Pericardial effusion in the course of myocardial infarction: incidence, natural history, and clinical relevance

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ABSTRACT Incidence and significance of pericardial effusion in patients with acute myocardial infarction (AMI) have not been established. To evaluate these issues, we studied prospectively 138 consecutive patients with AMI. An echocardiogram was obtained in each 1, 3, and 10 days and 3 and 6 months after admission. Fifty four patients with unstable angina and 57 without heart disease were studied as controls. Echocardiographic diagnostic criteria of pericardial effusion were established from 33 additional patients undergoing surgery. Pericardial effusion was found in 28% of patients with AMI. Twenty-five percent of patients with AMI had pericardial effusion on the third day, vs 8% of patients with unstable angina (p < .02) and 5% of patients without heart disease (p < .01). At 1, 3, and 10 days and 3 and 6 months prevalence of pericardial effusion was 17%, 25%, 21%, 11%, and 8%, respectively. There was no case of tamponade. Pericardial effusion was more common in anterior AMI (p < .02) and in patients with heart failure (p < .05) but it was not significantly associated with early pericarditis, peak creatine kinase–MB, the level of anticoagulation, or mortality. Thus, pericardial effusion is a common event in patients with AMI (incidence of 28%), but does not result in specific complications. The reabsorption rate of pericardial effusion is slow and, in our experience, mild or moderate pericardial effusion does not preclude heparin therapy. Circulation 73, No. 2, 294–299, 1986.

THE INCIDENCE of pericardial effusion (PE) during acute myocardial infarction (AMI) is not well established: It was formerly considered to be an uncommon occurrence,1–3 but there have been marked discrepancies between recently reported series4–5 and so questions regarding PE and AMI have not yet been answered. In addition, although individual cases of massive hemopericardium associated with free wall rupture6,7 or with anticoagulant therapy have been described,8,9 the causes and the clinical significance of PE in most patients have not yet been confirmed. Therefore, it is not known whether the finding of PE favors the diagnosis of subclinical early postinfarction pericarditis, or whether it is predictive of the subsequent development of the postinfarction syndrome. It is also not established whether the finding of PE in patients with AMI is an indication to modify prophylactic anticoagulant therapy. Thus, the present echocardiographic study was designed to determine prospectively the incidence, natural history, clinical relevance, and related factors of PE in the course of AMI.

Material and methods

Patients. A total of 282 patients were distributed in four groups. Group I included 138 consecutive patients admitted to our coronary unit with AMI. AMI was diagnosed by the presence of at least two of the three following diagnostic criteria: prolonged suggestive chest pain, characteristic electrocardiographic (ECG) changes (new Q waves), and elevation of serum creatine kinase (CK)–MB level. Seven out of these 138 patients died within a few hours after admission before the first echocardiographic study could be recorded. The remaining 131 patients (115 men and 16 women, with ages ranging from 35 to 81 years, mean age 58 ± 12 years) were prospectively studied with sequential echocardiographic recordings on days 1, 3, and 10 after admission, and 3 and 6 months after discharge. Ten patients were excluded because their echocardiographic recordings were considered of inadequate quality. Accordingly, group I consisted of 121 analyzable patients.

Group II was a control group including 54 patients admitted for unstable angina. Ages and sex distribution were comparable to those of patients in group I. Diagnostic criteria of unstable angina were effort angina with a clearly progressive pattern or angina at rest with repeated attacks or with attacks lasting longer than 15 min; and absence of new Q waves on the echocar-
gram and of elevated serum CK-MB levels. None of these patients had a previous history of myocardial infarction or had undergone cardiac surgical procedures. Echocardiographic study was performed in this group on the third day after admission. Two patients were excluded because their echocardiograms were of inadequate quality.

Group III was another control group consisting of 57 subjects without any clinical, radiologic, or ECG evidence of cardiovascular disease and in whom any previous or present condition that might have been associated with PE was ruled out. Ages and sex distribution of these subjects were comparable to those of patients in group I. Two patients were excluded because their echocardiograms were of inadequate quality.

