Detection of Pulmonary Congestion by Chest Ultrasound in Dialysis Patients

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OBJECTIVES This study sought to investigate clinical and echocardiographic correlates of the lung comets score.

BACKGROUND Early detection of pulmonary congestion is a fundamental goal for the prevention of congestive heart failure in high-risk patients.

METHODS We undertook an inclusive survey by a validated ultrasound (US) technique in a hemodialysis center to estimate the prevalence of pulmonary congestion and its reversibility after dialysis in a population of 75 hemodialysis patients.

RESULTS Chest US examinations were successfully completed in all patients (N = 75). Before dialysis, 47 patients (63%) exhibited moderate to severe lung congestion. This alteration was commonly observed in patients with heart failure but also in the majority of asymptomatic (32 of 56, 57%) and normohydrated (19 of 38, 50%) patients. Lung water excess was unrelated with hydration status but it was strongly associated with New York Heart Association functional class (p < 0.0001), left ventricular ejection fraction (r = −0.55, p < 0.001), early filling to early diastolic mitral annular velocity (r = 0.48, p < 0.001), left atrial volume (r = 0.39, p = 0.001), and pulmonary pressure (r = 0.36, p = 0.002). Lung water reduced after dialysis, but 23 patients (31%) still had pulmonary congestion of moderate to severe degree. Lung water after dialysis maintained a strong association with left ventricular ejection fraction (r = −0.59, p < 0.001), left atrial volume (r = 0.30, p = 0.01), and pulmonary pressure (r = 0.32, p = 0.006) denoting the critical role of cardiac performance in the control of this water compartment in end-stage renal disease. In a multiple regression model including traditional and nontraditional risk factors only left ventricular ejection fraction maintained an independent link with lung water excess (beta = −0.61, p < 0.001). Repeatability studies of the chest US technique (Bland-Altman plots) showed good interobserver and inter-US probes reproducibility.

CONCLUSIONS Pulmonary congestion is highly prevalent in symptomatic (New York Heart Association functional class III to IV) and asymptomatic dialysis patients. Chest ultrasound is a reliable technique that detects pulmonary congestion at a pre-clinical stage in end-stage renal disease. (J Am Coll Cardiol Img 2010;3:586-94) © 2010 by the American College of Cardiology Foundation
Chronic volume expansion, either clinically apparent or occult, is a pervasive complication in patients with end-stage renal disease (ESRD) maintained on dialysis. Even though the independent prognostic power of volume overload remains scarcely defined in epidemiologic studies, recent findings in a large multietnic cohort of American patients documented that fluid accumulation between dialysis is a powerful predictor of death and cardiovascular complications in this population (1). There has been a quest for methods aimed at estimating body fluids volume and for personalizing fluids removal in ESRD (2,3). The main issue for the achievement of dry weight by dialysis is that volume subtraction should be tailored to the individual patient’s hemodynamic tolerance taking into full account cardiac performance, which is very often compromised in ESRD patients (4,5).

Extravascular lung water (LW) is a relatively small but fundamental component of body fluids volume (6,7). This component represents the water content of the lung interstitium that is strictly dependent on the filling pressure of the left ventricle (LV), that is, the hemodynamic parameter considered as the golden standard for guiding fluids therapy in critical care.

In recent years, the use of chest ultrasound (US) to detect LW has received growing attention in clinical research in intensive care patients (8) and in patients with heart failure (9). In the presence of excessive LW, the US beam is reflected by subpleural thickened interlobular septa, a low impedance structure surrounded by air with a high acoustic mismatch. This US reflection generates hyperechoic reverberation artifacts between thickened septa and the overlying pleura that are defined as “lung comets” (10). Lung comets represent the US equivalent of Kerley B lines in standard chest X-rays. These artifacts (Fig. 1) are easily detected with standard US probes. Remarkably, lung comets are strongly related to LV filling pressure (capillary wedge pressure) and the measurement of LW by US has been formally validated against a golden standard technique such as the indicator thermodilution method in a series of patients submitted to cardiac catheterization (11). A recent proof-of-concept study aimed at testing the regression of lung comets along with fluids removal was based just on hemodialysis patients (12), and chest US is increasingly applied to detect and monitor pulmonary congestion in patients with chronic heart failure (9) and to grade disease severity in acute respiratory distress syndrome/acute lung injury (13).

The aim of the present study is 3-fold: 1) to estimate the feasibility of LW measurements by chest US in hemodialysis patients and to determine the prevalence of pulmonary congestion in these patients; 2) to investigate the relationship between LW, body fluids volume status, and echocardiographic parameters of cardiac performance; and 3) to study the effect of standard ultrafiltration dialysis on LW.

