Chest ultrasound and hidden lung congestion in peritoneal dialysis patients

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Abstract

Background. Chest ultrasound (US) is a non-invasive well-validated technique for estimating extravascular lung water (LW) in patients with heart diseases and in end-stage renal disease. We systematically applied this technique to the whole peritoneal dialysis (PD) population of five dialysis units.

Methods. We studied the cross-sectional association between LW, echocardiographic parameters, clinical [pedal oedema, New York Heart Association (NYHA) class] and bioelectrical impedance analysis (BIA) markers of volume status in 88 PD patients.

Results. Moderate to severe lung congestion was evident in 41 (46%) patients. Ejection fraction was the echocardiographic parameter with the strongest independent association with LW ($r = -0.40$ $P = 0.002$). Oedema did not associate with LW on univariate and multivariate analysis. NYHA class was slightly associated with LW ($r = 0.21$ $P = 0.05$). Among patients with severe lung congestion, only 27% had pedal oedema and the majority (57%) had no dyspnoea (NYHA Class I). Similarly, the prevalence of patients with BIA, evidence of volume excess was small (11%) and not significantly different ($P = 0.79$) from that observed in patients with mild or no congestion (9%).

Conclusions. In PD patients, LW by chest US reveals moderate to severe lung congestion in a significant portion of asymptomatic patients. Intervention studies are necessary to prove the usefulness of chest US for optimizing the control of fluid excess in PD patients.

Keywords: chest ultrasound; congestive heart failure; bioelectrical impedance; lung comets; peritoneal dialysis

Introduction

Patients with kidney failure on dialysis (chronic kidney disease Stage 5-D) represent a selected population with a high burden of cardiovascular co-morbidities. The severity of cardiac involvement in kidney failure is epitomized by the fact that over three-quarters of these patients display left ventricular (LV) hypertrophy [1] and that about a half of them show clear-cut evidence of LV systolic dysfunction [2]. Preventing volume overload is highly recommended for LV dysfunction and heart failure by the American Heart Association [3], as well as in nephrology guidelines like Kidney Disease Outcomes Quality Initiative [4], and the European Best Practice guidelines for dialysis patients [5].

Notwithstanding progress in dialysis techniques, volume overload and cardiopulmonary congestion remain a major problem, particularly so in patients on peritoneal dialysis (PD) with minimal or no diuresis [6]. Chest ultrasound (US) has now emerged as a reliable technique for detecting and grading the severity of pulmonary congestion in patients suffering from heart diseases [7]. This technique allows the direct quantification of water accumulated in the lung interstitium [lung water (LW)] [7, 8], i.e. a body fluid compartment strictly dependent on pulmonary wedge pressure, the critical haemodynamic variable that dictates LV filling pressure. We have recently applied this method in haemodialysis (HD) patients [9]. Since the dynamics of fluid removal and the equilibrium between body fluid compartments are different between HD and PD [10], in this study, we applied the same technique to perform a multi-centre survey in PD patients. The aim of the present study was to investigate the relationship between LW, body volume status, dyspnoea and echocardiographic parameters of cardiac performance in the whole PD population of five nephrology units.

Materials and methods

Study population

The study protocol conformed to the Declaration of Helsinki and was approved by the local ethics committee. All patients provided informed consent.

We invited all patients of five dialysis units who were undergoing chronic PD to take part in this study (Reggio Calabria $n = 32$, Acireale $n = 25$, Catania $n = 18$, Padova $n = 9$ and Taurianova $n = 4$). Fifty-seven patients were on continuous ambulatory PD and 31 on automated PD. Dialysis prescription aimed at obtaining a total Kt/V of at least 1.8/week.
In 40 patients, one bag was an icodextrin (7.5 g/dL) solution. The median duration of PD treatment was 21 months (interquartile range 10–44 months). The median residual diuresis by 24-h urine collection was 700 mL/24 h (interquartile range 0–1200).

The cause of chronic renal disease was glomerulonephritis in 21, nephroangioklesclerosis in 17, tubulo-interstitial nephritis in 9, polycystic kidneys in 13 and unknown in 17 patients. Eleven patients had diabetic nephropathy but diabetes as a co-morbidity was present in 11 additional patients.

