Patient With Bilateral Pleural Effusion*

Are the Findings the Same in Each Fluid?

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Study objectives: To determine whether, in patients with bilateral pleural effusions, the main cellular and biochemical features of the pleural fluid on the right side differ from or correlate with those on the left side. We examined lactate dehydrogenase (LDH), glucose, and total protein (TP) levels, RBC count, nucleated cell count (NCC), and differential cell count.

Patients and methods: Twenty-seven patients with bilateral pleural effusions, including 13 patients with effusions after coronary artery bypass graft surgery, 12 patients with congestive heart failure, 1 patient with malignant pericarditis, and 1 patient with renal failure, were studied retrospectively.

Results: The right-sided and the left-sided pleural effusions did not differ in the mean TP (p = 0.38), glucose (p = 0.31), and LDH (p = 0.39) levels, RBC count (p = 0.31), NCC (p = 0.96), and the percentage of neutrophils (p = 0.22), lymphocytes (p = 0.73), mononuclear cells (MNCs) (p = 0.49), and eosinophils (p = 0.65). The bias ± precision was 0.1 ± 0.64 g/dL for TP, 2.7 ± 23 mg/dL for glucose, 41 ± 362 IU/L for LDH, 6,100 ± 62,900 cells/µL for RBC count, 36 ± 1,043 cells/µL for NCC, 2.9 ± 11.6% for the percentage of neutrophils, 1.15 ± 17% for the percentage of lymphocytes, 2.3 ± 17% for the percentage of the MNCs, and 0.15 ± 5.4% for the percentage of eosinophils. Moreover, there was a close correlation between the right-sided and the left-sided pleural effusions concerning TP level (r = 0.85, p < 0.001), glucose level (r = 0.78, p < 0.001), LDH level (r = 0.71, p < 0.001), RBC count (r = 0.66, p < 0.001), NCC (r = 0.60, p = 0.001), and the percentage of neutrophils (r = 0.77, p < 0.001), lymphocytes (r = 0.77, p < 0.001), MNCs (r = 0.74, p < 0.001), and eosinophils (r = 0.84, p < 0.001).

Conclusion: Since the pleural fluid findings tend to be similar in both sides of patients with bilateral pleural effusion, we suggest that diagnostic thoracentesis may not need to be performed on both sides, unless there is a specific clinical indication. (CHEST 2003; 124:167-176)

Key words: bilateral; glucose; lactate dehydrogenase; nucleated cell count; pleural effusion; protein; thoracentesis

Abbreviations: CABG = coronary artery bypass graft; LDH = lactate dehydrogenase; MNC = mononuclear cell; NCC = nucleated cell count; TP = total protein

Simultaneous accumulation of pleural fluid in both pleural cavities may occur in a variety of diseases. By far, the most frequent cause is congestive heart failure.1 The etiologic spectrum of bilateral pleural effusion also includes metastatic malignant pleural disease,2 lupus pleuritis,3 rheumatoid pleuritis,4 post-coronary artery bypass graft (CABG) pleural disease,5 benign asbestos pleural disease,6 pulmonary infections,7 drug-induced pleuritis,8 renal failure,9 pericardial disease,10 pulmonary embolism,11 or even tuberculous pleuritis.12 Even though bilateral pleural effusion is fairly common in clinical practice, the relationship between the main pleural fluid characteristics in the right and left side has not been previously examined. Thus, it is not known if the fluid that accumulates in the one hemithorax has different characteristics than the fluid in the other hemithorax. Accordingly, it is not clear if a diagnostic thoracentesis should be performed on both sides, or if a unilateral thoracentesis would be sufficient.

We conducted a retrospective study to determine

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CHEST / 124 / 1 / JULY, 2003 167

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whether, in patients with bilateral pleural effusions, the main pleural fluid cellular and biochemical features differ between the right and the left side. For this purpose, we compared the lactate dehydrogenase (LDH), total protein (TP), and glucose levels, as well as the RBC count, nucleated cell count (NCC), and the differential cell count on the right and left sides. We hypothesized that there would be no significant difference between the pleural fluid cellular and biochemical features on the right and left sides.

