Pericardial Involvement During the Course of Myocardial Infarction*
A Long-term Clinical and Echocardiographic Study

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Study objective: This study investigated the long-term course of infarct-related pericarditis and pericardial effusion. Focus was given to the following issues: incidence and timing of pericarditis and pericardial effusion during the acute phase and 3 years follow-up, size, hemodynamic and clinical consequences of effusions, and potential risks of thrombolytic or anticoagulant therapy in patients with pericardial effusion.

Patients and study design: Serial echocardiographic examinations were performed in 192 consecutive patients with first myocardial infarction during the acute phase (day 1, 5, 10, 21) and during 3 years follow-up (year 1, 2, and 3 after infarction). The follow-up was 100%. Clinical, angiographic, and autopsy data were analyzed.

Results: Pericardial effusion was detected at least once during serial echocardiographic examinations in 82 of 192 patients (43%). The incidence in different subgroups (with or without thrombolysis, open or closed artery at 3 weeks, infarction in left anterior descending, left circumflex, or right coronary artery perfusion bed) was similar. Most (48%) effusions were first detected on the fifth day, and most (50%) disappeared between days 21 and 365. However, in nine patients, the effusion persisted beyond 1 year (up to 3 years in three patients). Only systolic separation of pericardial layers was detected in 59% of effusions, circular effusion in 3.6% of all effusions. No cardiac tamponade developed. Heart failure or death complicated 49% of infarctions with pericardial involvement and 16% of infarctions without effusion (p<0.01). Mortality alone was 8% among patients without effusion and 15% among those with more than minimal effusion (not significant).

Conclusions: Pericardial effusion can be detected by serial echocardiographic examinations in 43% of myocardial infarctions. It appears during the initial 5 days and disappears slowly during several weeks to several months. Anticoagulant and thrombolytic therapy does not increase the frequency or the size of effusions.

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LAD=left anterior descending; LCX=left circumflex;
RCA=right coronary artery

Key words: anticoagulant therapy; echocardiography; myocardial infarction; pericardial effusion; pericarditis

Pericarditis is a common complication of acute myocardial infarction. Its incidence depends on its definition. The frequency of echocardiographic pericardial effusion is reported to be between 24% and 37%. The frequency of clinical pericarditis is much less: between 5% among all infarctions and 21% among anterior Q-wave infarctions. Pericarditis or pericardial effusion is attributed either to epicardial irritation in transmural infarctions, to increase in hydrostatic pressure due to the heart failure, or (in rare instances) due to subacute rupture of free left ventricular wall. There are relatively few published reports on this topic, and to our knowledge, none of them followed up the patients systematically by serial echocardiograms from the first day until the third year after myocardial infarction.

Thus, our prospective long-term study was aimed to answer the following questions: What is the incidence of pericarditis and pericardial effusion during the initial 3 weeks and subsequent 3 years after myocardial infarction? When does pericardial effusion appear and when does it disappear during the course of myocardial infarction? What are the size and hemodynamic consequence of pericardial effusion during myocardial infarction? Is the clinical course of an infarction with effusion different from that without an effusion? What is the relationship between clinical pericarditis and echocardiographic pericardial effusion? Does thrombolytic or anticoagulant therapy influence the incidence, size, and hemodynamic consequence of pericardial effusion?

METHODS

The Group of Patients

Between January 1, 1983 and December 31, 1987, a total of 192 consecutive patients with first acute myocardial infarction (Q-wave type) were included in the study. All patients were followed up from the first day of infarction until 3 years later as a part of another study investigating the effects of thrombolytic therapy on left ventricular function. Complete (100%) follow-up was obtained. The inclusion criteria were the following: first myocardial infarction with ST elevations in at least two ECG leads, age younger than 65 years, less than 6 h between the onset of symptoms and admission to the hospital, initial echo performed within

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the first 24 h after the onset of symptoms, and no previous known myocardial, pericardial, valvular, renal, collagen, or neoplastic disease.

There were 158 male and 34 female patients in the group. The mean age was 54 ± 8 years (range, 28 to 65 years). Eighty-eight patients were treated by intracoronary streptokinase, 64 by intravenous streptokinase, and 40 did not receive thrombolytic agents. Ninety-four patients had an anterior infarction and 98 patients had an inferior/posterior infarction. The diagnosis of infarction was confirmed by increase in creatine kinase value (more than twice above normal) and by serial ECG changes (Q waves developed in 171 patients, and only ST-T changes developed in 21 patients with very early and successful thrombolysis).

