Drainage of Large Pleural Effusions Increases Left Ventricular Preload

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**Objectives:** The aim of the study was to investigate if pleurocentesis in patients with pleural effusion would lead to changes in systolic and diastolic function of the left ventricle.

**Design:** The study was descriptive, and patients were their own controls.

**Setting:** The setting was a single-center university hospital.

**Participants:** Patients with pleural effusion requiring pleurocentesis were eligible for inclusion.

**Interventions:** The participants who had pleurocentesis performed were available for analysis.

**Measurements and Main Results:** Prior to pleurocentesis and approximately 1 hour after, patients were examined primarily with transthoracic echocardiography. The examination included measurements of left ventricular volumes and measures of diastolic function assessed by Doppler echocardiography. Thirty-five patients were included, and 11 later were excluded, yielding a study population of 24. Preload, expressed as left ventricular end-diastolic volume, increased significantly from before to after pleurocentesis (p = 0.014). None of the diastolic parameters showed significant results. Significant changes were observed for heart rate, supplementary O₂, respiratory frequency, and saturation.

**Conclusions:** Pleurocentesis increased left ventricular preload and improved respiratory function. © 2014 Elsevier Inc. All rights reserved.

**KEY WORDS:** pleural effusions, drainage, preload, left ventricular, pleurocentesis, echocardiography, hemodynamics

PLEURAL EFFUSION (PLE) is a frequent complication in various patient populations, often leading to impaired respiratory function.¹ ² Previous reports indicated that PLE can cause hemodynamic compromise through a mechanism resembling cardiac tamponade.³ ⁵ Despite this, detailed knowledge about the hemodynamic effects of PLE is still sparse.

PLEs are located in close proximity to the heart and pulmonary vessels and may directly or indirectly influence these structures by increasing the external pressure. The possible effects are numerous and include increased right ventricular afterload if pulmonary vessels are compressed and decreased preload as the right and left ventricular transmural pressure (defined as intraventricular pressure minus intrapleural pressure pressures) decreases due to increased external pressure on cardiac structures from increased intrapleural pressure.⁶ The individual contributing factors are difficult to single out and require description of the basic hemodynamic determinants of circulatory function. Echocardiography and dynamic cardiac magnetic resonance imaging are the only noninvasive methods providing thorough knowledge about these fundamental physiologic parameters with the possibility of measuring at the bedside with echocardiography. The current study was the first to systematically address the changes in basic hemodynamic determinants induced by pleurocentesis in human subjects. The authors hypothesised that pleurocentesis in patients with PLE would lead to changes in systolic and diastolic function of the left ventricle. This study investigated the effects of pleurocentesis on left ventricular preload, systolic function, and filling patterns using echocardiography.

**METHODS**

The study was approved by the local Committee on Biomedical Research Ethics and conducted in agreement with the Helsinki II declaration. Written informed consent was obtained from all participants.

Patients (age ≥ 18) with suspected PLE who were referred for pleurocentesis were eligible for inclusion. The PLE was suspected by the clinical staff on various clinical indications, such as dyspnea and abnormal chest X-rays, and confirmed by ultrasonography at the Department of Medical Imaging. Exclusion criteria were suspected empyema and positive-pressure ventilation. Patients received standard treatment according to hospital guidelines; however, no fluid was administered to the patients between the measurements.

Transthoracic echocardiography was performed prior to pleurocentesis and approximately 1 hour after. Arterial blood pressure, respiratory rate, arterial oxygen saturation, and oxygen supply were measured. In addition, the degree of dyspnea was quantified. The volume of the drained effusion was measured at the time of the second echocardiogram. The primary endpoint was change in left ventricular end-diastolic volume (LVEDV) from before to after pleurocentesis. The authors measured the time from the first echocardiogram to insertion of the pleural drain and the time from insertion of the pleural drain to the second echocardiogram.

All echocardiographic data were collected by 3 experienced examiners using a Vivid E9 echocardiography system equipped with M5S cardiac probe or Vivid S6/Q with an M4S cardiac probe (GE Healthcare, Horten, Norway). Each patient was examined by the same operator and using the same system before and after pleurocentesis.

