Pleural Fluid Characteristics of Patients With Symptomatic Pleural Effusion After Coronary Artery Bypass Graft Surgery

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Background: This study describes the pleural fluid characteristics of patients who develop symptomatic pleural effusions after coronary artery bypass graft surgery (CABG).

Methods: Post-CABG patients who underwent a therapeutic thoracentesis for a symptomatic pleural effusion were included unless another explanation for the pleural effusion was present.

Results: During the study, 71 patients (mean age, 61 years) were identified; 49 were men and 22 were women. All patients underwent internal mammary artery grafting. Early effusions (<30 days after CABG) occurred in 45 patients (63%) and late effusions (≥30 days after CABG) developed in 26 (37%). Early effusions were bloody (median red blood cell count, 706 × 10^12/L [706 000 mm^3]) with a high eosinophil count (median, 0.385), whereas effusions that occurred in the late period were yellow exudates with predominant lymphocytes (median, 0.68) and monocytes (median, 0.20). The mean pleural fluid level of lactate dehydrogenase was more than 3 times the upper limit of the reference range in serum in early effusions, whereas late effusions had significantly lower lactate dehydrogenase levels.

Conclusions: Characteristics of early and late effusions differ significantly, suggesting a different pathogenesis of the effusions. Patients who develop a symptomatic pleural effusion after CABG should undergo a therapeutic thoracentesis; however, further investigations are warranted only in patients who have pleural fluid characteristics different from those described.

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Coronary artery disease remains an important cause of morbidity and mortality in the United States, with 175 000 patients requiring coronary artery bypass graft surgery (CABG) per year. Approximately 50% of patients undergoing CABG develop a pleural effusion.1-3 The incidence of post-CABG pleural effusions is higher in patients who receive internal mammary artery (IMA) grafts than in those who receive saphenous vein grafts.2 This difference is attributed to the performance of pleurotomy to harvest the IMA grafts. Most effusions are small, asymptomatic, and left sided; regress spontaneously; and are of no clinical significance. Occasionally a patient may develop a moderate to large symptomatic pleural effusion after CABG.

Most effusions are diagnosed in the early postoperative course; however, some attain their maximal size weeks to months after surgery. The pathogenesis of the post-CABG effusion remains obscure, and the pleural fluid characteristics have not been described. The purpose of the present study was to describe the pleural fluid findings in patients who develop symptomatic pleural effusions after CABG.

RESULTS

During the 8-month study period (September 1, 1997, to May 1, 1998), 113 patients underwent a therapeutic thoracentesis for a symptomatic pleural effusion within 12 months of undergoing CABG. Forty-two patients were excluded from the study because they had other potential reasons for their pleural effusion, such as pneumonia (n = 13), pulmonary embolism (n = 4), drug reactions (n = 7), congestive heart failure (n = 11), valve repair (n = 5), malignancy (n = 1), or rheumatoid arthritis (n = 1). Seventy-one patients met our selection criteria after CABG (mean age, 61 years; 49 men and 22 women). The total number of patients who underwent CABG during this period at...
PATIENTS AND METHODS

The present study was conducted at Saint Thomas Hospital, Nashville, Tenn, a tertiary care referral center where more than 2000 CABGs are performed annually. To identify patients who had a pleural effusion after CABG, we reviewed the medical records of 226 patients who underwent a therapeutic thoracentesis for a symptomatic pleural effusion under ultrasound guidance between September 1, 1997, and May 1, 1998; of these, 113 patients underwent CABG. In the other 113 patients who had undergone a thoracentesis the diagnoses included malignancy (n=43), congestive heart failure (n=31), parapneumonic effusion (n=20), postvalve replacement (n=6), abdominal aortic aneurysm repair (n=1), rheumatoid arthritis (n=3), chylothorax (n=1), and unknown (n=6).

The medical records of the 113 patients who had undergone CABG were further reviewed and data were collected regarding (1) age and sex, (2) type of surgery, (3) side and size of effusion, (4) timing of occurrence of effusion after CABG, (5) characteristics of the pleural fluid as listed below, (6) list of medical problems, (7) medication list, and (8) left ventricular ejection fraction by echocardiography or left ventriculography.

PATIENT INCLUSION CRITERIA

To be included in the present study, patients were required to meet the following criteria: (1) CABG within 1 year of the therapeutic thoracentesis and (2) no other explanation for the pleural effusion (eg, congestive heart failure, pulmonary embolism, drug reaction, or pleuropulmonary infection). The pleural fluid characteristics in the 2 groups differed significantly (Table 2). Although early and late effusions were exudative, early post-CABG effusions were bloody, with high RBC and eosinophil counts. The median RBC count was $706 \times 10^3/\text{L}$ ($706000 \text{ mm}^3$) in early effusions and $7 \times 10^3/\text{L}$ ($7000 \text{ mm}^3$) in late effusions ($P < .001$). The total white blood cell count in the early group was $30 \times 10^9/\text{L}$ ($30000 \text{ mm}^3$) and in the late group was $1.2 \times 10^9/\text{L}$ ($1200 \text{ mm}^3$). The differential cell count in the early group showed 0.385 eosinophils, 0.125 lymphocytes, 0.065 monocytes, and 0.242 neutrophils. Late effusions showed a 0.68 lymphocyte predominance and 0.20 monocytes, 0.08 neutrophils, and no eosinophils.