Clinical Assessment

All patients were examined by careful auscultation and asked for any chest pain at least twice daily during the first 5 days and then once daily during 3 weeks of hospital stay. Clinical diagnosis of pericarditis was made when a diagnostic pericardial friction rub was heard by two experienced cardiologists and/or when a typical inspiratory pleuropapercardial (precordial) pain appeared (for details, see the Results section). Heart failure was diagnosed when at least two of the following criteria occurred together: S3 gallop, pulmonary basal rales, orthopnea, and/or pulmonary congestion on the chest radiograph.

Echocardiography

Complete echocardiographic examination (two-dimensional, M-mode, and Doppler) was performed on days 1, 5, 10, and 21, and 1, 2, and 3 years after infarction. Special care was given to good quality recording of all levels of short-axis views as well as parasternal long-axis view (with derived M-mode) for effusion and wall motion assessment, and apical views for wall motion analysis only. Ultrasound studies were analyzed separately by two cardiologists (experienced echocardiographers), and in case of any discrepancy (in regional wall motion assessment or in effusion diagnosis), a consensus was reached.

Pericardial effusion was diagnosed with slight modification of the M-mode criteria of Horowitz et al; in addition to these criteria, pericardial effusion was diagnosed also when there was no pericardial separation on the initial echocardiogram and a systolic separation at least 3 mm developed later during the hospital course. Every effusion was classified as minimal, small, or circular. Minimal effusion was diagnosed when a new (not present
during the initial examination) posterior systolic separation of pericardium and epicardium appeared during the follow-up. Small effusion was diagnosed when the posterior separation (at least 3 mm) was present during the whole cardiac cycle. Circular effusion was diagnosed when separation was present anteriorly as well as posteriorly. When a different amount of pericardial fluid was found during different examinations, the largest effusion was considered for the purpose of this study.

Coronary Arteriography

Coronary arteriography with left ventriculography was performed in the third week after infarction in 171 patients. Angiogram (or autopsy in those patients who died during this period) revealed one-vessel disease in 96 patients, two-vessel disease in 62 patients, and three-vessel disease in 34 patients. The infarct-responsible artery was left anterior descending (LAD) in 94 patients, right coronary artery (RCA) in 72 patients, and left circumflex artery (LCX) in 26 patients.

Statistical Analysis

A χ² test was used for statistical analysis.

RESULTS

Incidence of Pericarditis and Pericardial Effusion

The incidence of pericarditis and pericardial effusion (detected at least once during the follow-up) is shown in Table 1. Effusion accompanied infarc-

<p>| Table 1—The Incidence of Pericardial Effusion (as Detected by Echocardiography) and of Pericarditis (as Detected by Pericardial Friction Rub and/or Pericardial Pain)* |
|-------------------------------------------------|--|-------------------------------------------------|--|-------------------------------------------------|--|-------------------------------------------------|--|-------------------------------------------------|--|-------------------------------------------------|--|</p>
<table>
<thead>
<tr>
<th>No. (%) of Effusions</th>
<th>No. (%) of Pericarditis</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients (n=192)</td>
<td>82 (43)</td>
</tr>
<tr>
<td>Intracoronary thrombolysis (n=88)</td>
<td>35 (40)</td>
</tr>
<tr>
<td>Intravenous thrombolysis (n=64)</td>
<td>27 (42)</td>
</tr>
<tr>
<td>No thrombolysis (n=40)</td>
<td>20 (50)</td>
</tr>
<tr>
<td>Open vessel (n=98)</td>
<td>38 (39)</td>
</tr>
<tr>
<td>Closed vessel (n=54)</td>
<td>24 (44)</td>
</tr>
</tbody>
</table>

*All differences are not significant.
tions in the perfusion beds of all three major coronary arteries: LAD in 46%, LCX in 38%, and RCA in 39%.