Echocardiography was performed with the patient in the left lateral position at end-expiration. Recordings were focused on the left ventricle and obtained in the apical 4-chamber view, apical 5-chamber view, apical 2-chamber view, and parasagittal long-axis view. Three ECG-triggered cine-loops from each view were stored for offline analysis.

Peripheral saturation was measured using peripheral pulse oximetry. Supplementary O₂ supply was measured as the O₂ volume/min that was distributed by the oxygen outlet. The ward staff managed O₂ supply according to their standard operational procedure, which is guided by the oximetry measurements and a clinical assessment. Dyspnea was quantified using a validated 10-point visual analog scale (VAS) with 0 being the lowest degree of breathlessness and 10 the highest.⁷ ⁸
An investigator blinded from patient data performed the echocardiographic analyses using commercially available software (Echopac, GE Healthcare, Horten, Norway). All measurements were repeated by a second observer to assess interobserver variability.

LVEDV and left ventricular end-systolic volumes (LVESV) were measured from the apical 4-chamber recordings using the methods of discs at end-diastole when the left ventricular chamber size is at its largest and at end-systole when ventricular chamber size is at its minimum. Ejection fraction (EF) was calculated as the difference between LVEDV and LVESV divided by LVEDV.

In the case of pericardial effusion, this was quantified as the greatest dimension of echo-free space between the 2 pericardial layers.

Stroke volume (SV) and cardiac output (CO) were calculated as follows: The velocity time integral (VTI) of the left ventricular outflow tract (LVOT) was traced manually from pulsed Doppler recordings of the 5-chamber view. The LVOT cross-sectional area was calculated from diameter measurements obtained in the parasternal long-axis view, and the SV was calculated by multiplication of VTI and LVOT cross-sectional area. Heart rate (HR) of the ECG of the pulsed Doppler 5-chamber recording was multiplied with SV for calculation of CO.

Early and atrial transmitral peak flow velocities (E and A) were analyzed from 4-chamber pulsed Doppler recordings. Early atrial and systolic peak velocities of the medial and lateral mitral annulus (e’, a’, and s’) were measured from the tissue Doppler 4-chamber view.

Calculations were performed on all patients pooled and also on subgroups based on the volume of PLE; ie, a subgroup with the largest volume of drained PLE and a subgroup with the smallest volume of drained PLE. This was done in order to assess the relationship between the size of PLE and the effects of pleurocentesis.

The lack of studies addressing the effects of pleurocentesis on LVEDV precluded meaningful sample size calculation. Instead, the authors chose a sample size of 20 based on a previous study with a similar design. A paired student’s t-test was performed to test differences between before and after pleurocentesis. Correlations were calculated as Pearson’s correlation coefficient. Normality was inspected visually from histograms and Q-Q plots. Body surface area was calculated from the formula of Dubois & Dubois. Results are presented as mean ± standard deviation unless otherwise stated. Only p values < 0.05 were considered significant. Interobserver bias was calculated as the mean difference in readings divided by the mean, expressed as a percentage and presented as mean bias with corresponding 95% confidence intervals (CI). Calculations were made using STATA (StataCorp LP, College Station, TX).

RESULTS

Thirty-five patients were enrolled; 11 later were excluded due to no pleurocentesis performed (n = 6), empyema (n = 1), patient request (n = 2), conversion from atrial fibrillation to sinus rhythm from before to after pleurocentesis (as rhythm conversion in itself changes the hemodynamics greatly) (n = 1), and logistical reason (pleurocentesis was delayed severely, caused unavailability of echocardiography staff) (n = 1). Thus, 24 patients (17 males) completed the study. The average age was 67.1 ± 12.7 years, average height was 175 ± 9 cm, and average weight was 72 ± 15 kg. The distribution of drained PLE was left (n = 11), right (n = 9), and bilateral (n = 4). The cause of PLE in the patients was sternotomy (n = 19), idiopathic (n = 2), cancer (n = 2), and heart failure (n = 1). The median time between the first echocardiogram and pleurocentesis was 120 minutes (range 50-270 minutes), and the median time between pleurocentesis and the second echocardiogram was 70 minutes (range 55-165 minutes). None of the patients were hemodynamically unstable before or after pleurocentesis, assessed as a systolic pressure below 90 mmHg or need for inotropes or vasoconstrictors. None of the patients had a concomitant pericardial effusion of more than 5 mm. Twelve patients received supplementary oxygen.