**METHODS**

The study protocol conformed to the Declaration of Helsinki and was approved by the local ethics committee. All patients provided informed consent. **Patients.** Between May 8 and July 7, 2009, we invited, to take part into the study, all patients undergoing chronic hemodialysis treatment and those who initiated hemodialysis during this period in the dialysis unit of our department (n = 78). Seventy-five patients (49 men and 26 women) accepted and were enrolled. Hemodialysis patients were being treated thrice weekly with standard bicarbonate dialysis by cuprophan or semisynthetic membranes. Forty-six patients were habitual smokers (17 ± 13 cigarettes/day). Sixty patients were on treatment with erythropoietin. Forty-two patients were being treated with various antihypertensive drugs (26 on monotherapy with angiotensin-converting enzyme inhibitors, calcium channel blockers, beta-blockers, angiotensin II receptor blockers, and other antihypertensive drugs) and the remaining 16 patients were on double or triple therapy with various combinations of these drugs. Patients were classified as symptomatic or asymptomatic on the basis of a slightly modified New York Heart Association (NYHA) scale (14). Total body water volume was estimated in each patient by bioelectrical impedance analysis (BIA) by using a standard apparatus (Akern BIA 101/S, Florence, Italy) and the subject’s nutritional and hydration status was interpreted in relationship to normative data in the Italian general population (15).

**Lung comets detection and lung comets score.** A standard (3.0-MHz) echocardiography probe (Toshiba Nemio XG, Toshiba, Tokyo, Japan) was used for the detection of lung comets. Examinations were performed in the supine position. Scanning of the anterior and lateral chest was performed on both sides of the chest, from the second to the fourth (on the right side to the fifth) intercostal...
spaces, at parasternal to mid-axillary lines, as previously described (8). Lung comets were recorded in each intercostal space and were defined as a hypoechoic, coherent US bundle at narrow basis going from the transducer to the limit of the screen (Fig. 1). These extended comets arise from the pleural line and should be differentiated from short comets’ artifacts that may exist in other regions. Lung comets starting from the pleural line can be either localized or scattered to the whole lung and be present as isolated or multiple artifacts (with a distance ≥7 mm between 2 artifacts). The sum of lung comets produces a score reflecting the extent of LW accumulation (0 being no detectable lung comet). More details are available in a 2-min movie on YouTube (16). On the basis of this score, we grouped patients into 3 categories of increasingly severe pulmonary congestion (mild: <14 comets; moderate: 14 to 30 comets; severe: >30 comets) as described in detail elsewhere (17). All measurements were made by an observer unaware of the result of clinical and echocardiography data.

Echocardiography. Echocardiographic measurements were obtained in each patient before and after dialysis by a standard echocardiography instrument (Toshiba Nemio XG). Details on the echocardiography protocol followed in our unit were previously described (18).

Reproducibility studies. The interobserver reproducibility of comets scoring was assessed in a set of 24 consecutive patients. One of 2 observers is an expert echocardiography technician who received specific training on chest US, and the second observer is a nephrology trainee with introductory level experience in renal US who was trained by the technician (in a 2-h practical session) to measure the lung score. The reliability of comets score over time was investigated in a series of 10 patients who maintained stable (±1 kg) body weight over 2 to 4 weeks. To test the agreement of comets scoring by different probes, these measurements were recorded in random order with the 3.5-mHz probe (a probe routinely applied for renal sonography) and the standard echocardiography (3.0-mHz) probe in a series of 21 consecutive patients and then read by a blind observer.

Statistical analysis. Data are expressed as mean ± SD, median, and interquartile range, or as percent frequency, as appropriate. Comparisons among groups were made by p value for linear trend (1-way analysis of variance or chi-square test). Among patients, comparisons were made by paired t test (normally distributed data) or by Wilcoxon signed
rank test (non-normally distributed data). Correlations between variables were investigated by Pearson product moment correlation coefficient (r), point-biserial correlation coefficient, or by Spearman rank correlation coefficient (rho), as appropriate. The agreement between continuous or discrete data was tested by the Bland-Altman method and by the concordance correlation coefficient, whereas that between categorical variables was tested by kappa statistics. Independent correlates of lung comets score were identified by multiple linear regression analysis. Significant independent correlates of lung comets score were identified by backward elimination strategy (p out: 0.10). Data are expressed as standardized regression coefficient (beta) and p value. All calculations were made using a standard statistical package (SPSS for Windows, version 9.0.1, Chicago, Illinois).