Group IV consisted of 33 patients (with ages and sex distributions comparable to those in Group I) with any of several cardiac conditions who underwent cardiac surgery and in whom an echocardiographic recording performed on the day previous to surgery was available. During operation, after opening the pericardium, pericardial fluid was aspirated through a catheter with special care to remove fluid from all pericardial sinuses and recesses. The volume of pericardial fluid was measured and the results were correlated to the echocardiographic findings.

Clinical findings. The following parameters were studied: (1) site of the infarction. Infarctions were classified as "Q wave infarction" (when new Q waves present) and "non-Q wave infarction" (when only changes in the ST-T segment were present). Q wave infarctions were subdivided into anterior (Q wave from V_1 to V_5 - V_6 and inferior (Q wave in leads II, III, and aVF). True posterior infarctions (R/S ratio higher than 1 in V_1) were included in the inferior subgroup, and lateral infarctions (Q waves in V_3, V_6 and/or lead I and aVL) were included in the anterior subgroup, except when associated with inferior infarction. (2) Myocardial enzyme curve. Measurements of SGOT, total CK, and CK-MB were carried out every 6 hr through the first 2 days after admission. Correlations were made with the peak value of CK-MB. (3) Heart failure. Heart failure was considered to be present when the patient had the characteristics of Killip's classes II, III, or IV. (4) Early postinfarction pericarditis. Since there are not well-established diagnostic criteria for this type of pericarditis, the two following different conventional definitions based on clinical parameters were established: (A) pericardial friction rub regardless of associated findings; and (B) pericardial friction rub and/or two of the following criteria: fever, pericardial pain, suggestive ECG changes. (5) X-ray changes. For all patients at least three x-ray chest films were available, two of which were obtained within the 4 first days after admission and the third of which was obtained on day 10. All were examined looking for changes in heart size, findings suggesting heart failure, and signs of pleural effusion. (6) Resuscitation maneuvers, electroversion, and electrocatheter insertion. The presence and time sequence of these events were tabulated along with the incidence of with PE. (7) Anticoagulant therapy. All the patients with AMI and those with unstable angina received subcutaneous calcium heparin at an initial dosage of 2500 IU/10 kg of body weight every 12 hr (full-dose heparin regimen) to maintain a ratio patient/control of partial thromboplastin time (PTT) in the 1.8 to 2.5 range. In those patients with past or present gastroduodenal ulcer, significant arterial hypertension, or old age, a dosage of 7500 IU/12 hr was administered (low-dose heparin regimen), with a subsequent lengthening of the patient's PTT to not more than 10 sec over his or her control PTT. Both the two dose regimens were adjusted over two successive control periods to keep the mentioned values in the preestablished ranges.

Echocardiographic study. Initially, all recordings were carried out with an M mode Ekoline 20A ultrasonoscope. In all cases in which images of persisting effusions (echo-free space in the posterior pericardial sac present in the first three recordings without changes) were found (five patients) or in which doubts regarding interpretation of findings arose among observers (16 patients), an additional two-dimensional study with an ATL Mark 300 mechanical sector scanner echocardiograph was carried out. Two-dimensional examinations were obtained in conventional views (long- and short-axis parasternal, four-chamber apical, and four-chamber and short-axis subcostal).