Materials and Methods

Saint Thomas Hospital is a tertiary-care medical center. Since September 1, 1997, we have maintained a database on all patients who undergo ultrasonically guided thoracentesis and who signed an informed consent approved by the Institutional Review Board. Every patient (both outpatients and inpatients) who undergoes ultrasound-assisted thoracentesis in Saint Thomas Hospital and signs the consent form is prospectively entered. We conducted a retrospective pilot study to examine whether, in patients with bilateral pleural effusions, the main pleural fluid features differ between the right and the left side. We searched this database that contains clinical and laboratory data for 1,312 pleural fluids for patients who underwent bilateral thoracentesis on the same day. The decision to perform the thoracentesis (unilateral or bilateral) was made by the patient’s primary care physician. Some patients who underwent bilateral thoracentesis at our hospital may have not been included in the study because they did not sign a consent form or did not undergo thoracentesis in the ultrasound laboratory. The etiology of the pleural effusion; the LDH level (Fig 2) and higher TP level (Fig 1) on the right side coexisted with a lower glucose level on the right side (Table 1, Figs 1–9). Among all the examined features, TP levels showed the highest correlation between the right and the left side (Table 1). The bias for every characteristic was low, and the 95% confidence interval for the bias included zero for every measurement analyzed. There was no case in which one side was an exudate and the other side a transudate. Moreover, we documented a close correlation between the right-sided and left-sided pleural effusions concerning all the characteristics we examined (Table 1, Figs 1–9). Among all the examined features, TP levels showed the highest correlation between the right and the left side. The glucose levels were also highly correlated, while LDH levels showed a lower correlation coefficient. The RBC counts showed a weaker correlation, a fact that may be due to the minor bleeding that frequently occurs during the thoracentesis and may lead to great, though clinically insignificant, changes in the number of the pleural fluid RBCs. The NCCs showed the weakest correlation, although the percentages of the various cell types were highly correlated.

The plots of the various measurements were examined to determine if there were instances when the value on one side differed markedly from the value on the other side. There appeared to be two patients in whom the levels of LDH differed markedly between the two sides (Fig 3). In patient 13, with post-CABG pleural effusions, a higher LDH level on the right side coexisted with a lower glucose level (Fig 2) and higher TP level (Fig 1) on the right side were calculated. The bias is the mean difference between values on the left and right sides. The precision is the SD of the difference between the two sides. For statistical analysis and construction of Figures, the SPSS 10.0 statistical program (SPSS; Chicago, IL) was used.

Results

Thirty-three patients were identified from the database who underwent bilateral thoracentesis on the same day. Twenty-seven patients with definitive diagnosis and available laboratory data were included in the study. Four patients were excluded because pleural fluid data were missing from one or both sides, and two patients were excluded because of no definite diagnosis.

The most common diagnoses were pleural effusion after CABG (13 cases) and congestive heart failure (12 cases). One patient had bilateral pleural effusions due to renal failure, while another patient had bilateral pleural effusions secondary to a malignant pericardial effusion due to bronchogenic carcinoma with negative pleural fluid cytology. A pneumothorax, due to a previous thoracentesis, was evident in the left hemithorax in this patient.

There was no significant difference in the mean values of any pleural fluid characteristic between the right and the left side (Table 1). The bias for every characteristic was low, and the 95% confidence interval for the bias included zero for every measurement analyzed. There was no case in which one side was an exudate and the other side a transudate. Moreover, we documented a close correlation between the right-sided and left-sided pleural effusions concerning all the characteristics we examined (Table 1, Figs 1–9). Among all the examined features, TP levels showed the highest correlation between the right and the left side. The glucose levels were also highly correlated, while LDH levels showed a lower correlation coefficient. The RBC counts showed a weaker correlation, a fact that may be due to the minor bleeding that frequently occurs during the thoracentesis and may lead to great, though clinically insignificant, changes in the number of the pleural fluid RBCs. The NCCs showed the weakest correlation, although the percentages of the various cell types were highly correlated.

