Diagnostic performance of pulmonary ultrasonography and a clinical score for the evaluation of fluid overload in haemodialysis patients

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Abstract
Introduction: There is no feasible benchmark in daily routine to estimate the hydration status of haemodialysis patients, which is essential to their management.
Objective: We performed a study in haemodialysis patients patients to assess the diagnostic performance of pulmonary ultrasound and clinical examination for the evaluation of fluid overload using transthoracic echocardiography as a gold standard.
Methods: 31 patients receiving chronic haemodialysis patients were included. Evaluation of hydration status was assessed weekly before haemodialysis sessions using clinical and Echo Comet Score from pulmonary ultrasound and transthoracic echocardiography (reference method).
Results: Five patients had a transthoracic echocardiography overload. Compared with transthoracic echocardiography, the diagnostic performance of the clinical overload score has a sensitivity of 100%, a specificity of 77%, a positive predictive value of 50% and a negative predictive value of 100% with a κ of 0.79. Only orthopnoea (*P*=0.008), jugular turgor (*P*=0.005) and hepatic-jugular reflux (*P*=0.008) were significantly associated with transthoracic echocardiography overload diagnosis. The diagnostic performance of Echo Comet Score by pulmonary ultrasound has a sensitivity of 80%, a specificity of 58%, a positive predictive value of 26% and a negative predictive value of 94%. Ten patients (32.3%) had an increase of extravascular pulmonary water without evidence of transthoracic echocardiography or clinical overload.
Conclusions: Our clinical score has a convincing diagnostic performance compared to transthoracic echocardiography and could be easily used in daily clinical routine to adjust dry weight. The evaluation of the overload using pulmonary ultrasound seems poorly correlated with the overload evaluated by transthoracic echocardiography. Extravascular pulmonary water undetected by clinical examination and transthoracic echocardiography remains a parameter that requires further investigation.

Keywords
Echocardiography
Fluid overload
Haemodialysis
Hydration status
Lung ultrasound

Abbrevations

BIS	bio-impedance spectroscopy
DW	dry weight
ECS	Echo-Comet Score
ESRD	end-stage renal disease
FO	lluid overload
IVC	inferior vena cava
LVEF	left ventricular ejection fraction
LVFP	left ventricular filling pressure
LR	likelihood ratio
PPV	positive predictive value
NPV	negative predictive value
NYHA	New York Heart Association
RBV	red blood volume
ROC	receiver operating characteristic
Se	sensibility
Sp	specificity

sPAP	systolic pulmonary arterial pressure
TTE	trans-thoracic echocardiography

Introduction

The definition of hydration status to determine optimal dry weight (DW) is essential for the management of haemodialysis patients. The DW concept in dialysis was conceived at the same time as dialysis in 1967 [1] and has evolved over time. DW is defined as the lowest weight tolerated by the patient at the end of the dialysis session at which there are minimal symptoms of hypovolemia or hypervolemia [2]. DW is an element of standard care for haemodialysis patients because inadequate DW is associated with increased cardiovascular morbidity and mortality [3-8]. Patients with end-stage renal disease (ESRD) requiring haemodialysis have a high risk of developing pulmonary congestion. The accumulation of pulmonary water can be infra-clinical and occurs gradually between dialysis sessions, especially in anuric patients [9] and is related in part to increased alveolar-capillary permeability [10].

Clinical examination is the classic tool for assessing hydration status at the patient's bedside. However, it can be faulted in finer evaluation. There is currently neither a validated clinical score to assess hydration status in haemodialysis patients nor a gold standard to define the DW. Various anthropometrical [11] or radiological tools [12-16] and biomarkers [17-20] have been tested. Among them, transthoracic echocardiography (TTE) provides a more accurate assessment of blood volume than clinical examination [21] by studying left ventricular filling pressure (LVFP), systolic pulmonary arterial pressure (sPAP) and inferior vena cava (IVC) diameter at the same time, but it requires training and its long duration is poorly suited to routine use by untrained users such as nephrologists.

In lung ultrasound, B-lines are artefactual images resulting from close contact between (alveolar) air and water (clogged septa). Lung ultrasound detects pulmonary congestion with a sensitivity (Se) and a specificity (Sp) respectively, of 93 and 93% in intensive care patients [22]. This technique has several advantages: it is fast (from 3 to 10 minutes) [13,15,23], non-irradiating and inexpensive. It can be performed with any ultrasound machine. The training is simple (about 2 hours) [14], with low inter-operator variability [24,25]. It can be used in daily practice to detect fluid overload (FO) and has been validated in congestive heart failure and intensive care [26,27].