The M mode criteria for the diagnosis of PE were drawn from our correlation study of echocardiographic and surgical findings: The amount of fluid found at operation in each patient was correlated with the echocardiographic patterns described by Horowitz et al.\(^1\) (figure 1). Types A, B, and C\(_2\) (no case of pattern C\(_1\) was found) represent patterns in which epicardial and posterior pericardium are not separated from each other throughout the cardiac cycle; these patterns were consistently found in patients in whom less than 50 ml of pericardial fluid was recovered at operation. There was complete overlap among values, precluding any estimation of the amount of fluid from the echocardiographic pattern. By contrast, all patients with D pattern had more than 50 ml fluid at operation, larger amounts than those associated with the other echocardiographic patterns. Type E represents pericardial thickening and was not associated with effusion. On the basis of these results, we accepted as a diagnostic finding of PE only the separation between pericardial sheets throughout the cardiac cycle, as in Horowitz's D pattern, and we assumed that this implied an amount of fluid greater than 50 ml. For two-dimensional examinations, it was accepted that the posterior echo-free space detected by M mode was caused by PE if the following criteria were met: (1) the echo-free space persisted throughout the cardiac cycle, without end-diastolic obliteration; (2) it ranged from atrioventricular junction to at least the vicinity of papillary muscle; (3) it was anterior to the descending aorta, and (4) it could be differentiated from other structures such as coronary sinus, descending aorta, and occasional pleural effusion or ventricular pseudoaneurysm.

\[\text{FIGURE 1. Amount of fluid found at operation in the pericardial cavity in all group IV patients in relation to echocardiographic pattern in the posterior left ventricular wall. On the top of each column the mean, SD, and range of the volumes (in ml) in each type are shown. All patients with pattern D had an effusion larger than 50 ml. END = endocardium; EP = epicardium; PER = pericardium.}\]
Echocardiographic recordings were interpreted by three different experienced observers who were unaware of the clinical features of the patients. When discrepancies arose, a consensus was reached. Since the number of our patients with PE who were operated on was not large enough to establish quantitative echocardiographic criteria of the amount of fluid, these criteria were arbitrarily established from the sum of epicardial and pericardial separations in the anterior and posterior spaces. Measurements were made at the level of the tips of the mitral valve. PE was therefore graded, as it has been by other authors, as mild (less than 10 mm), moderate (10 to 20 mm), or severe (more than 20 mm).

Statistical analysis. Data related to quantitative variables are given as mean ± SD. Comparisons have been made by means of Student's t test for grouped data, χ² test, or Fisher's exact test, depending on the variables in each case.

Results

Frequency of PE. Of the 121 patients with AMI (group I), echocardiographic diagnosis of PE was made during the clinical evolution in 34 (28%); on the third day after admission, 28 (25%) of the 114 survivors had PE. The three observers were in agreement about the interpretation of the two-dimensional studies in all 21 cases in which doubts had been raised by the M mode echocardiogram or in which a pattern of effusion was persistent on the latter. Two-dimensional recordings confirmed that the M mode echo-free space corresponded to PE in 11, whereas in the remaining 10 this space could have been related to other adjacent structures.

PE was diagnosed in four (8%) of the 52 patients with unstable angina (group II) (p < .02 as compared with the prevalence on the third day after admission in group I). PE was diagnosed in three (5%) of the 55 subjects without heart disease (group III) (p < .01 compared with group I, p = NS compared with group II). Comparisons are shown in figure 2.

Evolution of PE. No patient was lost to follow-up. In figure 3 the prevalence of PE at the time of each of the five successive control measurements is shown. The peak prevalence (25%) was found on day 3. In each patient the amount of fluid also had a tendency to peak around the third day. The appearance of fluid was detected very early, whereas its disappearance was progressive, a prevalence as low as that found in group II (unstable angina) being reached 6 months after the acute episode. In four patients signs of PE were present on all five recordings, although in two of them the volume was variable.

Quantification and location of PE. PE was mild in 30 (88%) and moderate in four patients (12%). Severe PE was not found in any patient. Location of PE associated with AMI was the same as that found with PE of any cause; that is, in mild PE there was only separation in the posterior space, whereas in moderate PE anterior separation was present only when posterior separation was already important. In the 21 patients in whom two-dimensional studies were carried out and localized effusion were not accessible to M mode echocardiography, intrapericardial masses suggesting clots or formation of bands or loculation were not observed.