**LW evaluation**

LW was estimated by lung US [7]. We described in detail the technique and tested its feasibility and reproducibility in HD patients [9]. In brief, a standard (3.0 MHz) echocardiography probe is applied on specific areas of the chest (see below). In the presence of extravascular LW, the US beam finds subpleural interlobular septa thickened by oedema. The reflection of the beam generates comet-tail reverberation artifacts, called B-lines or US lung comets. US scanning of the anterior and lateral chest is obtained on the right and left hemithorax, from the second to the fourth (on the right side to the fifth) intercostal spaces and from the parasternal to the axillary line. The sum of lung comets observed in these areas produces a score reflecting the extent of LW accumulation (zero being no detectable lung comet) (Figure 1). The severity of lung congestion was categorized according to pre-set thresholds into three classes, as described elsewhere [9], and patients with a lung comets score between 15 and 30 and those with a score > 30 were considered as having moderate and severe lung congestion, respectively.

One operator was responsible for lung comets determination in each of the four largest centres. Patients of the smallest centre (n = 4 patients) were evaluated in the reference laboratory in Reggio Calabria. As described elsewhere in detail [9], the inter-operator reproducibility of lung comets determination is excellent. The sonographers of the nephrology units participating into this study were preliminarily trained at CNR-IIBM, Reggio Calabria, and the agreement of lung comets measurements between them and the trainer sonographer was confirmed to be excellent.

**New York Heart Association score**

Patients were stratified into four classes of dyspnoea according to the New York Heart Association (NYHA) classification. Categories of increasing severity in the NYHA classification show a progressively higher mortality risk in dialysis patients [11]. Furthermore, we documented a fairly good agreement between independent assessors in the same population [11].

**Echocardiographic evaluation and volume status assessment**

Sixty-one patients in the five units underwent echocardiography and volume status assessment by bioelectrical impedance analysis (BIA). Echocardiographic measurements were obtained for each patient at empty abdomen by standard echocardiography instruments. Details on the echocardiography protocol followed in our unit were previously described [12].

LV ejection fraction was obtained according to the standard Simpson formula. Diastolic function (E/E′ ratio) was obtained using tissue Doppler [13].

BIA was performed using a standard apparatus (Akern BIA/101S; Florence, Italy) and subjects’ hydration status was interpreted in relation to normative data in the Italian PD population [14].

Estimation of pedal oedema was performed by clinicians of the participating centres who were not informed of the echocardiogram and BIA results. Oedema was classified as present/absent but no attempt at sub-categorization was made.

**Laboratory methods**

Biochemical parameters were determined by routine auto-analyser methods in each centre.

**Statistical analysis**

Data are presented as mean ± SD, median and inter-quartile range or as per cent frequency and comparison between groups were made by t-test, Mann–Whitney test or chi-squared test, as appropriate. Variables which were not normally distributed were log transformed. The independent association between lung comets, clinical and laboratory variables was analysed by simple and multiple linear regression analyses. In multiple regression analyses, we entered the univariate predictors of lung comets score (P < 0.1) (i.e. NYHA class, systolic pressure, ejection fraction, left atrial volume) as well as residual diuresis and oedema, which were unrelated to lung comets score at crude analysis. We forced these variables into the final model because they are commonly held as clinical markers of volume overload. We did so because even if not significantly associated to the outcome variable, residual diuresis and oedema can modify the effect of other independent predictors on the same outcome.

All calculations were made using a standard statistical package (SPSS for Windows).

**Results**

On the basis of the pre-established thresholds [9], lung congestion was classified as severe (>30 lung comets) in 21 patients (24%), moderate (15–30 lung comets) in 20 (23%) and mild to absent (<15 lung comets) in the remaining 47 (53%) patients (Table 1 Figure 2). Table 1 shows the main baseline characteristics of the patients divided into these three groups. Categorical analysis

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**Fig. 1.** Left panel: asymptomatic patient with absence of comets. Central panel: one lung comet. Right panel: patient with severe LW accumulation as evidenced by the high number of lung comets.
showed that systolic pressure was lower in patients with moderate to severe lung congestion compared to those with mild or no congestion (Table 1). The proportion of patients on any type of anti-hypertensive therapy was not significantly different in the three groups as was the proportion of those on diuretics, angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers. Patients with moderate or severe congestion were treated with a similar number of anti-hypertensive drugs than those with mild or no congestion (Table 1).