**Timing of Pericardial Effusion During the Course of Myocardial Infarction**

The appearance and disappearance of pericardial effusion, as detected by serial echocardiography, are shown in Figure 1 and Table 2. Most effusions were detected for the first time on day 5 (n=39; i.e., 47% of effusions), and first echocardiogram showing resolution of previously present effusion was most frequently detected 1 year after infarction (n=41; i.e., 50% of all effusions).

Only seven patients had a minimal or small effusion present already on day 1. In all these seven patients, the size of effusion increased during the hospital stay and the effusion disappeared later. There was no clinical evidence for other causes of effusion. On the contrary, in 14 patients, the effusion was first detected on day 21 in two patients even 1 year after infarction and in one patient 3 years after infarction. These three “late” effusions were clinically silent, found accidentally during a routine echocardiographic follow-up. In fact, two of them theoretically could have appeared much earlier, anytime after day 22. In nine patients, the effusion persisted beyond 1 year (up to 3 years in three patients).

**Table 2—The Appearance and Disappearance Time of Effusions**

<table>
<thead>
<tr>
<th>Effusion (Appearance)</th>
<th>Effusion (Disappearance)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day</td>
<td>First Echo With</td>
</tr>
<tr>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>5</td>
<td>39</td>
</tr>
<tr>
<td>10</td>
<td>19</td>
</tr>
<tr>
<td>21</td>
<td>14</td>
</tr>
<tr>
<td>Effusion persisting beyond 3rd year</td>
<td>4</td>
</tr>
</tbody>
</table>

*Total: n=82.

**Table 4—Relation Between the Size of Effusion and Clinical Signs of Pericarditis**

<table>
<thead>
<tr>
<th>Clinical Pericarditis</th>
<th>Without Pericarditis</th>
</tr>
</thead>
<tbody>
<tr>
<td>No effusion</td>
<td>6</td>
</tr>
<tr>
<td>Minimal effusion</td>
<td>3</td>
</tr>
<tr>
<td>Small effusion</td>
<td>4</td>
</tr>
<tr>
<td>Circular effusion</td>
<td>3</td>
</tr>
</tbody>
</table>

*The largest effusion during any of the examinations is given per patient. Total patients: n=192.

**Size, Clinical, and Hemodynamic Consequences of Pericardial Effusions During Myocardial Infarction**

Most effusions (48 patients including 3 with effusion and pericarditis, i.e., 59%) were minimal. Circular effusion was detected only in three patients (3.6%). The mean diastolic separation of pericardium and epicardium posteriorly was 5 mm in small effusions and 18 mm in circular effusions. The mean anterior diastolic separation in circular effusions was 5 mm. No patient developed clinical or echocardiographic signs of cardiac tamponade. There was no death attributed to free left ventricular wall rupture.

Mortality among patients with small or circular effusion was 15% compared with 8% in those without effusion (difference not significant).

The relation between ejection fraction, heart failure, and death and the presence and extent of pericardial involvement is shown in Table 3 and Figure 2. Interestingly, 11 of 13 patients with heart failure or death in the presence of preserved ejection fraction (>50%) had pericardial involvement (3 of them pericarditis, 8 varying degrees of effusion).

**Relation Between Clinical Pericarditis and Echocardiographic Pericardial Effusion**

Clinical pericarditis was diagnosed in 16 patients: 6 without evidence of effusion, and 10 with effusion (Table 4). Pericardial friction rub with typical pleuropерicardial chest pain was detected in all six patients without effusion and in seven of those with effusion. Three patients with effusion had only peri-
cardiac pain without friction rub. Thus, there was no significant relation between clinical pericarditis and echocardiographic effusion.

Influence of Thrombolytic or Anticoagulant Therapy on the Incidence, Size, and Consequences of Pericardial Effusions

As shown in Table 1, the incidence of pericardial effusion (and of pericarditis) was even slightly (not significantly) higher among patients without thrombolytic and anticoagulant therapy. There was also no difference in size of effusions.

DISCUSSION

The Incidence of Pericardial Effusion

The 43% incidence of pericardial effusion is somewhat higher than previously published\(^1,2,5\) and similar to another report from this country.\(^8\) The explanation for higher incidence in these two Czech reports is a methodologic one: only these two reports are based on multiple (at least four during hospital stay, and additional later) serial echocardiographic examinations during initial 3 weeks of infarction, thus having a higher chance to detect a small, transient effusion. It was routine in Czechoslovakia during the 1980s (when the data for both reports have been collected) to keep all patients with myocardial infarction in the hospital for 3 weeks.