Relationship between PE and clinical findings. In table 1 the correlation between PE and different clinical variables is shown. No significant correlation was found between PE and the amount of myocardial enzyme release, the implantation of an electrocatheter, the performance of resuscitation maneuvers or electroversion, or whether the infarction was a first episode or a reinfarction. Disturbances of rhythm or conduction were not more frequent in patients with PE. However,
PE was more often associated with anterior infarctions (p < .02), than with non-Q wave infarctions or Q wave infarctions; there was no significant difference between the incidence of PE in patients with Q wave and those with non–Q wave infarction. Congestive heart failure was significantly associated with PE (p < .05); 10 of the 22 patients with heart failure had PE. In no patient with PE did changes in the cardiac silhouette at x-ray examination suggest appearance, progression, or clearing of PE.

In table 2 the cases of pericarditis in the group with AMI are shown. It can be seen that its prevalence increases when more inclusive diagnostic criteria are adopted. However, PE was not observed more frequently in patients with pericarditis, regardless of the criteria used for defining the latter.

Two patients had free wall rupture demonstrated at necropsy. One of them had PE evident on the echocardiogram recorded previous to death.

**Anticoagulant therapy and PE.** There was no difference in the incidence of PE among patients receiving full and low doses of heparin (table 3). The groups of patients were found to be comparable with respect to age, sex, site of the infarction, and incidence of heart failure and pericarditis.

**Clinical course.** No case of PE resulting in tamponade was observed; therefore, pericardiocentesis was not performed in any patient. Although clearing of effusion was usually slow, no finding suggesting constrictive pericarditis was found in any patient throughout the follow-up. Mortality was similar both in patients with and without PE during the hospital stay and the 6-month follow-up (table 1). Finally, no instance of Dressler's postinfarction syndrome was detected during the follow-up period among the 104 patients surviving the acute phase of myocardial infarction.

**Discussion**

The first aim of our study was to establish the incidence of PE during AMI. The only two available echocardiographic studies dealing with this topic, published very recently, report widely different incidences (5.6% and 37%, respectively). When our study was designed, we were conscious of relevant methodologic issues and in particular we were aware of the fact that diagnostic echocardiographic criteria of PE should be properly defined. Horowitz et al. postulated that the echocardiogram could detect PE resulting in 15 ml of fluid or more onwards; however, this might be an overestimation of the sensitivity of the echocardiogram, since a part of the pericardial fluid may be located in pericardial sinuses and recesses and therefore may not be accessible with echocardiography. In addition, in healthy individuals up to 20 to 25 ml of pericardial fluid may frequently be found. If Horowitz's assumptions were true, this would mean that echocardiography could diagnose as PE physiologic amounts of fluid. Therefore, we studied a series of our own

