Factors Associated With Pericardial Effusion in Acute Q Wave Myocardial Infarction

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To elucidate the clinical characteristics associated with pericardial effusion in the early phase of myocardial infarction, 330 patients with acute Q wave infarction were studied. According to echocardiography, 83 patients had pericardial effusion on the third day of hospitalization, and careful auscultation revealed that a pericardial rub was absent in 45 patients and was present in 38 patients. Based on seven clinical variables, multivariate analysis was performed to determine the important variables related to the occurrence of pericardial effusion with and without pericardial rub. Pulmonary capillary wedge pressure and left ventricular segments with advanced asynergy were the significant factors related to the occurrence of pericardial effusion without a pericardial rub. The presence of ventricular aneurysmal motion, left ventricular segments with advanced asynergy, and alveolar arterial oxygen difference were related to pericardial effusion with a pericardial rub. Therefore, a hemodynamic factor was the major mechanism associated with the increase in extravascular myocardial fluid and the consequent occurrence of hydropericardia in the absence of a pericardial rub, whereas an increase in the microvascular permeability in the myocardium with excessive fluid exuding through the irritated epicardial surface was the mechanism related to pericardial effusion with a pericardial rub in the early phase of acute myocardial infarction. (Circulation 1990;81:477–481)

Pericardial effusion is one of the complications occurring during the course of acute myocardial infarction, but there is marked variability in its reported incidence, mechanisms, and clinical significance.1–5 Echocardiography is the procedure of choice for the detection of pericardial effusion, and although pericardial effusion demonstrated by echocardiography may indicate fluid retention, this is not diagnostic of pericardial injury. A pericardial rub is not rare after acute myocardial infarction and has been reported in patients with pericardial involvement near the infarct.1,6–9 Therefore, it is clinically important to distinguish between irritant and hemodynamic factors contributing to the occurrence of pericardial effusion in the early phase of acute myocardial infarction.

Because hydropericardia appears to result from an increase in the production of myocardial interstitial fluid or interference of fluid drainage,9 we hypothesized that hydrostatic pressure, osmotic pressure, and myocardial vascular permeability affect the production of pericardial fluid. In this investigation, we studied seven clinical factors that may affect the production of pericardial fluid to elucidate the differences in the clinical settings associated with the occurrence of echocardiographically demonstrated pericardial effusion with and without a pericardial rub in patients after their first acute Q wave infarction.

Methods

Patients

We studied 330 consecutive patients after their first acute Q wave myocardial infarction (anterior infarction, 203 patients; inferior infarction, 127 patients) who were admitted to the coronary care unit within 24 hours from the onset of chest pain and who survived the first 3 days after admission. It is a routine procedure in our hospital to insert a Swan-Ganz catheter in patients with acute myocardial infarction who were admitted within 24 hours from the onset of chest pain. All the patients were examined by a physician, and written, informed consent was obtained before the Swan-Ganz catheter insertion. None of the patients had chronic renal failure, collagen disease, cardiac surgery within the previous 6 months, or metastatic disease. During this period, a technically satisfactory echocardiogram could not be obtained in 37 patients, and they were not included in this study.
Clinical Evaluation

The diagnosis of myocardial infarction was made when the patients had an ST elevation with a new Q wave (anterior infarction, two or more in V6, inferior infarction, II, III, and aVF) in serial electrocardiograms and at least twice a normal elevation in the level of serum creatine kinase with MB isoenzyme 5% or more. All patients were monitored continuously in the coronary care unit, and all were examined by careful auscultation at least twice daily. Pericardial rub was considered as a to-and-fro scratchy or grating noise heard in systole, mid-diastole, and presystole or in only one of these phases, and the diagnosis of pericardial rub was made after confirmation by at least two cardiologists. Hemodynamic measurements including cardiac output, pulmonary capillary wedge pressure, and right atrial pressure were determined by the Swan-Ganz method. Pulmonary capillary wedge pressure and right atrial pressure were determined at least once every 4 hours, and cardiac output was determined every 12 hours. The lowest cardiac output and highest pulmonary capillary wedge pressure and right atrial pressure during 24 hours before the echocardiographic study were recorded. Total protein, albumin, and globulin levels were measured at the time of admission and once daily for the first 3 days. Colloid osmotic pressure was calculated according to the Nitta-Staub’s equation:\[\text{Colloid osmotic pressure} = a(2.8C + 0.18C^2 + 0.012C^3) + b(0.9C + 0.12C^2 + 0.004C^3),\]
where a is albumin fraction, b is globulin fraction, and C (g/dl) is total protein. Arterial blood was taken from the radial or femoral arteries at the time of admission with the patients breathing room air. The alveolar arterial oxygen difference was calculated by assuming a respiratory quotient equal to 0.8.