Recently, several studies have evaluated this technique in the haemodialysis population [28]. The number of B-lines is correlated with an elevated LVFP by TTE, and the increase of total and lung water by bio-impedance spectroscopy (BIS) [12-14,29-31]. The number of B-lines decreases during a dialysis session and is correlated with weight loss and water loss in BIS [14,29]. The relationship between the presence of asymptomatic pulmonary water on ultrasound, the DW and the occurrence of adverse events is yet to be clarified.

We conducted a prospective study to compare the performance of lung ultrasound and clinical examination with TTE as the diagnostic gold standard to assess FO in haemodialysis patients.

The secondary objective was to determine which clinical signs best correlate with pulmonary and cardiac FO.

Materials and methods

Patients

Volunteer patients over 18 years old in haemodialysis for more than 3 months at the University Hospital Centre in Marseilles, France, haemodynamically stable and without any cardiovascular, infectious or haemorrhagic event in the previous three months were included. All patients had at least three dialysis sessions per week.

The data was collected prospectively. Procedures followed were in accordance with the Helsinki Declaration of 1975, as revised in 2000. All patients received a written information and have given their express consent for the use of their health data. This study is approved to be in conformity with General Data Protection Regulation, and registered in the Health Data Portal of Assistance *Publique-Hôpitaux de Marseille* under the reference PADS19-344. Patients who missed more than one dialysis session in the previous month and patients with a history of pulmonary fibrosis or active lung infection were not included. The persistence of a residual diuresis was assessed for all patients and was defined by a diuresis volume superior to 500 mL per day.

Fluid overload assessment

The hydration status evaluation was performed during the mid-week dialysis session by a physician trained in clinical examination, cardiac and pulmonary ultrasound.

The TTE evaluated three parameters:

• IVC diameter using the two-dimensional motion-mode method (M-mode), measured in sub-xiphoid view in the hepatic portion at non-forced end-expiratory and end-inspiratory phases. IVC collapsibility index was calculated as follows: (maximum IVC diameter at expiration - minimum IVC diameter)/maximum IVC diameter *100. A collapsibility index greater than 40% is the threshold to define hypovolemia in spontaneous ventilation [32];

• sPAP was evaluated by measuring the tricuspid regurgitation velocity peak plus the estimated right atrial pressure. The right atrial pressure was rated at 10 mmHg if the IVC diameter was greater than 2 cm and at 5 mmHg in other cases, according to the Brennan et al. classification [33]. sPAP was considered elevated above a value of 35 mmHg [34];

• LVFP was evaluated using two measurements: the velocity ratio of the early to late filling flow (E/A ratio) using pulsed Doppler at the mitral annulus and the velocity ratio of the early filling flux (E) to the early velocity of the mitral annulus in lateral position (E') in tissue Doppler mode (E/E' ratio) [35,36]. Only the E/E' ratio was measured in the case of chronic atrial fibrillation [37]. It was considered high for values greater than 13 and low for values below 8 in patients with preserved left ventricular ejection fraction (LVEF), according to the 2012 French *Haute Autorité de santé* (HAS) guidelines [38].

We defined the echocardiographic FO as E/E' ratio >13 or a combination of the following criteria: E/E' ratio between 8 and 13, IVC collapsibility <40% and sPAP >35 mmHg.

This definition was chosen using semiotic evidence bundles conventionally used in clinical practice and values described in the literature for ESRD patients [39-43], in the absence of a validated echocardiographic score to define overload in haemodialysis patients. We chose this definition as the gold standard in our study because of the absence of a suitable benchmark to assess FO in ESRD patients, and because it has been shown that the E/E' ratio correlates well with the elevation of LVFP in cardiac catheterization in patients with ESRD [39]. In addition, the thresholds appear to be similar to those in the non-haemodialysis population [42], with elevated values representing an independent risk factor for mortality [39].