The incidence of pleural effusions immediately after surgery in patients undergoing CABG has been reported to be 42% to 89%. This wide variability in the incidence of post-CABG effusions is probably related to the technique used to diagnose the pleural effusion because higher rates have been reported when ultrasound or computed tomography is used. The incidence of pleuropulmonary complications is higher with use of IMA grafts compared with saphenous vein grafts. This difference has been attributed to the necessity to enter the adjacent pleural space while mobilizing and harvesting the IMA. Most post-CABG effusions are small, are left sided, and regress spontaneously. Occasionally a patient may de-
velop a moderate to large symptomatic pleural effusion after CABG. The prevalence of large effusions after CABG is not definitely known but has been reported to be 1% to 4%. Most effusions occur in the early postoperative period; however, some effusions reach their maximum size only months after CABG. In the present study, none of the effusions were identified more than 90 days after surgery. Accordingly, one should be hesitant to attribute pleural effusion more than 90 days after CABG to the surgery. The mechanism of the formation of pleural fluid after CABG is not clear, and the analysis of pleural fluid characteristics has been poorly documented in the literature.

In a study by Hulburt et al., 200 patients were followed up after surgery (100 with IMA grafts and 100 with saphenous vein grafts); 4% of patients receiving IMA grafts required a thoracentesis or tube thoracostomy by the sixth postoperative day. Two months after surgery, 10.5% of patients receiving IMA grafts and reported that 8.5% required a thoracentesis immediately after surgery. At 3 months, 20% of patients had a pleural effusion but only 1.5% required thoracentesis. Landymore and Howell7 reported that none of their 67 patients required a thoracentesis during 3 months of follow-up. None of these 3 studies described the pleural fluid characteristics. In our recent study,5 we reported that 0.51% of patients undergoing CABG were readmitted to the hospital for a pleural effusion after CABG. None of the patients in this previous study are included in the present series. In the present series, 57 patients had a moderate to large pleural effusion after CABG for which there was no other explanation. During the study period, approximately 1600 patients underwent CABG. Accordingly, the incidence of moderate to large pleural effusion that we discovered that could be attributed to the CABG was approximately 3.5%. The true incidence of post-CABG effusion is probably much higher than this because our study included only symptomatic patients, and many patients who had an uncomplicated course were followed up at their local hospital.

These patients were further classified into early and late categories. Patients who underwent a thoracentesis within 30 days after CABG were classified as early (n = 45 [63%]) and those who presented more than a month after the surgery were categorized as late (n = 26 [37%]). The pleural fluid findings in the 2 groups differed significantly. The fluid was invariably exudative in both groups, but the mean LDH levels were 3 times higher in the early group compared with the late group. We speculate that the source of the LDH was the RBCs because the early effusions tended to be bloody, with high RBC levels. Pleural fluid glucose and protein levels did not differ significantly in the 2 groups. The leukocyte differential cell count showed eosinophilia in the early group (median, 0.382%), whereas the late pleural effusions tended to be yellow exudates with a higher percentage of lymphocytes (median, 0.68). In our previous study5 we found a similar difference in the pleural fluid characteristic in early and late effusions, although pleural fluid findings were not available for the majority of the patients.

These differences in the pleural fluid findings of the 2 groups may provide clues as to the etiology of the effusions. The pathogenesis of early effusions is probably related to trauma during surgery that results in bleeding into the pleural space. The high RBC count (median, 700 × 10^3/L), indicating a median hematocrit of 0.20, provides strong evidence for the traumatic origin. The high eosinophil count is probably related to blood in the pleural space because it is known that bloody pleural effusions are frequently eosinophilic. Late pleural effusions probably have a different pathogenesis. Because of the late presentation, it is unlikely to be related to blood in the pleural space at the time of surgery. The high lymphocyte count suggests an immunologic etiology. Postcardiotomy syndrome is characterized by fever, pericarditis, and pleuritis, which occurs within 6 weeks after cardiac operation and is similar to Dressler (postmyocardial infarction) syndrome. The etiology of postcardiotomy syndrome is hypothesized to be an autoimmune reaction directed against the epicardium, possibly in concert with a new or reactivated viral infection. The incidence of postpericardiotomy syndrome is reported to be 10% to 40%. Engle et al15 demonstrated that anticardiolipin antibodies appear in the serum of some patients with this syndrome. A rise in viral titers has also been demonstrated. Although speculative, it is possible that late lymphocytic pleural effusions after CABG may

### Table 1. Laterality of Pleural Effusions and IMA Grafts

<table>
<thead>
<tr>
<th>Side of Effusion</th>
<th>Right</th>
<th>Left</th>
<th>Bilateral</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMA Graft</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>4</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Left</td>
<td>13</td>
<td>26</td>
<td>3</td>
</tr>
<tr>
<td>Bilateral</td>
<td>4</td>
<td>5</td>
<td>9</td>
</tr>
</tbody>
</table>