The relationship between lung congestion by chest US and symptoms of dyspnoea as defined by NYHA are shown in Figure 2 and Table 1.

On χ² analysis, NYHA categories were not different among the three classes of lung congestion (P = 0.57). However, when the same variable was analysed in a regression analysis, it was weakly associated with lung comets score ($r = 0.21; P = 0.05$).

The majority of patients with evidence of moderate (60%) to severe lung congestion (57%) were asymptomatic (NYHA Class I) (Figure 2, Table 1). The proportion of patients on any type of anti-hypertensive therapy was not significantly different in the three groups as was the proportion of those on diuretics, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers. Patients with moderate or severe congestion were treated with a similar number of anti-hypertensive drugs than those with mild or no congestion (Table 1).

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The majority of patients with evidence of moderate (60%) to severe lung congestion (57%) were asymptomatic (NYHA Class I) (Figure 2, Table 1). The proportion of patients with peripheral oedema, that of anuric patients, and residual diuresis was similar among the three groups of lung congestion (Table 1) and these variables were not associated (P > 0.1) with lung comets score on regression analysis.

On multiple regression analysis (Table 2), NYHA class and residual diuresis were the sole independent predictors of lung congestion. Both NYHA class and residual diuresis were directly associated with lung congestion (Table 2).

In the 61 patients who underwent echocardiographic evaluation, ejection fraction and left atrial volume resulted in...
in the echocardiographic parameters with the strongest association with lung comets score. The association was inverse for ejection fraction and direct for left atrial volume (Table 3, Figure 3, Figure 4). Among those patients with moderate and severe lung congestion, only 15 and 11%, respectively, had BIA evidence of volume excess and this proportion was not significantly different (P = 0.79) from that observed in patients with mild or no congestion (9%). In a multiple regression analysis including systolic blood pressure, NYHA class, oedema, residual diuresis, left atrial volume and ejection fraction (Table 4), only ejection fraction (standardized β = −0.36, P = 0.007) and left atrial volume (standardized β = 0.29, P = 0.05) were strong and independent predictors of LW.

Discussion

This study shows that estimation of LW by chest US allows the identification of a substantial proportion of PD patients with moderate to severe lung congestion with no symptoms or signs of fluid excess.

In patients with heart disease, chest US closely reflects direct invasive measurement of extravascular LW [7, 8] and we have previously validated this method in HD patients [9]. However, due to differences in ultrafiltration potential and tolerability, observations in HD patients cannot be extrapolated to PD. Therefore, we performed a survey applying lung US to the whole population of five dialysis units.

Table 2. Multiple regression analysis of lung comets scorea

<table>
<thead>
<tr>
<th></th>
<th>β</th>
<th>P</th>
</tr>
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<tbody>
<tr>
<td>NYHA class</td>
<td>0.31</td>
<td>0.006</td>
</tr>
<tr>
<td>Residual diuresis</td>
<td>0.30</td>
<td>0.006</td>
</tr>
<tr>
<td>Systolic arterial pressure</td>
<td>−0.16</td>
<td>0.12</td>
</tr>
<tr>
<td>Oedema</td>
<td>−0.11</td>
<td>0.31</td>
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aData are expressed as standardized regression coefficient (β) and P-value. Significant correlations are indicated in bold.

The present survey shows that the PD population has a high risk of lung congestion. In fact, 46% of patients had moderate to severe lung congestion. Notably, among the simple clinical markers of fluid overload, pedal oedema was not associated with lung congestion, while NYHA class, despite being associated with LW, was not helpful in identifying patients with moderate to even severe lung congestion. Indeed, the vast majority of patients with these levels of lung congestion were asymptomatic (NYHA Class I). We also observed that residual diuresis, which is a key prognostic marker in PD patients, on multivariate analysis was directly associated with LW. We believe that the direct association between residual diuresis and lung congestion merely reflects the fact that volume expansion stimulates pressure/volume diuresis. This functional link might explain why pulmonary congestion (an alteration in part reflecting volume expansion) goes in parallel with urine output. Due to the cross-sectional nature of the study, the latter explanation remains hypothetical.