We have developed a clinical score to define the presence of FO using the following criteria: Major criteria – dyspnoea New York Heart Association (NYHA) ≥ III, orthopnoea; Minor criteria – jugular turgor and hepatic-jugular reflux in half-sitting position, pulmonary crackles at auscultation, peripheral oedema (evaluated by searching an indentation after pressing the two inferior limbs (over the dorsum of the foot, behind and above the medial malleolus) and the sacral region) and pre-dialysis high blood pressure. The association of two major or three minor criteria or the combination of one major and one minor criterion defined FO (*Table 1*). This score was defined collegially by the study investigators prior to the study, by choosing the signs recognized the most sensitive and specific of fluid overload [44]. Then, inter-observer reliability of this score was measured by Cohen's

kappa (κ) coefficient in 10 patients by 2 independent observers prior to the study [45]. This score was obtained at the beginning of the dialysis session.
Lung ultrasound assessed the number of anterior and lateral B-lines in a supine position. Lung water quantification was evaluated by the Echo Comet Score (ECS) using the 28-region technique described by Jambrik et al. [23]. The sum of the B-lines at each site led to a score of over 280 indicating the importance of extravascular pulmonary water. The presence of B-lines was considered "mild" (5 to 14 B-lines), "moderate" (15 to 29 B-lines) or "severe" (more than 30 B-lines) [40]. Cardiac and pulmonary ultrasounds were done in the first 30 minutes of the dialysis session using an ultrasound machine (Philips® CX50 POC, Amsterdam, Netherlands), after the clinical examination.
Clinical, anthropometric and demographic characteristics were collected at baseline. Intra-dialytic hypotension was defined as systolic blood pressure fall more than 20 mmHg, or more than 10 mmHg associated with signs of poor tolerance, according to Kidney Disease Outcomes Quality Initiative (KDOQI) recommendations [41].
Biological data were collected before the dialysis session. The relative changes in blood volume during the dialysis session were evaluated by the relative blood volume (RBV) monitor incorporated into the dialysis machine (Nikkiso® DBB05, Tokyo, Japan).

Statistical analysis

Categorical variables were tested by Chi-square test and expressed as counts and percentages. The quantitative values were tested by a Mann-Whitney test and expressed as median and interquartile (IQR) ranges (25^{th}-75^{th} percentiles) and calculation of correlation by Spearman test and linear regression. All tests were non-parametric. A $P<0.05$ was considered significant. We express the diagnostic weight as likelihood ratio (LR) to describe the discriminatory power of clinical examination and lung ultrasound to define FO compared to the diagnostic gold standard (TTE). LRs and Receiver operating caracteristics (ROC) Curves were calculated using the Evidence-Based Medicine Calculator (©Knowledge Translation Program). Values greater than 1 increase the probability of disease. LRs less than 1 decrease the probability of disease. LRs of 2, 5, and 10 increase the probability of disease by about 15%, 30%, and 45%, respectively (in absolute terms). LRs of 0.5, 0.2, and 0.1 decrease probability by 15%, 30%, and 45%, respectively. We analysed clinical examination and lung ultrasound findings with tables comparing LRs of each different parameters to express the greatest diagnostic value [46].

Results

General characteristics of the study population

Thirty-one patients were included between December 2016 and April 2017.
Characteristics of the study population are shown in *Table 2*. 83.9% of the patients were classified as hypertensive. Antihypertensive medications were prescribed to 67.8% of the study population. Most commonly prescribed were beta-blockers (32.3% of patients), followed by renin angiotensin system blockade (12.9% of patients), and calcium channel blockers (9.7% of patients). Loop diuretics were prescribed for 41.3% of patients. 19.3% of the patients had chronic heart failure, 41.9% had ischemic cardiopathy, 16.1% had atrial fibrillation, and 35.4% had diabetes mellitus. 61.3% of the patients had a residual diuresis.

Prevalence of fluid overload according to TTE

Characteristics of the patients relative to hydration status are presented in *Table 3*. At TTE, patients had a median E/A ratio of 0.82 [0.59-1.1], a median E/E' ratio of 7.5 [5.7-10.6], a median IVC collapsibility of 17.4% [6.6-47.6], a median sPAP of 10.0 mmHg [5.0-28.2]. Five (16.1%) participants had FO according to the TTE definition (*Table 4*). In the TTE FO group, the median inter-dialytic weight variation was +2.3% [1.6-3.0].

Clinical and lung ultrasound characteristics of patients with fluid overload

The diagnostic performances of the clinical FO score according to TTE FO were: Se: 100% [95%CI: 57-100]; Sp: 81% [95%CI: 62-92]; positive predictive value (PPV): 50% [95%CI: 24-76]; negative predictive value (NPV): 100% [95%CI: 85-100], LR: 5.21 [95%CI: 2.37-11.43] (*Table 5, Figure 1A*). The ROC curve of the clinical score is shown in *Figure 1B*. Inter-observer reliability test showed a substantial agreement with a κ of 0.77.