Table 1 presents the data on all patients (n = 24) and division of patients into separate subgroups of the largest (n = 12) and the smallest (n = 12) amount of drained PLE. Six patients (2 from the subgroup of the largest drained PLE) had no atrial component in the diastolic measures (A, E/A, a’, e’a’) before and after pleurocentesis, and these measurements were made on the remaining 18 patients.

Pleurocentesis increased LVEDV significantly both overall (p = 0.014) and in the patients with the largest amount of drained PLE (p = 0.004). Figure 1 depicts the correlation between increase in LVEDV and the amount of drained PLE. SV increased significantly for all patients pooled (p = 0.009) and for patients with the largest drained PLE (p = 0.012). None of the diastolic parameters reached statistical significance.

Significant changes were also observed for HR, supplementary O2 supply, RF, saturation, and VAS for all patients (Table 1).

Interobserver variability was 6.0% (95% CI 1.9%; 10.1) for volumes (LVEDV and LVESV), −5.2% (95% CI −7.1%; −3.3%) for tissue Doppler measurements (e’, a’, and s’), 5.4% (95% CI 3.2%; 7.6%) for transmitral flow values (E, A), and −7.9% (95% CI 12.2%; −3.6%) for VTI. The overall interobserver variability was −1.7% (95% CI −3.4%; 0.3%).

DISCUSSION

This study showed that drainage of large PLE led to an increase in LVEDV. In addition, an increase in SV and a decrease in HR were observed while CO remained unchanged. Although the patients studied were not critically ill, a significant improvement to the hemodynamic status was observed along with substantial improvements in all measures of respiratory function due to pleurocentesis.

It previously has been reported that rapid removal of large PLEs may cause relative hypovolemia due to fluid redistribution to the pleural cavity. None of the patients in this study experienced hemodynamic collapse as a consequence of pleurocentesis.

The observations in this study were most evident when dividing the patients into the largest and smallest amount of drained PLE, as the patients with the largest amount experienced the most significant improvements. This is in line with a previous report suggesting that the volume of PLE is decisive for the hemodynamic effects. Vaska et al examined PLE in dogs by infusing saline into the pleural spaces, resulting in increased intrapericardial pressure leading to tamponade-like pathophysiology. The increased intrapericardial pressure may be transmitted to the pericardial space or the pulmonary vessels, resulting in impaired cardiac filling and reduced stroke volume. This is in line with the observed changes in this study. Three mechanisms may explain the observed changes.

Firstly, external compression of the heart from accumulating PLE decreases right ventricular (RV) transmural pressure. This
has been reported in a porcine model as decreased transmural CVP, a surrogate measure for right-sided transmural pressure with incremental volumes of PLE. The same mechanism is responsible for the occurrence of right atrial collapse as a consequence of PLE reported by Sadaniantz. A fall in right-sided transmural pressure gives rise to decreased RV end-diastolic volume, and, thus, decreased RV preload.

Consequently, the SV of the RV falls, and this effect is transmitted to the LV a few beats later.

Secondly, the observed changes may be the result of increased RV afterload as a result of direct compression of the pulmonary vessels or indirectly by increased pressure on the lung and, subsequently, the small pulmonary vessels. Increases in pulmonary artery resistance and pulmonary wedge pressure previously have been reported as a consequence of PLE. Increased RV afterload attenuates LV preload.

Thirdly, PLE may facilitate a decrease in LV transmural pressure with a concomitant lower LV preload. Ahmed et al reported that pleurocentesis in ICU patients with PLE decreases pulmonary capillary wedge pressure (PCWP), a surrogate measure of LV end-diastolic pressure. Thus, pleurocentesis may have decreased the absolute LV filling pressure.

