Clinical Correlates of PR-Segment Depression in Asymptomatic Patients With Pericardial Effusion

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OBJECTIVES
The purpose of this study was to determine the clinical correlates of PR-segment depression among consecutive asymptomatic patients with pericardial effusion (PE) detected by routine echocardiography.

BACKGROUND
Pericardial effusion is a relatively common finding in clinical practice, but not many studies have evaluated electrocardiographic (ECG) changes associated with the occurrence of PE. Among 4,061 consecutive patients referred to our echocardiography laboratory, 176 asymptomatic patients had PE correlated with their clinical history and ECG findings.

RESULTS
PR-segment depression was detected in 40 patients (23%). There were no significant differences in age, gender distribution or heart rate between patients with and without PR-segment depression. Fifteen post-pericardiotomy patients (33%), 19 patients (40%) with malignant disease and 6 patients (46%) with connective tissue disease had PR-segment depression, whereas no patient with heart disease (dilated cardiomyopathy, hypertensive heart disease, old myocardial infarction, valvular heart disease), renal disease or hypothyroidism had PR-segment depression, nor widespread ST-segment elevation. Among 40 patients with PR-segment depression, 8 had ST-segment elevation in the leads of epicardial derivation, 8 had upright T waves, 20 had low to inverted T waves with an isoelectric ST-segment and 4 had ST-T-wave changes due to bundle branch block.

CONCLUSIONS
PR-segment depression was a relatively common ECG sign associated with clinically silent PE, and it was an ECG indicator of inflammatory pericardial involvement. (J Am Coll Cardiol 2002;39:2000–4) © 2002 by the American College of Cardiology Foundation

Pericardial effusion (PE) is a relatively common finding in clinical practice; echocardiography is the procedure of choice for detecting PE. Although PE demonstrated by echocardiography may indicate fluid retention, this is not diagnostic of pericardial injury (1). Pericardial rub and stage I ST-segment elevation (ST-segment elevation in all leads except aVR and V₁) are two specific signs of pericardial inflammation (1,2). PR-segment depression is almost as characteristic as the classic ST-segment deviation and is detected in most patients with pericarditis (3,4). Moreover, PR-segment depression is observed longer after acute pericardial injury, when the ST-segment has already returned to baseline (2). However, not many studies have evaluated electrocardiographic (ECG) changes associated with the occurrence of PE. Accordingly, we designed a study to evaluate the frequency and clinical correlates of PR-segment depression in patients with PE detected by routine echocardiography.

METHODS
Patients. Among 4,061 consecutive patients who were referred to our echocardiography laboratory between November 10, 1997 and May 9, 2001, we studied 176 clinically stable asymptomatic patients (age 19 to 89 years) with PE who were in sinus rhythm. Exclusion criteria were sinus tachycardia (>120/min) and P-wave abnormalities. The study procedure was approved by the institutional review board of Kochi Medical School.

Echocardiography. M-mode and two-dimensional echocardiography was performed with a Toshiba SSH 160A phased-array sector scanner (Toshiba Co. Ltd., Tokyo, Japan), with a 3.75- or 2.5-MHz transducer used by an experienced echocardiographer. Echocardiography was performed with the patients in the 45° left lateral decubitus position, and all classic views were recorded on videotape for subsequent analysis by observers who were unaware of the ECG data. Anterior and posterior PE were measured as the maximal diastolic epicardial-pericardial separation recorded at the level of the tip of the mitral valve. However, anterior separation was considered representative of effusion only in the presence of a posterior echo-free space. Pericardial effusion was classified as small (pattern C; <10 mm), moderate (pattern D; 10 to 20 mm) or large (pattern D; >20 mm), as described by Horowitz et al. (5) and Weitzman et al. (6). A detailed chart review was performed to assess the most likely causes of PE in each patient.