### Table 1

<table>
<thead>
<tr>
<th>Relationship between PE and clinical findings in patients with AMI</th>
<th>PE</th>
<th>non-PE</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>34 (28%)</td>
<td>87 (72%)</td>
<td></td>
</tr>
<tr>
<td>Age (mean ± SD)</td>
<td>61.8 ± 9.8</td>
<td>56.7 ± 12.3</td>
<td>NS</td>
</tr>
<tr>
<td>Sex</td>
<td>M</td>
<td>30 (29%)</td>
<td>75 (71%)</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>4 (12%)</td>
<td>12 (75%)</td>
</tr>
<tr>
<td>Peak CK-MB (IU)</td>
<td>83.6 ± 66.2</td>
<td>88.5 ± 51.1</td>
<td>NS</td>
</tr>
<tr>
<td>No. of infarctions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First infarction</td>
<td>31 (28%)</td>
<td>80 (72%)</td>
<td>NS</td>
</tr>
<tr>
<td>Reinfarction</td>
<td>3 (30%)</td>
<td>7 (70%)</td>
<td></td>
</tr>
<tr>
<td>Temporary pacing</td>
<td>1 (10%)</td>
<td>9 (90%)</td>
<td>NS</td>
</tr>
<tr>
<td>Resuscitation maneuvers and/or electroversion</td>
<td>2 (50%)</td>
<td>2 (50%)</td>
<td>NS</td>
</tr>
<tr>
<td>Major arrhythmias</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supraventricular</td>
<td>4 (50%)</td>
<td>4 (50%)</td>
<td>NS</td>
</tr>
<tr>
<td>Ventricular</td>
<td>8 (31%)</td>
<td>18 (69%)</td>
<td>NS</td>
</tr>
<tr>
<td>Atrioventricular block</td>
<td>1 (11%)</td>
<td>8 (89%)</td>
<td>NS</td>
</tr>
<tr>
<td>Site of infarction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>20 (38%)</td>
<td>32 (68%)</td>
<td>&lt;.02</td>
</tr>
<tr>
<td>Inferior</td>
<td>10 (29%)</td>
<td>47 (54%)</td>
<td></td>
</tr>
<tr>
<td>Type of infarction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q wave infarction</td>
<td>30 (27%)</td>
<td>80 (73%)</td>
<td>NS</td>
</tr>
<tr>
<td>Non-Q wave infarction</td>
<td>4 (36%)</td>
<td>7 (64%)</td>
<td></td>
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<tr>
<td>Heart failure</td>
<td>10 (45%)</td>
<td>12 (55%)</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Hospital mortality</td>
<td>6 (35%)</td>
<td>11 (65%)</td>
<td>NS</td>
</tr>
<tr>
<td>Late mortality (6 month)</td>
<td>2 (33%)</td>
<td>4 (67%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

### Table 2

<table>
<thead>
<tr>
<th>Relationship between PE and pericarditis in patients with AMI</th>
<th>Patients</th>
<th>PE</th>
<th>non-PE</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definition</td>
<td>(n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>14</td>
<td>6 (42%)</td>
<td>8 (58%)</td>
<td>NS</td>
</tr>
<tr>
<td>B</td>
<td>21</td>
<td>8 (38%)</td>
<td>13 (62%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Definition A = pericardial friction rub regardless of associated findings; definition B = pericardial friction rub and/or two of the following criteria: fever, pericardial pain, suggestive ECG changes.

### Table 3

<table>
<thead>
<tr>
<th>Relationship between PE and the level of anticoagulation in patients with AMI</th>
<th>Patients</th>
<th>PE</th>
<th>non-PE</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full-dose heparin</td>
<td>50</td>
<td>16 (32%)</td>
<td>34 (68%)</td>
<td>NS</td>
</tr>
<tr>
<td>Low-dose heparin</td>
<td>71</td>
<td>18 (25%)</td>
<td>53 (75%)</td>
<td></td>
</tr>
</tbody>
</table>
comparing the fluid findings on the echocardiogram with the amount removed at surgery. As is shown in figure 1, amounts of less than 50 ml can result in any echocardiographic pattern from A to C2 (without separation between pericardial sheets or with separation lasting for less than one cardiac cycle). Thus, the diagnostic capabilities of the echocardiogram begin when the accumulated fluid is in excess of 50 ml. This amount correlates with an epicardial–pericardial separation that persists throughout the cardiac cycle (D pattern). Although Horowitz et al.10 believe that the C2 pattern, in which epicardium and pericardium come to contact in end-diastole, is also indicative of PE, we have not considered this diagnostic of PE since this would have entailed a significant loss of specificity. We think that a value of 50 ml is more useful in the separation of abnormal volumes of pericardial fluid from physiologic ones.