Ten out of 31 patients (32.3%) had FO according to the clinical score. The number of patients with clinical FO was significantly higher in patients with TTE FO: 100% versus 19.2%, *P*=0.0002. Five patients (19.2%) had clinical FO but no TTE FO (*Table 4*). Three clinical signs of FO were significantly associated with TTE FO: orthopnoea (60.0% versus 3.8%; *P*=0.0082; LR: 10.5); jugular turgor (100% versus 26.9%; *P*=0.0047; LR: 3.7); hepatic-jugular reflux (100% versus 30.8%; *P*=0.0076; LR: 3.24) (*Table 4*, *Figure 1A*). There was no significant difference between the TTE overload and no TTE overload groups for all other clinical signs. There was no significant difference in terms of the occurrence of intra-dialytic hypotension between the two TTE groups (*Table 4*). Serum albumin was not different between the TTE overload and no TTE overload groups: 37.8 [35.6-39.0] g/L vs 36.7 [34.4-41.3], respectively (*P*=0.89).

The diagnostic performance of lung ultrasound according to TTE FO was Se: 80% [95%CI: 38-96]; Sp: 58% [95%CI: 39-75]; PPV: 26% [95%CI: 11-52]; NPV: 94% [95%CI: 72-99], with a LR of 1.89 [95%CI: 1.01-3.54] (*Table 5*, *Figure 1A*). The ROC curve of the clinical score is shown in *Figure 1C*. By considering only the patients with moderate to severe pulmonary overload (ECS >15), lung ultrasound had a Se of 80% [95%CI: 38-96], a Sp of 62% [95%CI: 43-78], a PPV of 29% [95%CI: 12-55], a NPV of 94% [95%CI: 73-99], and a LR of 2.08 [95%CI: 1.08-4.00] (*Table 5*). Finally, by considering only the patients with severe pulmonary overload (ECS >30), lung ultrasound had a Se, Sp, PPV and NPV of 80% [95%CI: 38-96], 69% [95%CI: 50-84], 33% [95%CI: 14-61], and 95% [95%CI: 75-99], respectively, and a LR of 2.60 [95%CI: 1.26-5.36] (*Table 5*).

Fifteen out of 31 patients (48.4%) had pulmonary water on chest ultrasonography: one patient had mild pulmonary overload, two patients had moderate overload, and 12 patients had severe overload. The median ECS was 3 [0-42]. Among patients with pulmonary water on ultrasound, the median ECS was 44.5 [30.0-66.2]. The number of patients with lung water on ultrasonography was not different between the two TTE groups (80.0% versus 42.3%; *P*=0.11). The ECS was not significantly higher in patients with TTE overload: 51 [18-146] versus 0 [0-33.7]; *P*=0.22 (*Table 4*). ECS were significantly correlated with E/E' ratio (r=0.40; *P*=0.02; R^2 0.40) (*Figure 1D*).

Clinical and TTE characteristics of the patients based on the presence of pulmonary water at lung ultrasound

There were not significantly more patients in overload according to the clinical score in patients with overload on the pulmonary ultrasound than in patients without pulmonary overload: 35.7 versus 29.4%; *P*=0.50. Ten patients (32.3%) had pulmonary water without clinical overload. Pulmonary water ultrasonography was significantly associated with the presence of crackles: 28.6% versus 0.0%; *P*=0.03. There was no significant difference between the two lung ultrasound groups for all other clinical signs. There were not significantly more patients with TTE overload in patients with pulmonary ultrasound overload than in patients without lung overload: 5.8 versus 28.6%; *P*=0.11. Pulmonary water ultrasonography was significantly associated with a higher sPAP: 7.5 mmHg [5.0-11.5] versus 25.5 mmHg [5.0-39.7]; *P*=0.012. There was no significant difference between the two lung ultrasound groups regarding other TTE data.

The diagnostic performance of the clinical overload score according to presence of pulmonary water on lung ultrasound was: Se: 33% [95%CI: 15-58], Sp: 69% [95%CI: 44-

86], PPV: 50% [95%CI: 24-76], NPV: 52% [95%CI: 32-72], with a LR of 1.07 [95%CI: 0.39-2.96, non-significant].

Discussion

In our study, it appears that lung ultrasonography data do not correlate with TTE data to assess FO in ESRD patients. It had a poor Sp and PPV, but a good NPV. FO clinical score appears to be a better tool for gauging TTE-assessed overload with greater Se, Sp, PPV, and NPV than lung ultrasound.

Clinical overload evaluated by the score proposed in this study appears well correlated with TTE overload data, in particular, orthopnoea, jugular turgor and hepatic-jugular reflux. Our score has the advantage of being simple and fast for a volume assessment in routine clinical practice, and with a good inter-observer reliability. Thus, it seems useful for detecting intravascular overload and would make it possible to avoid the realization of TTE to assess DW.