Echocardiography

Two-dimensional and M-mode echocardiography were performed with an SSD 870 phased-array sector scanner (Aloka, Tokyo). All classic views were recorded on videotape for subsequent analysis by observers who were unaware of the patients’ clinical data. The presence of pericardial effusion was assessed on the third day of hospitalization with the method described by Horowitz et al.\(^\text{11}\) An epicardial-pericardial separation that persisted throughout the cardiac cycle (D pattern) was considered diagnostic of pericardial effusion.\(^\text{11}\) To quantify the size of the effusion, measurements were obtained at the level of tips of the mitral valve as described by Weitzman et al.\(^\text{12}\) Total effusion was graded as mild (<10 mm), moderate (10–20 mm), or severe (>20 mm). A two-dimensional echocardiogram was additionally used in doubtful cases. Regional left ventricular wall motion abnormalities were assessed by two-dimensional echocardiography obtained on the third day of hospitalization. Analysis of the left ventricular wall was performed with 11 segments obtained by long- and short-axis images,\(^\text{13}\) and the number of segments with advanced asynergy (akinesia or dyskinesia) was calculated. Functional left ventricular aneurysmal motion was defined by two-dimensional echocardiography as an area of thinned myocardium that was dyskinetic in systole with distinct diastolic deformity and preserved adjacent wall motion.\(^\text{14}\)

Coronary Arteriography

A coronary arteriogram was performed before each patient was discharged from the hospital. Coronary artery lesions with 70% or more reduction in diameter were considered to be obstructive. Each patient was classified as having one-, two-, or three-vessel disease. The proximal left anterior descending lesion was defined as a lesion before the first septal branch, and the proximal right coronary artery lesion was defined as a lesion before the acute marginal branch.

Statistical Analysis

Results are reported as the mean±SD. A Student’s t test and a paired t test were used for quantitative data, and \(\chi^2\) analysis was used for qualitative data. One-way layout analysis of variance and Scheffé’s multiple comparison were used to compare the groups without pericardial effusion, with pericardial effusion but without pericardial rub, and with pericardial effusion and pericardial rub. Discriminant analysis was performed to evaluate the important variables discriminating the two pericardial effusion groups with or without pericardial rub. The categorical variable of aneurysmal motion was subdivided as either being absent or present. A \(p\) value below 0.05 was considered significant.

Results

Incidence of Pericardial Effusion

Of the 330 patients with Q wave myocardial infarction, pericardial effusion was detected by echocardiography in 83 patients (57 men and 26 women; mean age, 63±12 years) on the third day after admission and was absent in 247 patients (180 men and 67 women; mean age, 61±12 years). There were no significant differences in the age and sex distribution between patients with or without pericardial effusion. Among the 83 patients with pericardial effusion, a pericardial rub was absent in 45 patients (group 1) and was present in 38 patients (group 2) during the first 3 days after admission. Pericardial effusion was mild in 37 patients and was moderate in eight patients (18%) in group 1, whereas 32 patients had mild and six patients (16%) had moderate pericardial effusion in group 2. There was no significant difference in the incidence of moderate pericardial effusion between the two groups. None of the patients had echocardiographic signs of severe pericardial effusion.

Clinical Characteristics of Pericardial Effusion

Without a Pericardial Rub

To determine the important variables associated with the occurrence of pericardial effusion without a
pericardial rub (group 1), seven clinical variables (alveolar arterial oxygen difference obtained at the time of admission, cardiac output, pulmonary capillary wedge pressure, right atrial pressure, colloid osmotic pressure, ventricular aneurysmal motion, and the number of advanced asynergic segments obtained on the third day after admission) were compared with those without pericardial effusion and were used in the discriminant analysis (Tables 1 and 2). As a result, pulmonary capillary wedge pressure and advanced asynergic segments were found to be the significant variables associated with the occurrence of pericardial effusion without a pericardial rub. The probability of discrimination (1-discriminant error) was 0.78.

**Clinical Characteristics of Pericardial Effusion With a Pericardial Rub**

The seven clinical variables were also used in the discriminant analysis to determine the important variables contributing to the occurrence of pericardial effusion with a pericardial rub. The probability of discrimination (1-discriminant error) was 0.74.

**Comparison of Selected Variables Between Groups 1 and 2**

When the four variables selected by the discriminant analysis were compared between the two groups, group 1 had significantly higher pulmonary capillary wedge pressure than group 2 ($p<0.001$). There were no significant differences in alveolar arterial oxygen difference, presence of aneurysmal motion, and number of advanced asynergic segments between the two groups. A coronary arteriogram was obtained in 37 patients in group 1 and in 26 patients in group 2. Thirteen patients in group 1 and 10 patients in group 2 had multivessel disease; the difference was not significant. There were also no significant differences between the two groups in the rate of proximal left anterior descending and proximal right coronary artery lesions (54% and 58% in groups 1 and 2, respectively).