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The explanation for these differences is not clear. Infection was not present, and although the RBC count was higher on the right side, the difference between the two sides was minor (Fig 4). The clinical significance of the differences in the values between the two sides is debatable, but could be possibly attributed to a more intense inflammatory reaction on the right side. In patient 27, who had renal failure, the difference between the LDH levels could probably be attributed to the presence of larger amounts of blood on the left side (Fig 4). Of note, in both of the patients with significantly different LDH levels between the two sides, the volume of the effusion was higher on the side with the higher LDH levels. When the NCCs were examined, the most striking difference was observed in patient 4 and patient 10 (Fig 5), who had heart failure. Although the reason for the differences in NCCs are

![Diagram](https://example.com/diagram.png)

**Figure 1.** The correlation between the pleural fluid TP levels on the right and left sides. [R] = right side; [L] = left side; Pt = patient. Solid line indicates best fit line. Dotted line indicates line of identity.

**Table 1—Comparison Between the Pleural Fluid Characteristics From the Two Sides**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Right Side</th>
<th>Left Side</th>
<th>p Value†</th>
<th>Bias Lower Bound</th>
<th>Bias Upper Bound</th>
<th>Precision</th>
<th>Correlation Coefficients</th>
<th>p Value‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>TP, g/dL</td>
<td>3.3 ± 1.2</td>
<td>3.2 ± 1.1</td>
<td>0.38</td>
<td>-0.1</td>
<td>0.36</td>
<td>0.64</td>
<td>0.85</td>
<td>≤ 0.001</td>
</tr>
<tr>
<td>Glucose, mg/mL</td>
<td>114 (44)</td>
<td>113 (38)</td>
<td>0.31</td>
<td>-2.7</td>
<td>-11.9</td>
<td>6.5</td>
<td>23</td>
<td>0.78</td>
</tr>
<tr>
<td>LDH, IU/L</td>
<td>355 (379)</td>
<td>361 (465)</td>
<td>0.39</td>
<td>41</td>
<td>-102</td>
<td>184</td>
<td>362</td>
<td>0.71</td>
</tr>
<tr>
<td>RBC, µL</td>
<td>1,847 (5,980)</td>
<td>3,525 (12,200)</td>
<td>0.31</td>
<td>6,100</td>
<td>-192,000</td>
<td>31,500</td>
<td>62,900</td>
<td>0.66</td>
</tr>
<tr>
<td>NCC, µL</td>
<td>620 (756)</td>
<td>555 (568)</td>
<td>0.96</td>
<td>-36</td>
<td>-457</td>
<td>358</td>
<td>1043</td>
<td>0.60</td>
</tr>
<tr>
<td>PMN, %</td>
<td>8.5 (14)</td>
<td>10 (14.5)</td>
<td>0.1</td>
<td>-2.9</td>
<td>-7.6</td>
<td>1.8</td>
<td>11.6</td>
<td>0.78</td>
</tr>
<tr>
<td>Lymphocytes, %</td>
<td>51 ± 25</td>
<td>50 ± 25</td>
<td>0.73</td>
<td>1.15</td>
<td>-5.7</td>
<td>8</td>
<td>17</td>
<td>0.77</td>
</tr>
<tr>
<td>MNC, %</td>
<td>23.5 (39.5)</td>
<td>18 (30)</td>
<td>0.72</td>
<td>2.3</td>
<td>-4.5</td>
<td>9.1</td>
<td>17</td>
<td>0.80</td>
</tr>
<tr>
<td>Eosinophils, %</td>
<td>0 (3)</td>
<td>0 (2.8)</td>
<td>0.65</td>
<td>-0.15</td>
<td>-2.3</td>
<td>2</td>
<td>5.4</td>
<td>0.73</td>
</tr>
</tbody>
</table>

*Data are expressed as mean ± SD if normally distributed and median (interquartile range) if not normally distributed, unless otherwise indicated.
CI = confidence interval; PMN = polymorphonuclear.
†Difference between the values in the right side and values in the left side.
‡Correlations between the two sides.
Figure 2. The correlation between the pleural fluid glucose on the right and left sides, logarithmic scale. Solid line indicates best fit line. Dotted line indicates line of identity. See Figure 1 legend for expansion of abbreviations.

Log Glucose [R] = 1.028 x log Glucose [L] - 0.783
r = 0.78  p < 0.001

Figure 3. The correlation between the pleural fluid LDH levels on the right and left sides, logarithmic scale. Solid line indicates best fit line. Dotted line indicates line of identity. See Figure 1 legend for expansion of abbreviations.