While TTE data (elevation of LVFP, sPAP, diameter and collapsibility of IVC) are markers of increased intravascular pressure, lung ultrasound seems rather to be a reflection of extravascular overload. It does not appear to be correlated with the echocardiographic data or clinical examination in our study. It was only correlated with crackles. Thus, it seems of interest for the detection of infra-clinical pulmonary FO, which is not identifiable using TTE. It could refine the accuracy of DW determination, particularly in patients for whom clinical evaluation of FO is difficult, since stating normohydration from only the intravascular fluid accumulation may lead to persistent fluid overload.

Because of the simplicity, the speed, and the excellent inter-observer reproducibility [43] of this examination, it appears a useful technique in which nephrologists should be trained.

Eleven of the 12 studies currently published on haemodialysis pulmonary ultrasound used ECS [28]. Our results are consistent with those of the Lung Water by Ultrasound Guided Treatment in Hemodialysis Patients (LUST) study, which reported the low sensitivity of pulmonary crackles and peripheral oedema compared to lung ultrasonography for evaluation of lung water in haemodialysis patients, but a good specificity in patients with high cardiovascular risk [30]. Our study provides TTE as the reference method, which is not evaluated in LUST study. Ours is therefore the first study comparing clinical signs with cardiac and pulmonary ultrasonography to detect FO at the chronic dialysis patient's bedside in unselected and stable ESRD patients.

Indeed, it has been shown that a decrease in ECS correlates with weight loss between the beginning and end of dialysis, while neither the diameter of the IVC [13,15] nor the E/A ratio varies [47]. In our study we confirm the existence of a correlation between LFVP evaluated in TTE and ECS, which is consistent to other studies [24,48].

This suggests that the extravascular compartment would balance more slowly than the intravascular area with ultrafiltration. The study of Agricola et al. showed a linear correlation between ECS and extravascular pulmonary water determined in transpulmonary thermodilution [48]. In our study, 15 out of 31 patients had overload on pulmonary ultrasound. However, the occurrence of a single episode of cardiac decompensation in our cohort suggests that in most cases this overload is well tolerated. The fact that the majority of the patients in the study had a residual diuresis probably limited the risk of cardiac decompensation.

Several questions remain unanswered. Our study shows 32.3% of clinically euvolemic patients with pulmonary water on ultrasound. There may be a risk of overtreating these patients with lung overload only with inappropriately high ultrafiltration volumes which may expose to risks, such as the occurrence of inter-dialytic hypotensions [49], fistula thrombosis [49,50], loss of residual diuresis [51,52] or decreased LVEF [53]. Conversely, FO could favour the occurrence of cardiovascular adverse effects, and even asymptomatic overload is an independent risk factor for mortality [3-6,54]. Asymptomatic lung congestion

is probably also dependent on other variable factors such as vascular hyper-permeability (due to a possible endothelial dysfunction) [10], as serum albumin was not different in our study between patients with TTE overload and no TTE overload. Detection of asymptomatic lung water by ultrasound could allow for better control of the hydration status and avoids the occurrence of cardiac events. The current LUST randomized trial (ClinicalTrials.gov identifier No. NCT02310061) may answer this question by comparing the mortality and the risk of cardiovascular events in chronic haemodialysis patients according to management based on a daily clinical volume assessment or pulmonary ultrasound examination in everyday practice.
The physicians in charge of the patients were blinded to study results that could have influenced the change in DW. The fact that clinical evaluations were performed before ultrasound evaluations limits an eventual assessment bias, as the ultrasound findings appear to be more objective than the clinical findings.
Our work has several limitations. It is a relatively small sample, not allowing for multivariate analyses, drawn from a single dialysis centre. The clinical score and TTE definition of FO were chosen empirically, in the absence of clearly defined and validated scores in the haemodialysis population in the literature.
We have not evaluated serum BNP in our study due to his poor sensitivity and specificity to assess fluid overload in dialysis patients [20]. We did not evaluated BIS neither, as this technique was not available in our center and already was compared to ECS in previous studies [29,31].

Conclusion

Evaluation of overload using the ECS by pulmonary ultrasound is poorly correlated with the overload evaluated by TTE. The presence of extravascular pulmonary water undetected by clinical examination and TTE remains a parameter which requires further investigation from a diagnostic and prognostic point of view in haemodialysis patients. The clinical score proposed in this study has a satisfying diagnostic performance compared to TTE with good inter-observer reliability, and could be easily used in daily clinical routine to adjust DW.