**RESULTS**

All eligible patients (n = 78) but 3 (1 patient with severe mental handicap, 2 patients that refused to take part for logistic reasons) agreed to participate in the study. Thus, 75 patients (96%) were actually enrolled. The demographic and clinical characteristics of the study population are reported in Table 1. Six patients had chronic obstructive pulmonary disease, 1 patient had a previous diagnosis of Wegener granulomatosis, and 46 were smokers. Seventy-three patients were virtually anuric (24-h diuresis, 0 to 250 ml/min), whereas the remaining patients had a 24-h urine volume ranging from 550 to 750 ml/24 h. On average, pre-dialysis arterial pressure was 138 ± 25/71 ± 12 mm Hg and post-dialysis was 124 ± 28/68 ± 13 mm Hg. Eleven patients (15%) had hypoalbuminemia (serum albumin: <3.6 g/dl) and 36 presented mild to moderate pedal edema before dialysis. Nineteen (25%) patients had a NYHA score ≥3.

**Pre-dialysis BIA.** On the basis of individual’s plot in the reactance/resistance nomogram, 24 patients (32%) were classified as “overhydrated,” 38 (51%) as at normal hydration status, and 13 (17%) as hypohydrated. Among patients with moderate to severe heart failure (NYHA functional class III to IV, n = 19), 15 (79%) were overhydrated by BIA.

**Chest US.** Chest US examinations were successfully completed in all cases (feasibility 100%). No data were rejected. The time needed for the chest US varied between 3 and 6 min (average: 4 min). Lung comets score significantly reduced (p < 0.001) after dialysis (Fig. 2). The mean and the median number of pre-dialysis lung comets (lung comets score) were 33 and 18, respectively. Lung comets score was <14 in 28 cases, 14 to 30 in 26 cases, and >30 in 21 cases.
cases. Overall, 47 of 75 patients (63%) had moderate to severe pulmonary congestion (i.e., a lung comets score ≥14) before dialysis. The score was higher in patients with symptomatic heart failure (NYHA functional class III to IV) than in patients without symptoms of heart failure, but the vast majority of asymptomatic patients (32 of 56, 57%) had a score ≥14, indicating moderate to severe pulmonary congestion. Patients with lung disease (n = 7) had a higher (median: 44, interquartile range 21 to 56 vs. median: 17, interquartile range 12 to 30) score than those without (p = 0.03).

On the basis of the pre-dialysis score, patients were divided into 3 pre-specified categories denoting increasingly severe LW accumulation (17) (no or mild: <14 comets, moderate: 14 to 30 comets, severe: >30 comets) (Table 1). Patients in the most severe category were older, more frequently smokers, with lower fractional urea clearance (Kt/V), and with NYHA functional class III to IV heart failure as compared to those in the other categories (Table 1). These associations were confirmed in correlation analyses (Table 1, last column), which also showed weak but significant relationships between lung comets and pre-dialysis systolic pressure (inverse association) and heart rate (direct association).

Lung comets score, BIA hydration status classification, and echocardiographic parameters. The lung comets score in patients identified as overhydrated by BIA (median: 20, interquartile range 13 to 57) did not significantly differ (p = 0.35) from that in patients with normal hydration status (median: 17, interquartile range 17 to 22) or that in hypohydrated patients (median: 15, interquartile range 7 to 45), and as much as 50% of the 38 patients who were normohydrated had a score indicating moderate to severe pulmonary congestion. The score was closely related to anatomical and functional echocardiographic parameters (Table 2). Indeed patients in the third lung comets category (>30 comets, severe congestion) had higher left ventricular mass index, left atrial volume, and left ventricular end-diastolic volume (LVEDV) than those in other 3 categories. Furthermore, patients in the third category displayed compromised LV systolic function as denoted by lower LV ejection fraction in comparison to other groupings. Correlation analyses substantially confirmed these categorical associations (Table 2, last column) and also revealed highly significant relationships of pre-dialysis lung comets with early left ventricular filling velocity (E), early filling to early diastolic mitral annular velocity (E/E’), pulmonary pressure, and LVEDV. The relationships between lung comets and LV ejection fraction, E/E’ ratio, and left atrial volume were the strongest among those considered in this study (Fig. 3).

In a multiple regression model including standard clinical correlates (p < 0.10) of lung comets score (age, smoking, Kt/V, systolic pressure and heart rate, and NYHA functional classification) as well as anatomical (LV mass index) and functional (ejection fraction, left atrial volume, pulmonary pressure, and E/E’ ratio) echocardiographic parameters of the left ventricle, results show only LV ejection fraction to be an independent correlate of the pre-dialysis score (beta = -0.61, p < 0.001). Forcing serum albumin into the model did not materially modify the link of the lung comets score with LV ejection fraction.

