (8.3)	0.31
COPD	174 (4.5)	85 (4.2)	62 (5.0)	27 (4.3)	89 (4.8)	0.55
Previous medication						
Aspirin	595 (15.2)	261 (12.8)	216 (17.3)	118 (18.8)	334 (17.8)	< 0.001
Clopidogrel	198 (5.1)	93 (4.6)	70 (5.6)	35 (5.6)	105 (5.6)	0.34
Prasugrel	16 (0.4)	9 (0.4)	7 (0.6)	0 (0.0)	7 (0.4)	0.19
Ticagrelor	23 (0.6)	11 (0.5)	8 (0.6)	4 (0.6)	12 (0.6)	0.92
Vitamin K antagonist	114 (2.9)	62 (3.1)	26 (2.1)	26 (4 .2)	52 (2.8)	0.04
NOAC	17 (0.4)	5 (0.2)	7 (0.6)	5 (0.8)	12 (0.6)	0.13
ACE-I or ARB	1044 (26.7)	473 (23.3)	375 (30.1)	196 (31.3)	571 (30.5)	0.00
Statin	816 (20.9)	366 (18.0)	298 (23.9)	152 (24.3)	450 (24.0)	< 0.001
Beta-blocker	690 (17.7)	300 (14.7)	243 (19.5)	147 (23.5)	390 (20.8)	0.00
Calcium blocker	480 (12.3)	193 (9.5)	189 (15.2)	98 (15.7)	287 (15.3)	< 0.001
Proton pump inhibitor	577 (14.8)	262 (12.9)	210 (16.8)	105 (16.8)	315 (16.8)	0.002
Diuretic	568 (14.5)	266 (13.1)	198 (15.9)	104 (16.6)	302 (16.1)	0.02

Data are expressed as mean ± standard deviation or number (%). 1-VD: single-vessel disease; 2-VD: two-vessel disease; 3-VD: three-vessel disease; ACE-

I: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; BMI: body mass index; COPD: chronic obstructive pulmonary disease; MI: myocardial infarction; MVD: multivessel disease; NOAC: non-vitamin K antagonist oral anticoagulant; PCI: percutaneous coronary intervention.

[a] Including patients with 2-VD and 3-VD.

[b] Comparison between patients with 1-VD versus 2-VD versus 3-VD.
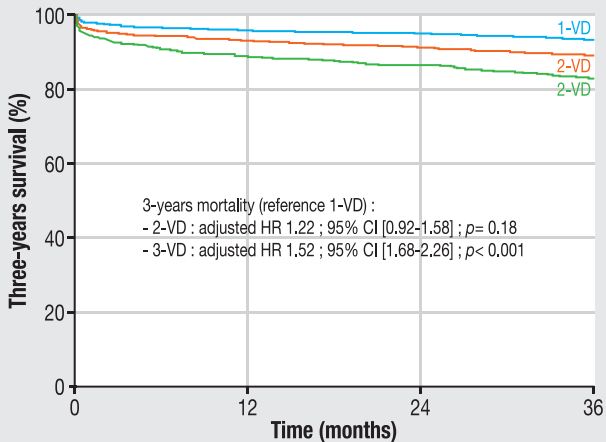
Table 2 Clinical presentation and management.