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Statement of ethics

Procedures followed were in accordance with the Helsinki Declaration of 1975, as revised in 2000. Since the echocardiography and lung ultrasound are realised in routine in our unit, and the data collected retrospectively, written consent were not necessary, but all patients were contacted and gave their express oral consent for the publication of their data. This study is registered in the local portal for access to health data (*Portail d'Accès aux données de Santé, Assistance-Publique-Hôpitaux de Marseille)* under the number PADS19-344.

Disclosure statement

The authors have no conflicts of interest to declare.

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Figure 1. Probability of fluid overload in echocardiography depending on clinical signs and lung ultrasound. **A.** Likelihood ratios. **B.** ROC curve of the clinical score according to echocardiography. **C.** ROC curve of lung ultrasound according to echocardiography. **D.** Correlation between E/E' ratio and Echo-comet score in pulmonary ultrasound.
LR: Likelihood ratios

Table 1
Clinical score of fluid overload

Major criterions
Dyspnea NYHA 3 or 4
Orthopnea
Minor criterions
Pulmonary crackles
Peripheral oedema
Jugular turgor
Hepatic-jugular reflux
Predialysis blood pressure above 150/100 mmHg
Clinical overload was defined by the association of 2 major criterions, or the association of 3 minor criterions, or the association of 1 major criterion and one minor criterion

Table 2
General characteristics of the population

Characteristics	**Population (n=31)**
Demographic	
Men, n (%)	22 (70.9)
Age (years)	63 [52-76]
Dry weight (kg)	70.5 [61.0-81.0]
Body mass index (kg/m²)	23.9 [21.9-27.3]
Residual diuresis, n (%)	19 (61.3)
High blood pressure, n (%)	26 (83.9)
Hypercholesterolemia, n (%)	12 (38.7)
Diabetes mellitus, n (%)	11 (35.4)
Smoking, n (%)	16 (51.6)
Chronic heart failure, n (%)	6 (19.3)
Atrial fibrillation, n (%)	5 (16.1)
Coronaropathy, n (%)	13 (41.9)
Baseline left ventricular ejection fraction (%)	64.5 [55.0-66.7]
Chronic obstructive pulmonary disease, n (%)	3 (9.7)
Chronic respiratory failure, n (%)	0 (0)
Dialysis	
Vascular access	

Catheter, n (%)	11 (35.5)
Fistula, n (%)	20 (64.5)
Technique	
Haemodialysis, n (%)	19 (61.3)
Haemodiafiltration, n (%)	10 (32.3)
Haemofiltration, n (%)	2 (6.4)
Sessions per week (n)	3 [3-3]
Duration of sessions (hours)	4 [4.0-4.7]
Dialysis vintage (months)	33 [8-102]
Biological data	
C-Reactive protein (mg/L)	8.1 [2.7-11.0]
Serum albumin (g/L)	36.9 [35.1-40.1]

Categorical variables are expressed in number (percentage). Quantitative values are expressed in median [1st and 3rd quartile].

Table 3
Characteristics of the population relative to hydration status

Characteristics	Population (n=31)
Clinical data	
Fluid overload according to clinical score, n (%)	10 (32.3)
KT/V of the session	1.35 [1.15-1.54]
Ultrafiltration volume during sessions (litres)	1.7 [1.2-2.1]
Weight gain since last session (kg)	1.3 [0.8-1.8]
Weight gain compared to dry weight (% dry weight)	2.3 [1.6-3.0]
Pre-dialysis blood pressure (mmHg)	
Diastolic	132 [120-149]
Systolic	72 [63-82]
Dyspnoea NYHA stage	
I	16 (51.6)
II	11 (35.5)
III	4 (12.9)
IV	0 (0)
Orthopnoea	4 (12.9)
Cough	7 (22.6)
Juguar turgor	12 (38.7)
Hepatic-jugular reflux	13 (41.9)
Pulmonary crackles	4 (12.9)
Peripheral oedema	7 (22.6)
Skin fold	5 (16.1)
Cramps	9 (29.0)
Global asthenia	13 (41.9)
Post-dialysis asthenia	17 (54.8)
Biological data	
Haematocrit (L/L)	0.33 [0.30-0.35]
Protidaemia (g/L)	68.1 [65.2-73.0]