*IMA indicates internal mammary artery.*

### Table 2. Characteristics of Early and Late Pleural Effusions After CABG

<table>
<thead>
<tr>
<th>Pleural Effusion</th>
<th>Early (n = 45)</th>
<th>Late (n = 26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red blood cell count, ×10^12/L</td>
<td>706 (187.5-1750)</td>
<td>7 (1.25-15)†</td>
</tr>
<tr>
<td>White blood cell count, ×10^9/L</td>
<td>1.45 (0.833-2.5)</td>
<td>0.975 (0.800-1.750)†</td>
</tr>
<tr>
<td>Lymphocytes, 10^6/L</td>
<td>0.125 (0.08-0.12)</td>
<td>0.68 (0.43-0.83)†</td>
</tr>
<tr>
<td>Monocytes, 10^6/L</td>
<td>0.065 (0.01-0.14)</td>
<td>0.20 (0.11-0.32)</td>
</tr>
<tr>
<td>Neutrophils, 10^6/L</td>
<td>0.242 (0.12-0.31)</td>
<td>0.08 (0.03-0.14)</td>
</tr>
<tr>
<td>Eosinophils, 10^6/L</td>
<td>0.385 (0.04-0.72)</td>
<td>0 (0-0.02)†</td>
</tr>
<tr>
<td>Lactate, mg/dL</td>
<td>1368 (760-2773)</td>
<td>556 (398-779)†</td>
</tr>
<tr>
<td>Protein, g/L</td>
<td>31 (26-41)</td>
<td>44 (41-48)</td>
</tr>
<tr>
<td>Glucose, mg/dL</td>
<td>102.5 (81-120)</td>
<td>107.0 (92-124)</td>
</tr>
</tbody>
</table>

*Data are given as median (25th-75th percentile). CABG indicates coronary artery bypass graft surgery.*

†P < .001 compared with the early group.
represent a subset of patients with a variant of, or a limited type of, postcardiotomy syndrome involving only the pleura. Although we did not measure anticrocinolin antibodies or viral titers in our patients, most responded to nonsteroidal drug therapy or a brief course of prednisone.

Our study has several clinical implications. First, large effusions related to CAGB can present in the late period. These effusions contain a high percentage of lymphocytes and resemble other lymphocytic exudates, such as those due to tuberculosis, malignancy, lymphoma, and other chronic infections. One factor that is different with post-CAGB effusions is that the LDH level is relatively low (the mean is less than the upper limit of the reference range in serum). We suggest that lymphocytic exudates after CAGB can be safely attributed to the CAGB itself unless the pleural fluid LDH level is more than twice the upper limit of the reference range in serum. We suggest that lymphocytic exudates after CAGB can be safely attributed to the CAGB itself unless the pleural fluid LDH level is more than twice the upper limit of the reference range in serum or there are factors (pulmonary infiltrates, fever, etc) that suggest an alternate diagnosis.

Second, not all effusions after CAGB are related to the surgery. Several other factors may contribute to the formation of effusions in patients undergoing CAGB, including congestive heart failure; pulmonary embolism; atelectasis; and use of drugs such as amiodarone, procarcinamide hydrochloride, and β-adrenergic blocking agents. It is important to include these in the differential diagnosis of effusions occurring in patients who have undergone CAGB.

No controlled studies have examined the management of pleural effusions in patients after CAGB. As already mentioned, most effusions are small, are left sided, and resolve spontaneously. However, as demonstrated in the present series, symptomatic pleural effusions after CAGB are not rare. We do not have controlled data on the management of post-CAGB effusions; however, on the basis of our experience, we recommend that these patients initially be treated with therapeutic thoracentesis and an anti-inflammatory agent such as indomethacin. The latter is particularly useful in late pleural effusions, which are predominantly lymphocytic, suggesting an immunologic basis for the effusion. If the effusion recurs, a second therapeutic thoracentesis with the possible addition of oral prednisone therapy for a brief period is recommended. If the effusion continues to recur, appropriate investigations to exclude other causes of effusion should be performed, and then more aggressive measures such as tube thoracostomy with pleurodesis might be considered.

In conclusion, we found 2 distinct categories of pleural effusions that occur after CAGB. Early effusions are usually bloody (mean hematocrit, 0.20), with a high eosinophil count, whereas effusions that occur in the late period (>30 days after CAGB) are yellow exudates with a predominance of lymphocytes. All effusions related to CAGB are exudative. In early effusions, the pleural fluid LDH level is high (mean, 3 times the upper limit in serum). Late effusions tend to have a lower LDH level, which is almost always less than twice the upper limit of the reference range in serum. The differences in the pleural fluid characteristics suggest that the 2 types of effusions have a different pathogenesis. Early effusions are probably related to trauma during surgery. Late effusions probably represent an immune reaction and may represent a variant or limited form of postcardiotomy syndrome. We recommend that patients who develop a symptomatic pleural effusion after CAGB undergo a therapeutic thoracentesis; however, further investigations are warranted only if the pleural fluid characteristics are other than those described. Further studies to understand the pathogenesis of post-CAGB effusions, and controlled trials for their management strategies, are indicated.

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REFERENCES