LVEDV is a reliable and precise measure of LV preload, and the authors observed that LVEDV increased in the group with the largest drained PLE and not in the group with the smallest PLE. This indicated that the effect of pleurocentesis on preload depends on the volume of the PLE. In addition, Figure 1 shows a dose-response relationship between size of PLE and changes in LVEDV. This was in accordance with a previous study in which incremental volumes of PLE caused significant decrease of LV preload in a porcine model along with a decrease in cardiac output, stroke volume, MAP, and mixed venous saturation. Concomitantly, central venous pressure and pulmonary artery pressure

**Table 1. Results**

<table>
<thead>
<tr>
<th></th>
<th>All patients (n = 24)</th>
<th>Largest drained PLE (n = 12)</th>
<th>Smallest drained PLE (n = 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T1 (± SD)</td>
<td>T2 (± SD)</td>
<td>p value</td>
</tr>
<tr>
<td></td>
<td>T1 (± SD)</td>
<td>T2 (± SD)</td>
<td>p value</td>
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<tr>
<td></td>
<td>T1 (± SD)</td>
<td>T2 (± SD)</td>
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<tr>
<td>Echocardiographic measures</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>LVEDV (mL)</td>
<td>99.2 ± 23.1</td>
<td>102.8 ± 22.3</td>
<td>0.014</td>
</tr>
<tr>
<td>LVEDV/BSA (mL/m²)</td>
<td>52.7 ± 11.0</td>
<td>54.8 ± 10.7</td>
<td>0.012</td>
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<tr>
<td>LVE SV</td>
<td>49.6 ± 14.5</td>
<td>49.5 ± 15.3</td>
<td>0.056</td>
</tr>
<tr>
<td>LVE SV/BSA (mL/m²)</td>
<td>26.4 ± 7.3</td>
<td>26.3 ± 7.2</td>
<td>0.946</td>
</tr>
<tr>
<td>SV (mL)</td>
<td>69.4 ± 12.9</td>
<td>73.2 ± 12.5</td>
<td>0.009</td>
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<tr>
<td>CO (L/min)</td>
<td>6.01 ± 1.80</td>
<td>5.95 ± 1.64</td>
<td>0.659</td>
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<tr>
<td>EF (%)</td>
<td>50.1 ± 7.6</td>
<td>52.4 ± 7.2</td>
<td>0.198</td>
</tr>
<tr>
<td>E (m/s)</td>
<td>0.94 ± 0.27</td>
<td>0.91 ± 0.31</td>
<td>0.263</td>
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<tr>
<td>A (m/s)</td>
<td>0.77 ± 0.29</td>
<td>0.72 ± 0.26</td>
<td>0.308</td>
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<tr>
<td>E/A</td>
<td>1.32 ± 0.61</td>
<td>1.37 ± 0.73</td>
<td>0.419</td>
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<tr>
<td>s' (cm/s)</td>
<td>8.6 ± 3.1</td>
<td>8.8 ± 2.9</td>
<td>0.660</td>
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<tr>
<td>e' (cm/s)</td>
<td>8.5 ± 1.9</td>
<td>8.6 ± 2.0</td>
<td>0.832</td>
</tr>
<tr>
<td>a' (cm/s)</td>
<td>9.5 ± 3.7</td>
<td>9.2 ± 4.2</td>
<td>0.313</td>
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<tr>
<td>E/e'</td>
<td>11.9 ± 5.2</td>
<td>11.6 ± 6.0</td>
<td>0.506</td>
</tr>
<tr>
<td>e'/a'</td>
<td>0.91 ± 0.42</td>
<td>1.07 ± 0.56</td>
<td>0.087</td>
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<tr>
<td>Other measurements</td>
<td></td>
<td></td>
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<tr>
<td>HR (min⁻¹)</td>
<td>85.3 ± 14.4</td>
<td>81.0 ± 14.8</td>
<td>0.003</td>
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<tr>
<td>MAP (mmHg)</td>
<td>87.3 ± 13.9</td>
<td>90.0 ± 11.2</td>
<td>0.300</td>
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<tr>
<td>O₂ (L/min)</td>
<td>1.7 ± 2.1</td>
<td>1.4 ± 1.6</td>
<td>0.044</td>
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<tr>
<td>RF (min⁻¹)</td>
<td>21.4 ± 4.1</td>
<td>19.4 ± 2.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sat (%)</td>
<td>95 ± 2</td>
<td>96 ± 2</td>
<td>0.002</td>
</tr>
<tr>
<td>VAS</td>
<td>3.3 ± 2.3</td>
<td>1.4 ± 1.3</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Abbreviations: A, atrial mitral inflow velocity; BSA, body surface area; CO, cardiac output; EF, ejection fraction, E, early mitral inflow velocity; HR, heart rate; LVEDV, left ventricular end-diastolic volume; LVE SV, left ventricular end-systolic volume; MAP, mean arterial pressure; O₂, supplementary oxygen volume; RF, respiratory frequency; SD, standard deviation; SV, stroke volume; Sat, saturation; VAS, visual analog scale; a', atrial mitral annular velocity; e', early mitral annular velocity; s', systolic mitral annular velocity.