**Medication**

Among the 83 patients with pericardial effusion, 27 patients received intravenous or intracoronary urokinase, whereas 76 patients with no evidence of pericar-

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**Table 1. Clinical Characteristics of Pericardial Effusion With and Without Pericardial Rub**

<table>
<thead>
<tr>
<th></th>
<th>No PE (n=247)</th>
<th>Group 1 (PE without PR) (n=45)</th>
<th>Group 2 (PE with PR) (n=38)</th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alveolar PaO2 D (Torr)</td>
<td>34±12</td>
<td>39±15</td>
<td>43±12</td>
<td>9.14</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CO (l/min)</td>
<td>5.02±1.23</td>
<td>4.43±1.36</td>
<td>4.50±1.06</td>
<td>6.41</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>PCW (mm Hg)</td>
<td>10±5</td>
<td>17±4</td>
<td>12±5</td>
<td>38.11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RA (mm Hg)</td>
<td>4±3</td>
<td>6±3</td>
<td>6±4</td>
<td>6.49</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>COP (mm Hg)</td>
<td>24±4</td>
<td>24±3</td>
<td>23±3</td>
<td>2.17</td>
<td>NS</td>
</tr>
<tr>
<td>Aneurysmal motion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>220 (89%)</td>
<td>32 (71%)</td>
<td>22 (58%)</td>
<td>$\chi^2=27.97$</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Present</td>
<td>27 (11%)</td>
<td>13 (29%)</td>
<td>16 (42%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asynergic segments</td>
<td>2.7±1.8</td>
<td>4.1±1.5</td>
<td>4.1±1.4</td>
<td>21.91</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

PE, pericardial effusion; PR, pericardial rub; Alveolar PaO2 D, alveolar arterial oxygen difference; CO, cardiac output; PCW, pulmonary capillary wedge pressure; RA, right atrial pressure; COP, colloid osmotic pressure; NS, not significant.

**Table 2. Relation Between Seven Clinical Variables and Pericardial Effusion With and Without Pericardial Rub**

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (PE without PR)</th>
<th>Group 2 (PE with PR)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Discriminant coefficient</td>
<td>F (adjusted)</td>
</tr>
<tr>
<td>Constant</td>
<td>-2.72</td>
<td>NS</td>
</tr>
<tr>
<td>Alveolar PaO2 D (Torr)</td>
<td>-0.01</td>
<td>0.26</td>
</tr>
<tr>
<td>CO (l/min)</td>
<td>-0.23</td>
<td>2.12</td>
</tr>
<tr>
<td>PCW (mm Hg)</td>
<td>0.30</td>
<td>44.25</td>
</tr>
<tr>
<td>RA (mm Hg)</td>
<td>-0.06</td>
<td>0.97</td>
</tr>
<tr>
<td>COP (mm Hg)</td>
<td>-0.03</td>
<td>0.24</td>
</tr>
<tr>
<td>Aneurysmal motion</td>
<td>0.64</td>
<td>1.19</td>
</tr>
<tr>
<td>Asynergic segments</td>
<td>0.25</td>
<td>4.71</td>
</tr>
</tbody>
</table>

PE, pericardial effusion; PR, pericardial rub; Alveolar PaO2 D, alveolar arterial oxygen difference; CO, cardiac output; PCW, pulmonary capillary wedge pressure; RA, right atrial pressure; COP, colloid osmotic pressure; NS, not significant.
dial effusion received urokinase. There was no significant difference in the number of the patients who received thrombolytic therapy between the group with (33%) and the group without (31%) pericardial effusion. We routinely give heparin to all patients with acute myocardial infarction in our coronary care unit. Eleven patients with pericardial effusion and 44 patients without pericardial effusion were receiving warfarin on the third day after admission, whereas 64 patients with pericardial effusion and 185 patients without pericardial effusion were receiving an antiplatelet agent (aspirin). Similarly, no significant difference was seen between the two groups regarding the use of anticoagulants and antiplatelet agent.

Discussion

Pericardial effusion is a relatively common early finding after acute myocardial infarction, but its incidence is variable. Among the 83 patients with pericardial effusion, a pericardial rub was absent in 45 patients (group 1) and was present in 38 patients (group 2). Although pericardial rub is less often detected than pericardial effusion, the 46% incidence of pericardial rub in our patients with pericardial effusion is less surprising. In this study, seven clinical variables were examined to evaluate the relative importance of each variable to the occurrence of pericardial effusion with or without pericardial rub.