Effect of dialysis on hydration status by BIA and on lung comets. Body weight reduced from 66.7 ± 18.0 kg pre-dialysis to 64.4 ± 17.4 kg after dialysis (-3.4%, p < 0.001). After dialysis, 7 out 24 patients (29%) moved from the overhydration to the normohydration or hypohydration area. The proportion of patients with moderate to severe pulmonary congestion fell from 47 (63%) to 23 (31%). The association between the comets score and hydration
status by BIA improved after dialysis: among patients who were normohydrated after dialysis (n = 25) only 4 (16%) had a score ≥14. Importantly there was a high correlation between pre-dialysis lung comets and the reduction in this score after dialysis (Fig. 3). LVEDV fell from 116 ± 37 ml to 103 ± 32 ml after dialysis, as did left atrial volume (from 14.1 ± 4.0 ml/m².7 to 12.6 ± 3.6 ml/m².7) whereas LV ejection fraction remained unmodified (57.4 ± 9.3% vs. 57.4 ± 9.5%), denoting improved LV performance. The decrease in lung comets after dialysis was also strongly related with pre-dialysis LV ejection fraction (r = -0.55, p < 0.001), pre-dialysis E/E’ ratio (r = 0.38, p = 0.001), pre-dialysis left atrial volume (r = 0.35, p = 0.003), pre-dialysis LVEDV (r = 0.32, p = 0.006), NYHA functional class (r = 0.32, p = 0.005), pre-dialysis LV end-diastolic diameter (r = 0.31, p = 0.007), pre-dialysis LV mass index (r = 0.29, p = 0.01), pre-dialysis pulmonary pressure (r = 0.23, p =

### Table 2. Echocardiographic Data of the Study Population

<table>
<thead>
<tr>
<th>Pre-Dialysis Echocardiographic Data</th>
<th>Pre-Dialysis Lung Comets Score</th>
<th>p for Trend</th>
<th>r (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVMI, g/m².7</td>
<td>&lt;14</td>
<td>71 ± 20</td>
<td>77 ± 17</td>
</tr>
<tr>
<td>Left ventricular end-diastolic volume, ml</td>
<td>116 ± 35</td>
<td>108 ± 33</td>
<td>126 ± 41</td>
</tr>
<tr>
<td>Left atrial volume, ml/m².7</td>
<td>12.3 ± 3.6</td>
<td>14.5 ± 3.2</td>
<td>16.0 ± 4.5</td>
</tr>
<tr>
<td>Early left ventricular filling velocity, cm/s</td>
<td>0.74 ± 0.21</td>
<td>0.77 ± 0.28</td>
<td>0.81 ± 0.28</td>
</tr>
<tr>
<td>E/E’ ratio</td>
<td>7.6 ± 1.6</td>
<td>8.4 ± 3.3</td>
<td>10.9 ± 5.6</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>62 ± 4</td>
<td>59 ± 6</td>
<td>49 ± 12</td>
</tr>
<tr>
<td>Pulmonary pressure, mm Hg</td>
<td>19 ± 12</td>
<td>18 ± 14</td>
<td>26 ± 17</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD or as percent frequency, as appropriate. Bold values are statistically significant. E/E’ = early filling to early diastolic mitral annular velocity; LVMI = left ventricular mass index.

### Figure 3. Correlation Analyses of Pre- and Post-Dialysis Lung Comets Scores

Relationship between pre-dialysis comets score and pre-/post-dialysis change in the same score and pre- (pink circles) and post-dialysis (green circles) relationships of the lung comets score with left ventricular ejection fraction (LVEF), E/E’ ratio, left atrial volume (LAV), and pulmonary pressure. Solid lines indicate pre-dialysis regression lines and dashed lines indicate post-dialysis regression lines. Data are expressed as Pearson product moment correlation coefficient (r) or Spearman rank correlation coefficient (rho), as appropriate. E/E’ = early filling to early diastolic mitral annular velocity.
0.05); however, it was largely independent of the volume of fluids removed across dialysis or changes in systolic and diastolic pressures or serum albumin (p = NS). Notably the strength of the association between the post-dialysis lung comets score and LV ejection fraction (r = −0.59, p < 0.001), left atrial volume (r = 0.30, p = 0.01) and pulmonary pressure (r = 0.35, p = 0.003) was of a degree similar to that observed before dialysis (Fig. 3). In the 7 patients with pre-existing pulmonary disease, the decrease in lung comet score (from 44 [median] to 18, −59%) did not significantly differ (p = 0.09) from that in patients without pulmonary disease (from 17 to 9, −47%).