Log LDH [R] = 0.734 x log LDH [L] + 0.738
r = 0.71  p < 0.001
Figure 4. The correlation between the pleural RBC count on the right and left sides, logarithmic scale. Solid line indicates best fit line. Dotted line indicates line of identity. See Figure 1 legend for expansion of abbreviations.

Figure 5. The correlation between the pleural fluid nucleated cells count on the right and left sides, logarithmic scale. Solid line indicates best fit line. Dotted line indicates line of identity. See Figure 1 legend for expansion of abbreviations.
not clear, they are clinically insignificant, as transudative fluid was present in each side in both patients. Patient 26, with pleural effusions due to malignant pericardial effusion, had a high eosinophil percentage on the left side while no eosinophils were found on the right side (Fig 9). This difference is also reflected in the difference in the percentages of the MNCs (Fig 8). Since the RBC count differed only slightly between the two sides (Fig 4), the presence of a left-sided pneumothorax due to previous thoracentesis is a reasonable explanation for the ipsilateral pleural fluid eosinophilia.

**Discussion**

In the present study, we examined whether, in patients with bilateral pleural effusion, the pleural fluid characteristics differ from one side to the other. We studied the TP, glucose, and LDH levels, RBC counts, NCCs, and differentials. Our results indicate the following: (1) there is no significant difference in the mean values of the measurements between the right side and the left side, (2) the bias for every pleural fluid characteristic is not clinically significant, and (3) there are highly significant correlations for all measurements between the values on the left side and the values on the right side.

Bilateral pleural fluid is a common clinical finding. Valdes and coworkers\textsuperscript{13} reported that 15\% of the 642 patients with pleural effusion who were admitted in the pneumonology and internal medicine department during a 5-year period had pleural fluid on both sides. The incidence of bilateral pleural effusion seems to be much higher in critically ill patients. Mattison and coworkers\textsuperscript{14} reported that 55\% of 62 patients with pleural effusion, who stayed in a medical ICU for at least 24 h, had pleural fluid in both hemithoraces. Interestingly, bilateral pleural effusion was present in 34\% of the total 100 consecutive ICU patients who were included in that study.\textsuperscript{14} In both of these studies,\textsuperscript{13,14} heart failure was the leading cause of bilateral pleural effusion. In the present study, heart failure was the second-leading cause of bilateral pleural effusions. Post-CABG pleural effusion was the most common cause of bilateral pleural effusion in our study due to the high number of CABG surgeries performed in our hospital. The high incidence (2.5\%) of bilateral thoracentesis in the present series can be attributed to the fact that our hospital is primarily a cardiac hospital with many...
patients with congestive heart failure and post-CABG effusions, both of which are commonly bilateral. Although bilateral pleural effusion is fairly common, there is no evidence to support any recommendation concerning the need for bilateral or unilateral diagnostic thoracentesis in these patients. Thus, the decision to perform bilateral or unilateral diagnostic thoracentesis relies on personal "clinical feeling" of the individual physician or on "local trends" of the institutions. In our experience, the practice of performing bilateral diagnostic thoracentesis is not uncommon among physicians in different hospitals. To the best of our knowledge, this is the first study attempting to clarify the relationship between the characteristics of the fluid in each pleural cavity. The laboratory tests included in the present analysis constitute the usual initial diagnostic workup for aspirated pleural fluid and provide the basis for the clinical decision making concerning further diagnostic evaluation of patients. The present study demonstrates that the fluids obtained from each hemithorax of patients with bilateral pleural effusion were usually very similar. In the minority of patients in whom noticeable numerical differences between the two sides were observed, the differences were of no clinical significance.

These results indicate that examining the fluid from both the pleural cavities instead of only one cavity would most frequently provide no additional information. This fact justifies the recommendation that in these patients, bilateral diagnostic thoracentesis may not be routinely performed. Additionally, we suggest that in cases in which therapeutic bilateral thoracentesis is needed, laboratory tests in fluid drained from one pleural cavity are adequate to characterize the effusions.

Certain benefits come of the management of patients with bilateral pleural effusions according to these recommendations. First, some cases of thoracentesis-related complications would be avoided. Pneumothorax can occur after 5 to 10% of thoracenteses, and ultrasound-guided thoracentesis does not significantly reduce the rate of this complication when performed by inexperienced personnel. Second, eliminating unnecessary medical procedures leads to a reduction of health-care costs. It is estimated that an ultrasound-guided pleural fluid aspiration combined with the usual laboratory tests included in the present study costs Medicare $453 per patient.