Two-dimensional echocardiography provides a noninvasive means for visualization of abnormal left ventricular wall motion, but this technique tends to overestimate the infarct size. Therefore, in this study, only advanced asynergy (akinesia and dyskinesia) was used to estimate the extent of myocardial infarction. As a result, patients in group 1 had significantly more segments with advanced asynergy than patients without pericardial effusion, and advanced asynergic segments were an important factor related to the occurrence of pericardial effusion in the absence of pericardial rub, which indicates that the patients in group 1 had more extensive myocardial damage.

Myocardial lymph drains to the subepicardium and ultimately to the mediastinum and right heart cavities. Thus, hydropericardia appears to result from an increase in the production of myocardial interstitial fluid or from interference of myocardial venous and lymph drainage by elevated central venous pressure. Fluid filtration across the microvascular system is governed by hydrostatic and osmotic pressure generated in the microvessels and interstitium. Because coronary flow drains into both the right atrium and left ventricle in diastole, the rise in right atrial and left ventricular diastolic pressure would increase the hydrostatic pressure of the myocardial microvessels. Interestingly, Gee et al found a significant increase in the extravascular myocardial water after an increase in the left atrial pressure in dogs when compared with a control series. Because there was no significant difference in the colloid osmotic pressure between the two groups, an increase in hydrostatic pressure is considered to be the factor associated with increased myocardial interstitial fluid volume. Therefore, although right atrial pressure was not selected as a variable in this study, our results from the multivariate analysis are in keeping with previous findings suggesting that the rise in the pulmonary capillary wedge pressure, resulting from the hemodynamic change imposed on the left ventricle from more extensive myocardial damage, is associated with the occurrence of pericardial effusion in the absence of a pericardial rub.

Patients with pericardial effusion in the presence of a pericardial rub (group 2) had a higher alveolar arterial oxygen difference that was associated with significantly more segments with advanced asynergy and a higher incidence of aneurysmal motion than those without pericardial effusion. Mechanisms considered as a cause of interstitial edema and congestion of the lung in acute myocardial infarction include increased hydrostatic pressure or increased pulmonary vascular permeability. The mechanism of increase in vascular permeability in acute myocardial infarction is still unclear but Gee et al found that activation of formed elements in blood may be involved in mediating vascular injury after acute myocardial infarction. Furthermore, the extravascular water content of the heart and lung increased in the absence of an increase in left atrial pressure after coronary artery ligation. Because pulmonary capillary wedge pressure in group 2 was not critically elevated, the higher alveolar arterial oxygen difference in group 2 patients than in those patients without pericardial effusion suggests that an increase in vascular permeability of heart and lung existed in group 2 patients.

The development of infarct expansion or functional left ventricular aneurysmal motion is associated with a larger amount of myocardial necrosis and anatomically transmural infarction. Transmural myocardial infarction extends to the epicardial surface and is responsible for producing pericardial inflammation in the infarct zone. Considering the result of discriminant analysis, a possible mechanism contributing to the occurrence of pericardial effusion with a pericardial rub is increased extravascular myocardial fluid due to increased vascular permeability associated with loss of interstitial fluid from the myocardium to the pericardial space through the damaged visceral pericardium as a result of higher incidence of anatomically transmural infarction.

Limitations

Two limitations of our study should be addressed. First, because of the transient nature of pericardial rub, patients with irritative pericardial involvement in whom a rub was missed could be included in the noninflammatory group. However, the difference in pulmonary capillary wedge pressure might have been larger if 100% of the patients in groups 1 and 2 had been correctly identified. Second, the small number of patients in the groups with the conditions of
interest, pericardial effusion without (45 patients) or with (35 patients) a pericardial rub, might have led to either the selection of variables by the discriminant analysis that in reality are unimportant or might have missed variables that are actually important. Nonetheless, an appraisal of our results in relation to results from other studies and the consistency of selected variables within our group of patients indicate that our conclusion would probably not be altered by a larger group of patients.

Conclusion

The present study demonstrates that patients in group I had higher pulmonary capillary wedge pressures than patients in group 2, despite nearly identical coronary angiographic findings, extent of infarction, and disturbance of pulmonary gas exchange in both groups. Thus, a hemodynamic mechanism is the major factor contributing to the occurrence of pericardial effusion in the absence of a pericardial rub, whereas an increase in capillary permeability and excessive fluid exuding through the irritated epicardial surface are mechanisms associated with pericardial effusion with a pericardial rub in the early phase of acute myocardial infarction.

References


KEY WORDS • pericardium • echocardiography • hemodynamics • vascular permeability • Q wave • infarctions
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