The Timing of Pericardial Effusion During the Course of Myocardial Infarction

This report confirmed that most pericardial effusions arise during initial 5 days, but effusion can first appear anytime during the initial 3 weeks. Sugiuara et al\(^13\) found echocardiographic evidence of pericardial effusion on the third day in 25% of Q-wave infarctions. In our study, the same frequency (26%) of effusions was found on the fifth day, with an additional 17% occurring later during the course of infarction.

The resolution of effusion is frequently slow, lasting 1 to 18 months.\(^8\) This study showed even persistence of effusion up to 3 years in three patients.

The Size of Pericardial Effusion

It was confirmed that most effusions are small,\(^5\) and a circular effusion is an exception during myocardial infarction. Tamponade in the absence of cardiac rupture is extremely rare and was not detected in this study or by others.\(^5,9\) If a large effusion with tamponade is present during the course of myocardial infarction, cardiac rupture should always be considered.\(^10\)

Prognostic Significance of Pericardial Effusion

Mortality in patients with more than minimal effusions was greater (15%) than in those without effusion (8%); however, the difference did not reach statistical significance. Other investigators did not find a significant relationship between pericardial effusion and in-hospital mortality.\(^9,12\) In contrast, Sugiuara et al\(^13\) found a mortality rate of 27% among 45 patients with pericardial effusion, compared with 12% among 67 patients with a pericardial friction rub (with or without effusion) and 6% among 218 patients without effusion and without friction rub. Wall et al\(^13\) found a 15% mortality rate among patients with a pericardial friction rub compared with 6% among those without a friction rub.

Our data show that clinical pericarditis and/or small to circular effusion is accompanied in 66% by heart failure or death, compared with 16% incidence of these events among patients without pericardial
involvement. This finding has possibly two explanations: (1) larger, fully transmural infarctions lead more frequently to heart failure and also to pericarditis; (2) heart failure itself, by increasing hydrostatic pressure, can precipitate the accumulation of fluid within the pericardial cavity. Our data show (Table 3, Fig 2) that it is difficult to establish the relative prognostic importance of decreased ejection fraction and pericardial involvement in myocardial infarction, because most patients with pericardial involvement also had decreased ejection fraction. However, as already mentioned, among patients with preserved ejection fraction, pericardial involvement might differentiate those at higher risk for subsequent events. However, this needs further confirmation.

The Relation Between Pericarditis and Effusion

The frequency of clinical pericarditis in this study resembles that reported by others.\(^5,^4\) As noted also by Galve et al.,\(^9\) the association between clinical pericarditis and echocardiographic pericardial effusion is weak. Clinical pericarditis is thus much less common than the echocardiographic detection of pericardial effusion. Further, clinical pericarditis can occur without effusion. Likewise, an echocardiographic finding of pericardial effusion is commonly clinically silent.

Is Thrombolytic and Anticoagulant Therapy Safe in Pericarditis Accompanying Myocardial Infarction?\(^2\)

Our observations with streptokinase and those reported by others with tissue plasminogen activator\(^1\) showed that thrombolytic and anticoagulant\(^11\) therapy does not increase frequency or size of pericardial effusion. Khandheria et al.\(^14\) described seven patients with combination of pericardial effusion and left ventricular mural thrombus treated safely by anticoagulants on a short- and long-term basis. Anticoagulant therapy, when it needs to be maintained, does not appear to precipitate tamponade physiology. However, clinical vigilance is required to control the level of anticoagulation and ensure hemodynamic tolerance if an effusion is present.

In conclusion, frequent echocardiographic examinations can detect pericardial effusion in a significant percentage of patients with myocardial infarction. Effusions usually develop during the initial 5 days of infarction and resolve slowly during the subsequent year. They are accompanied by a higher frequency of congestive heart failure and, possibly, by higher mortality. Effusions in the absence of cardiac rupture are usually small and rarely cause cardiac tamponade. Clinical pericarditis and echocardiographic hydropericardium appear to be separate entities. Thrombolytic and anticoagulant therapy in the presence of infarct-related pericarditis or pericardial effusion appears well tolerated.

REFERENCES