The main finding of our study, which confirms previous observations in HD patients [9], was the strong association of lung congestion with ejection fraction and left atrial volume. This association was independent of clinical markers of volume excess and other potential founders. This observation further emphasizes the fact that LW reflects pulmonary wedge pressure and is determined not only by volume status but also by LV function.

In line with the association between LW and ejection fraction, we also found that systolic blood pressure tended to be lower in those patients with more severe LW accumulation, likely reflecting a more compromised pump function since the use of anti-hypertensive drugs was not enhanced in these patients.

Our study has limitations. Firstly, the sample size was relatively small. Secondly, the cross-sectional design prevents us from making conclusions about the clinical usefulness of LW measurements. Thirdly, we did not collect data on the peritoneal permeability, which is a key factor influencing volume status in PD patients.

In conclusion, this study shows that PD patients may present substantial LW accumulation in the absence of dyspnoea and obvious clinical evidence of volume excess.

Table 3. Lung comets score versus echocardiographic parametersa

<table>
<thead>
<tr>
<th>Lung comets score</th>
<th>&lt;15 (n = 36)</th>
<th>15–30 (n = 14)</th>
<th>&gt;30 (n = 11)</th>
<th>P</th>
<th>r (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVMI (g/m²)</td>
<td>59 ± 20</td>
<td>50 ± 23</td>
<td>63 ± 22</td>
<td>0.58</td>
<td>0.10 (0.44)</td>
</tr>
<tr>
<td>LV end-diastolic volume (mL)</td>
<td>107 ± 28</td>
<td>110 ± 62</td>
<td>118 ± 42</td>
<td>0.45</td>
<td>0.11 (0.41)</td>
</tr>
<tr>
<td>Left atrial diameter (mm)</td>
<td>36 ± 7</td>
<td>36 ± 8</td>
<td>41 ± 7</td>
<td>0.05</td>
<td>0.25 (0.07)</td>
</tr>
<tr>
<td>Left atrial volume (mL)</td>
<td>42 ± 16</td>
<td>44 ± 19</td>
<td>60 ± 26</td>
<td>0.008</td>
<td>0.30 (0.02)</td>
</tr>
<tr>
<td>Left atrial volume/height²</td>
<td>12 ± 5</td>
<td>11 ± 4</td>
<td>16 ± 8</td>
<td>0.02</td>
<td>0.29 (0.02)</td>
</tr>
<tr>
<td>Early LV filling velocity (cm/sec)</td>
<td>59 ± 17</td>
<td>61 ± 22</td>
<td>63 ± 15</td>
<td>0.53</td>
<td>0.11 (0.40)</td>
</tr>
<tr>
<td>E/A ratio</td>
<td>0.71 ± 0.32</td>
<td>0.74 ± 0.33</td>
<td>0.85 ± 0.35</td>
<td>0.26</td>
<td>0.18 (0.18)</td>
</tr>
<tr>
<td>E/E’ ratio</td>
<td>7.6 ± 3.1</td>
<td>8.1 ± 3.6</td>
<td>7.8 ± 2.9</td>
<td>0.85</td>
<td>0.13 (0.34)</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>61 ± 8</td>
<td>56 ± 15</td>
<td>53 ± 12</td>
<td>0.05</td>
<td>−0.40 (0.002)</td>
</tr>
<tr>
<td>Hyperhydration status (BIA) (%)</td>
<td>9 ± 15</td>
<td>15 ± 11</td>
<td>79 ± 0.72</td>
<td>0.02</td>
<td>0.87</td>
</tr>
</tbody>
</table>

aLVMI, left ventricular mass index; E/A, early to atrial filling velocity; E/E’, early filling to early diastolic mitral annular velocity. P tests the differences among the groups. r is the Pearson coefficient of correlation between lung comets score and the variables. Significant differences between groups and significant correlations are indicated in bold.
Chest ultrasound in PD

Chest ultrasound (US) is a promising technique with potential for refining volume control in PD patients. Our observations form a rational basis for designing a clinical trial aimed at testing the usefulness of lung US for prevention and treatment of cardiopulmonary congestion in PD patients.

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Ethics Committee: the study protocol conformed to the Declaration of Helsinki and was approved by the local ethics committee. All patients provided informed consent.

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References


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