* p value < 0.05.

Fig 1. Correlation between the increase in left ventricular end-diastolic volume from before to after pleurocentesis and the volume of effusion drained. Pearson correlation = 0.58, p = 0.003.
increased, although it should be emphasized that the volumes of PLE were much greater (up to 75mL/kg) than in the authors’ study. In addition, a recently published human case report supports the authors’ hypothesis and the presented data on the effect of PLE on LV preload.17

SV increased significantly after pleurocentesis similar to LVEDV; ie, the patients with the largest drained PLE improved significantly (Table 1). This finding is consistent with the Frank-Starling law of the heart, which is increased preload resulting in increased stroke volume in preload-responsive individuals. However, CO did not change, which may reflect that the patients were able to produce an adequate CO before pleurocentesis and, therefore, lowered HR when SV was increased.

EF did not change significantly in this study. Given the way EF is calculated, an increase in LVEDV, with the difference between LVEDV and LVESV being constant, would tend to decrease EF. EF did not change as the increased preload caused a greater SV.

The ratio of early mitral inflow velocity to early mitral annular velocity of the left ventricle, E/e’, previously has been shown to correlate with left ventricular filling pressures during sinus rhythm18,19 and atrial fibrillation20 and is useful in patients with normal ejection fraction.21 E/e’ did not change despite a small but significant increase in LVEDV. This potentiates previous concerns that E/e’ may be insensitive to rapid intra-individual changes in LV preload,22,23 especially in the setting of normal diastolic function. Some of the patients in the current study had normal diastolic function expressed by an E/e’ ≤8; in these patients, a linear relationship between filling pressure and E/e’ may not exist.

The results of this study suggested that pleurocentesis can be part of hemodynamic optimization in patients with moderate-to-large pleural effusions. Therefore, evaluation of the pleural cavity may be beneficial as an integral part of patient evaluation, especially in settings of respiratory or circulatory instability in which preload improvement is pivotal for hemodynamic stability.

In addition to the hemodynamic measurements, the authors observed that oxygen saturation, supplementary oxygen supply, and respiratory frequency improved significantly after pleurocentesis. Along with these results, the significant improvements in VAS for dyspnea showed that the patients in this study experienced improvements in their respiratory function, underlining the beneficial therapeutic and subjective effects of pleurocentesis. However, the authors did not find that the results of this study changed the indication for performing pleurocentesis. In addition, the beneficial effects of pleurocentesis always should be weighed against potential risks, eg, hemorrhage and infection.

This study only investigated acute changes of pleurocentesis. It is possible that the observed changes may have been amplified at a later stage of recovery with further lung expansion, re-opening of collapsed alveoli, and subsequent reduction in right ventricular afterload. This may have yielded even more pronounced beneficial changes of pleurocentesis. However, it is also possible that subsequent re-accumulation of PLE would diminish the observed changes in preload.

LVEDV and LVESV were derived from 4-chamber recordings, as this was the only view available for such an analysis. However, as the authors looked at intradividual changes rather than absolute volume measures, this did not influence the results.

The patients in this study were not critically ill, and the observed changes cannot readily be transferred to this population. Critically ill are, however, often subject to positive-pressure ventilation, which has similar effects on transmural pressures and, therefore, potentially aggravates the effects of PLE.24 Pleurocentesis of large PLEs increases left ventricular preload and improves respiratory function.

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