Our study, like those of Wunderick11 and Kaplan et al.,3 has been carried out with M mode echocardiography because it is well established that this technique has, because of better axial resolution, higher diagnostic capabilities than the two-dimensional scan for the qualitative diagnosis of PE,13 especially with small effusions such as those found in AMI. On the other hand, localized PE in patients with AMI seems to be exceptional.14 However, we have additionally used two-dimensional technique in all doubtful cases or in patients with persistent PE. This allowed us to rule out false positive diagnoses of PE, such as those secondary to left ventricular pseudoaneurysm,15 coronary sinus,16 or pleural effusion.17

In our healthy control subjects the prevalence of posterior echo-free space (5%) was identical to that found in the Framingham Study for individuals of the same age and sex.18 This echo-free space is not necessarily caused by effusion, since it may be secondary to adipose tissue.19 In our control patients with unstable angina we found a somewhat higher incidence (8%) that was not statistically different from that found in healthy individuals. This finding, along with the evolution of the PE prevalence in successive control patients (figure 3), shows quite distinctly the close association of PE with the events related to the acute phase of infarction. When we compare our results with those of the other two series,4,5 it seems difficult to find a satisfactory explanation for the low incidence of PE in the series by Wunderick4 (5.6%), because this is just the frequency found in healthy individuals. On the other hand, the higher incidence (37%) found by Kaplan et al.5 could be explained by the greater variability in a series that was smaller than ours (43 patients vs 121), and by the fact that they consider as evidence of PE the C2 pattern of Horowitz et al.,10 which, in our experience, is nonspecific with regard to A and B patterns.

We have also determined the natural history of PE in patients with AMI. It is remarkable that, although PE appears very early after AMI, its reabsorption is slow. Therefore, insofar as in a sizeable number of patients PE may persist for even months after the infarction, the finding of mild PE is of small value in the confirmation of a clinical suspicion of Dressler’s post-infarction syndrome.

From our results it can be inferred that early postinfarction pericarditis does not play a significant role in the occurrence of PE. The lack of correlation between pericarditis and PE has been shown for two different sets of diagnostic criteria so as to avoid conclusions based on an incorrect definition. One reason why this type of pericarditis, as clinically defined, is not significantly associated with PE is probably that its occurrence is localized on the area of necrosis. A practical conclusion to be drawn from our findings is that the detection of PE should not be used, as it often is, as a criterion of early postinfarction pericarditis.

By contrast, in our series congestive heart failure turned out to be a factor clearly associated with PE. We even detected a tendency for a greater incidence and amount of PE in the patients with more advanced Killip class. In fact, this is a well-known association that holds true for heart failure of many causes.20

In our series PE was significantly more common in patients with anterior AMI, whereas incidence of heart failure was similar in patients with anterior and inferior infarctions. This phenomenon cannot be easily explained; it can be speculated, however, that inferior infarctions make the detection of small amounts of PE more difficult due to posterior wall akinesia, which would lead to an underestimation of PE in those cases. On the other hand, we have not found that Q wave infarctions are more frequently associated with PE than non-Q wave infarctions. This fact may be related to the small specificity of this ECG classification regarding the transmural or nontransmural character of any infarction.21,22

In the present study it has not been possible to carry out a comparison between the incidence of PE in patients receiving heparin and those not receiving heparin, since in our coronary unit it is a routine measure to give anticoagulant drugs to all patients with AMI. Nevertheless, we think that heparin is not a causal factor of PE in AMI because (1) in the studies by Wunderick4 and Kaplan et al.5 there was no difference
in the incidence of PE between patients receiving and those not receiving heparin; (2) in our study no difference was found in the incidence of PE in patients on the two heparin regimens (full dose and low dose), and (3) although all the patients in our series were anticoagulated with heparin, no case of severe effusion or tamponade was found. This is the basis of our belief that there are no grounds to routinely withdraw or reduce the dosage of heparin when mild or moderate PE is discovered during the course of AMI.

In conclusion, the present study shows that (1) PE is a common occurrence in patients with AMI; (2) owing to its small size, PE has a subclinical evolution that does not influence prognosis; (3) PE is present early in the course of AMI, but its reabsorption is slow; (4) PE should not be considered a secondary manifestation of pericarditis, and (5) mild or moderate PE should not, by itself, lead to a modification in the dosage of heparin.

We are indebted to the members of the Coronary Care Unit and to Cardiac Surgery Service for allowing us to study their patients and for their collaboration.

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