**Reproducibility studies.** The reproducibility of the lung comets score over time in 10 stable patients who maintained a pre-dialysis body weight within ±1 kg of the initial study was good in that the difference between the 2 measurements was always less than 2 SD of the average measurement (concordance index = 0.83, 95% confidence interval: 0.60 to 0.93) (Fig. 4). The agreement between the expert and the naive observer was quite satisfactory: in over 24 independent measurements, only in 2 cases did the between-observer difference exceed 2 SD, and in 1 of these cases (very high score), the difference did not modify the categorization of the severity of pulmonary congestion (severe in both cases) (Fig. 4). Equally good was the reproducibility of the comets score as measured with the echocardiography probe (3.0 mHz) and the standard renal probe (3.5 mHz) in that just in 1 case did the interprobe difference exceed 2 SD (Fig. 4).

**DISCUSSION**

Chest US is a simple, easy to perform, and quick technique that provides reproducible estimates of LW in hemodialysis patients. By this technique, LW is strikingly increased in the vast majority of symptomatic and asymptomatic ESRD patients and appears strongly associated with altered LV performance but scarcely related with hydration status before dialysis. Standard ultrafiltration dialysis markedly reduces LW and improves LV performance but fails to normalize this parameter in most cases. Overall findings in this study indicate that
chest US gives reliable information that can be potentially useful for complementing the characterization of cardiac performance and body fluids status in hemodialysis patients.

**Fluids overload and pulmonary congestion in ESRD and in heart failure.** Accumulation of fluids in the lung is the most concerning consequence of fluids overload and pulmonary congestion, and congestive heart failure is a notorious, frequent complication in ESRD (19). The risk of pulmonary congestion due to fluids overload is particularly high in the presence of compromised LV function (20). In these cases, even a minor degree of fluids excess may translate into clinical symptoms of pulmonary congestion. The joint effect of fluids excess and LV dysfunction on pulmonary water is of paramount importance in ESRD because about 30% of patients entering chronic dialysis display frank symptoms of heart failure (21) and because as much as 48% of asymptomatic patients stabilized on dialysis have compromised LV function (5). Pulmonary capillary wedge pressure, which reflects LV filling pressure, is the driving force determining fluids extravasation into the lungs, a phenomenon that only occurs after substantial fluids accumulation in patients without heart disease (22) but even in the absence of fluids retention in patients with LV failure (23).

**LW and LV function in ESRD.** Patients with ESRD accumulate water in the lungs as their extracellular volume expands (24,25). We found that chest US, a technique with a very short learning curve that can be performed by standard equipment, provides reproducible estimates with good interobserver and interprobe agreement. Importantly, our observations in an inclusive population of ESRD patients, comprising 19 (25%) with NYHA functional class III to IV heart failure, show that LW before dialysis is highly dependent on LV function but largely independent of total body water. The close, inverse association between LW and ejection fraction, both before and after dialysis, clearly points to LV dysfunction as a main driver of pulmonary congestion.

Extending observations in patients with heart failure (10), our study provides evidence that chest US captures pulmonary congestion at a pre-clinical stage in most patients. Indeed as many as 57% of asymptomatic dialysis patients had moderate to severe congestion. As in patients with heart failure, detection of LW accumulation at a pre-clinical stage in dialysis patients may represent an important clue for preventing decompensated heart failure (23).

**Study limitations.** Although we specifically tested the reproducibility of the lung comet score in dialysis patients, the precision of US LW estimates in this population remains unknown. Because the uremic lung may have an altered water permeability (22,26), the issue deserves further study in ESRD patients. Yet the problem of precision of LW estimates appears to be of greater relevance for mechanistic rather than for outcome-oriented studies.

Our study is based on the dialysis population of a single center in its entirety without any prejudicial exclusion of patients. However, larger studies aimed at assessing the prognostic value and the usefulness of chest sonography in the clinical decision process are needed to solidly establish the value of this technique in ESRD.

**CONCLUSIONS**

Chest US is a reliable technique for estimating LW in dialysis patients. Subclinical pulmonary congestion is prevalent in asymptomatic and normohydrated dialysis patients. Chest US may prove useful in clinical practice to tailor ultrafiltration and drug treatment to ESRD patients, an issue that will be investigated in specifically designed observational and interventional studies.

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