Red Blood Volume at first hour (%)	-3.5 [-1.6 to -4.9]
Red Blood Volume at the end of session (%)	-6.0 [-3.1 to -10.1]
Echocardiography	
Fluid overload according to TTE Score, n (%)	5 (16.1)
Inferior vena cava collapsibility (%)	17.4 [6.6-47.6]
E/A ratio	0.82 [0.59-1.10]
E/E' ratio	7.5 [5.7-10.6]
sPAP (mmHg)	10.0 [5.0-28.2]
Lung ultrasound	
Presence of lung water, n (%)	15 (48.4)
Echo Comet Score /280	3 [0-42]

Categorical variables are expressed in number (percentage). Quantitative values are expressed in median [1st and 3rd quartile].
NYHA: New York Heart Association; sPAP: systolic pulmonary arterial pressure; TTE: transthoracic echocardiography

Table 4
Clinical and ultrasound characteristics of the population, depending on their fluid status according to gold standard: transthoracic echocardiography (TTE)

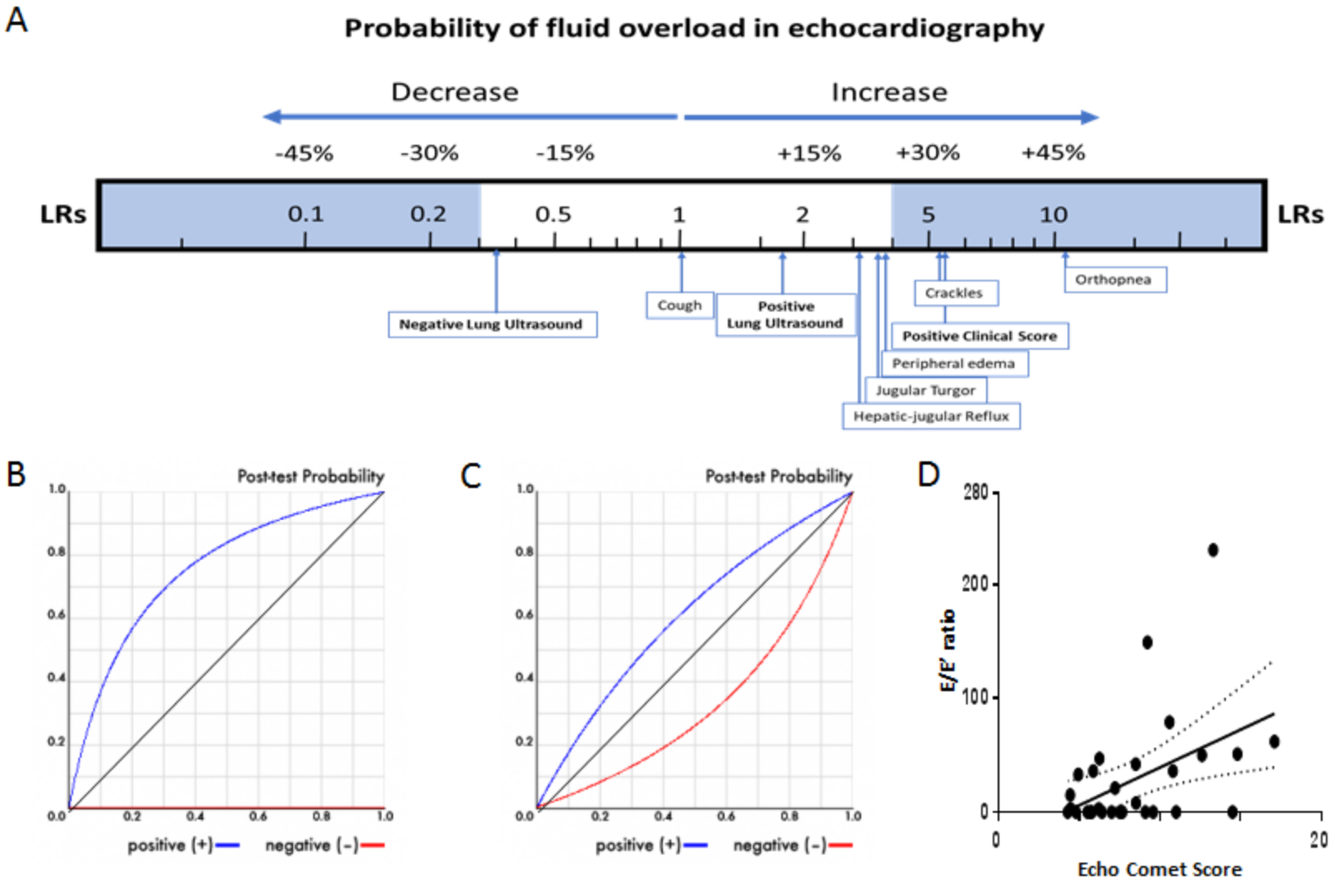
	No fluid overload (n=26)	**Fluid overload (n=5)**	***P***
Echocardiography			
Inferior vena cava collapsibility (%)	28.0 [7.1- 51.6]	10.7 [5.1-11.8]	**0.0002**
E/A ratio	0.8 [0.6-1.0]	1.3 [1.2-1.4]	**0.04**
E/E' ratio	6.7 [2.6-8.7]	14.5 [12.0-15.9]	**0.0011**
sPAP (mmHg)	5.0 [5.0-19.5]	38.5 [21.0-44.9]	**0.0049**
Clinical			
Dyspnoea NYHA score ≥3	4 (15.4)	0 (0.0)	0.99
Orthopnoea	1 (3.8)	3 (60.0)	**0.0082**
Cough	6 (23.1)	1 (20.0)	0.74
Jugular turgor	7 (26.9)	5 (100.0)	**0.0047**
Hepatic-jugular reflux	8 (30.8)	5 (100.0)	**0.0076**
Pulmonary crackles	2 (7.7)	2 (40.0)	0.11
Peripheral oedema	4 (15.4)	3 (60.0)	0.06
Skin fold	4 (15.4)	1 (20.0)	0.61
Cramps	8 (30.8)	1 (20.0)	0.84
Global asthenia	10 (38.5)	3 (60.0)	0.34
Post-dialysis asthenia	15 (57.7)	2 (40.0)	0.88
Red Blood Volume at first hour (%)	-2.5 [-0.97 to -4.4]	-5.8 [-4.0 to -7.1]	**0.019**
Red Blood Volume at the end of session (%)	-5.2 [-2.5 to -10.0]	-7.8 [-6.2 to -10.8]	0.08
Lung ultrasound			
Presence of lung water, n (%)	11 (42.3)	4 (80.0)	0.11
Echo Comet Score /280	0 [0-33.7]	51 [18-146]	0.22