Nevertheless, our results should be interpreted with caution. Besides its retrospective design and the
small sample size, the main limitation of the present study is that the great majority of the patients had bilateral pleural effusions as a result of either heart failure or CABG surgical operation, conditions in which the pathogenesis of pleural effusion on both sides is common. In heart failure, pleural fluid mainly derives from the excess interstitial pulmonary fluid. Although the pathogenesis of post-CABG pleural effusions is not clearly defined, it is believed that either direct surgical trauma of the pleura (in effusions developing in the first month after the operation) or an autoimmune mechanism triggered by the pericardial injury (in effusions found after the first month) are responsible for pleural fluid accumulation. The causative factor was also the same for both the right-sided and left-sided effusion in the two remaining patients, ie, renal failure and constrictive pericarditis. Since a common pathogenetic mechanism would be expected to lead to accumulation of pleural fluid of similar quality in both right and left pleural cavities, the composition of the population of the present study may partly explain the findings of the present study. However, this case selection also raises the possibility that the recommendation not to perform thoracentesis on both sides is not applicable in every patient with bilateral pleural effusion.

When the fluid in only one pleural cavity is examined, one may lose useful clinical information when localized pleural disease overlaps with a condition that causes systematic involvement of both the pleural cavities, ie, parapneumonic or malignant effusion in a patient with heart failure. In those cases, pleural fluid in the locally affected hemithorax may differ from the pleural fluid in the contralateral hemithorax that reflects the systematic disease procedure. More rarely, bilateral pleural effusions may also have the same etiology, ie, parapneumonic or metastatic malignancy, and still differ significantly. The characteristics of the pleural fluid in parapneumonic effusions accompanying bilateral pneumonia will depend on the extent of the pleural inflammatory response, which may differ from one side to the other. Furthermore, if only one of the pleural cavities is infected, the ipsilateral pleural fluid is expected to have a significantly higher NCC, a greater number of neutrophils, higher LDH levels, and lower glucose levels and pH than the reactive fluid from the other pleural cavity. In that case, it is very important that the complicated or empyemic effusion be promptly recognized and more aggressively treated than the contralateral, uncomplicated effusion. Likewise, in malignant bilateral pleural effusions, the LDH level, the glucose level, and the pH

Figure 8. The correlation between the percentage of pleural fluid MNCs on the right and left sides. Solid line indicates best fit line. Dotted line indicates line of identity. See Figure 1 legend for expansion of abbreviations.
may differ between the two sides if there is significant difference in the extent of pleural infiltration by the tumor cells. Since low pleural fluid glucose levels and pH are indicative of a greater tumor burden and predict failure of pleurodesis and shorter survival, the physician may need to be aware of the discrepancy to design optimal patient management.

For the above-mentioned reasons, if there is a coexisting unilateral parenchymal abnormality, pleural effusions of significantly different sizes, parapneumonic effusions, or metastatic malignant effusions, we suggest that bilateral diagnostic thoracentesis should be considered. Bilateral thoracentesis may also be required when the pleural fluid characteristics from one side are discordant to the patient’s clinical condition (i.e., unexplained fever), or when the pleural fluid in the nonpunctured hemithorax persists despite the successful treatment of the underlying disease. The possibility that many clinicians follow this practice could be a source of selection bias in our study. We believe this bias did not affect our conclusions. When we reviewed our database for patients who underwent bilateral thoracentesis separated by 1 to 3 days, we found eight patients. Analysis of the data in these eight patients gave comparable results to those reported for patients who underwent bilateral thoracentesis on the same day.

In conclusion, in patients with bilateral pleural effusions, the main pleural fluid cellular and biochemical features on the right side tend to be similar with the corresponding ones on the left side. For this reason, we suggest that diagnostic thoracentesis need not be routinely performed on both sides, unless there is a specific clinical indication. However, given the limitations of the present study already discussed, a prospective study that would include all patients who present with bilateral pleural effusions with a much broader range of etiologies is required to confirm this recommendation.

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