	All patients	1-VD	2-VD	3-VD	MVD[a]	P[b]
	(n = 3907)	(n = 2034)	(n = 1247)	(n = 626)	(n = 2034)	
Admission clinical presentation						
Atypical chest pain	178 (8.6)	88 (8.3)	54 (8.2)	36 (10.4)	90 (8.9)	0.43
Anterior MI	1648 (42.2)	934 (45.9)	493 (39.5)	221 (35.3)	714 (38.1)	< 0.001
Killip class						< 0.001
1	3467 (88.7)	1850 (91.0)	1101 (88.3)	516 (82.4)	1617 (86.3)	
2	278 (7.1)	116 (5.7)	93 (7.5)	69 (11.0)	162 (8.6)	
3	85 (2.2)	33 (1.6)	28 (2.2)	24 (3.8)	52 (2.8)	
4	65 (1.7)	29 (1.4)	22 (1.8)	14 (2.2)	36 (1.9)	
LVEF < 40%	308 (15.1)	211 (16.9)	127 (20,3)	646 (16.5)	773 (17.6)	0.01
GRACE score	143 ± 32	139 ± 32	145 ± 31	150 ± 33	147 ± 32	< 0.001
SRI score	24 ± 13	22 ± 13	25 ± 13	26 ± 14	25 ± 13	< 0.001
Heart rate (beats/min)	77 ± 18	77 ± 18	77 ± 18	78 ± 19	77 ± 19	0.35
SBP (mmHg)	136 ± 28	135 ± 27	138 ± 28	137 ± 28	137.5 ± 28	0.07
DBP (mmHg)	81.5 ± 18	81 ± 18	82 ± 18	81 ± 18	82 ± 18	0.45
Delays						

Time from symptoms to call (minutes); n	75 (30; 203); 3890	65 (30;180); 2026	80 (30;221); 1242	90 (30;211); 622	84.5 (30;219); 1864	0.02
Time from call to primary PCI (minutes); n	150 (109;238.5); 3717	146 (105;229); 1955	150 (10;245); 1182	165 (116;261.5); 580	155 (111;250); 1762	0.15
Management						
University hospital	1595 (40.8)	863 (42.4)	492 (35.5)	240 (38.3)	732 (39.1)	0.09
Radial access	2589 (79.9)	1353 (80.9)	827 (79.7)	409 (77.0)	1236 (78.8)	0.03
TIMI 0/1 before PCI	2234 (67.9)	1165 (67.6)	700 (67.5)	369 (69.9)	1069 (68.3)	0.58
Thromboaspiration	1240 (32.2)	704 (35.1)	383 (31.1)	153 (25.3)	536 (29.2)	< 0.001
Drug-eluting stent	2019 (52.5)	1028 (51.2)	685 (55.6)	306 (50.6)	991 (53.9)	0.12
TIMI 2/3 after PCI	3421 (95.7)	1796 (96.2)	1102 (95.9)	523 (93.2)	1625 (95.0)	0.008
No reflow	56 (1.8)	31 (1.9)	19 (1.9)	6 (1.2)	25 (1.6)	0.73
IABP	74 (1.9)	26 (1.3)	16 (1.3)	32 (5.1)	48 (2.6)	< 0.001
Diuretics	812 (20.8)	376 (18.5)	295 (23.7)	141 (22.5)	436 (23.3)	0.001

Data are expressed as number (%), mean ± standard deviation or median (interquartile range). 1-VD: single-vessel disease; 2-VD: two-vessel disease; 3-VD: three-vessel disease; DBP: diastolic blood pressure; GRACE: Global Registry of Acute Coronary Events; IABP: intra-aortic balloon pump; LVEF: left ventricular ejection fraction; MI: myocardial infarction; MVD: multivessel disease; PCI: primary coronary intervention; SBP: systolic blood pressure; SRI: Simple Risk Index; TIMI: Thrombolysis In Myocardial Infarction.

[a] Including patients with 2-VD and 3-VD.

[b] Comparison between patients with 1-VD versus 2-VD versus 3-VD.

3-years mortality (reference 1-VD) :
- 2-VD : adjusted HR 1.22 ; 95% CI [0.92-1.58] ; *p*= 0.18
- 3-VD : adjusted HR 1.52 ; 95% CI [1.68-2.26] ; *p*< 0.001

Number at risk

1-VD	2,034	1,945	1,859	1,783
2-VD	1,247	1,157	1,100	1,048
2-VD	626	555	520	482

Three-years survival (%) vs Time (months)

G1 : Single VD with PCI success
G2 : MVD with complete revacularization before discharge
G3 : MVD without complete revacularization before discharge
G4 : Primary PCI failure

Number at risk

	0	12	24	36
G1	1,796	1,723	1,646	1,580
G2	649	607	567	535
G3	936	850	811	769
G4	155	131	127	122