Categorical variables are expressed in number (percentage). Quantitative values are expressed in median [1st and 3rd quartile].
NYHA: New York Heart Association; sPAP: systolic pulmonary arterial pressure

Table 5
Fluid overload diagnostic performances of the clinical signs and the lung ultrasound compared to the diagnostic gold standard by transthoracic echocardiography (TTE) definition

Variable	Sensitivity (%) [95%CI]	Specificity (%) [95%CI]	Likelihood ratio [95%CI]	
			Present	Absent
Clinical signs				
Clinical score	100 [57-100]	81 [62-92]	5.21 [2.37-11.43]	-
Dyspnoea (NHYA score ≥3)	0 [0-43]	85 [67-94]	-	1.18 [1.00-1.39]
Orthopnoea	60 [23-88]	96 [81-99]	15.79 [2.01-121.28]	0.42 [0.14-1.22]
Cough	20 [4-62]	77 [58-89]	0.87 [0.13-5.73]	1.04 [0.64-1.69]
Jugular turgor	100 [57-100]	73 [54-86]	3.72 [1.97-7.00]	-
Hepatic-jugular reflux	100 [57-100]	69 [50-84]	3.25 [1.13-5.79]	-
Pulmonary crackles	40 [12-77]	92 [76-98]	5.20 [0.94-28.76]	0.65 [0.32-1.34]
Peripheral oedema	60 [23-88]	85 [67-94]	3.90 [1.23-12.33]	0.47 [0.16-1.40]
Lung ultrasound				
Mild to severe overload	80 [38-96]	58 [39-75]	1.89 [1.01-3.54]	0.34 [0.06-2.06]
Moderate to severe overload	80 [38-96]	62 [43-78]	2.08 [1.08-4.00]	0.33 [0.06-1.93]
Severe overload	80 [38-96]	69 [50-84]	2.60 [1.26-5.36]	0.29 [0.05-1.70]

NYHA: New York Heart Association


A
Probability of fluid overload in echocardiography
Decrease
Increase
-45%
-30%
-15%
+15%
+30%
+45%
LRs
0.1
0.2
0.5
1
2
5
10
LRs
Negative Lung Ultrasound
Cough
Positive Lung Ultrasound
Crackles
Orthopnea
Positive Clinical Score
Peripheral edema
Jugular Turgor
Hepatic-jugular Reflux
B
Post-test Probability
positive (+)
negative (–)
C
Post-test Probability
positive (+)
negative (–)
D
E/E' ratio
Echo Comet Score