Electrocardiography. A 12-lead ECG was obtained on the day of echocardiography. Atrial repolarization was assessed by studying the PR-segment with a magnifying glass. At least 0.5 mm of PR-segment depression from the TP segment in both the limb (more than two leads in leads I, II, aVL and aVF) and precordial leads (more than two leads in
leads V₃ through V₆) was considered diagnostic of PR-segment depression. ST-segment elevation was defined as 0.5 mm or more from the TP segment in both the limb and precordial leads. PR-segment and ST-segment deviations were considered present only after diagnosed by two cardiologists who had no knowledge of the clinical findings. A P-wave abnormality in the standard leads was diagnosed when one or more of the following findings were made: 1) P-wave configuration other than the rounded form normally seen (notched, peaked or other abnormal configurations); 2) amplitude of ≥0.2 mm in lead II; and 3) duration of >100 ms in any lead.

**Statistical analysis.** Results are presented as the mean value ± SD. A statistical analysis between the two groups was performed by the Student t test for continuous variables and the Fisher exact probability test for discrete variables. A p value <0.05 was considered significant.

**RESULTS**

**Clinical characteristics.** Table 1 summarizes the causes of PE in 176 patients. One hundred fifty patients had minor PE, 20 patients had moderate PE and 6 patients had major PE. No patient had clinical or echocardiographic evidence of cardiac tamponade.

**PR-segment depression.** Among 176 patients with PE, PR-segment depression was detected in 40 patients (23%). There were no significant differences in age, gender distribution, heart rate or the amount of PE between patients with and without PR-segment depression (Table 2). Fifteen post-pericardiotomy patients (33%), 19 patients (40%) with malignant disease and 6 patients (46%) with connective tissue disease had PR-segment depression. The time from pericardiotomy to echocardiography was three to six weeks in patients with PR-segment depression, and it was one week to six months in patients with no PR-segment depression. No patient with primary heart disease (e.g., dilated cardiomyopathy, hypertensive heart disease, old myocardial infarction (MI), valvular heart disease), chronic renal failure, nephrotic syndrome or hypothyroidism had PR-segment depression.

**ST-T–wave changes.** Among 105 patients with PE associated with pericardiotomy, malignant disease or connective tissue disease, 8 had ST-segment elevation and PR-segment depression in the leads of epicardial derivation, consistent with the stage I ECG change of pericarditis, 8 had upright T waves with PR-segment depression (early stage II ECG change) and 20 had low to inverted T waves with PR-segment depression (late stage II ECG change) (Figs. 1 and 2, Table 3). In contrast, 12 patients had low to inverted T waves with an isoelectric PR segment (late stage II ECG change), 4 had inverted T waves with an isoelectric PR segment (stage III ECG change) and 26 had normal ST-T waves with an isoelectric PR segment (stage IV ECG change). Primary widespread ST-T–wave changes were not determined in 27 patients, because of bundle branch block, old MI or left ventricular (LV) hypertrophy. Interestingly, four patients with ST-T waves due to bundle branch block had PR-segment depression. No patient with primary heart disease, chronic renal failure, nephrotic syndrome or hypo-

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**Table 1. Etiology of Pericardial Effusion (n)**

<table>
<thead>
<tr>
<th>Heart disease</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dilated cardiomyopathy</td>
<td>11</td>
</tr>
<tr>
<td>Hypertensive heart disease</td>
<td>13</td>
</tr>
<tr>
<td>Old myocardial infarction</td>
<td>19</td>
</tr>
<tr>
<td>Valvular heart disease</td>
<td>11</td>
</tr>
<tr>
<td>Post-pericardiotomy</td>
<td></td>
</tr>
<tr>
<td>Coronaery artery bypass graft</td>
<td>30</td>
</tr>
<tr>
<td>Valvular heart disease</td>
<td>8</td>
</tr>
<tr>
<td>Dissecting aneurysm</td>
<td>2</td>
</tr>
<tr>
<td>Atrial septal defect</td>
<td>5</td>
</tr>
<tr>
<td>Malignant disease</td>
<td></td>
</tr>
<tr>
<td>Lung cancer</td>
<td>9</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>3</td>
</tr>
<tr>
<td>Gastrointestinal cancer</td>
<td>8</td>
</tr>
<tr>
<td>Other cancers</td>
<td>21</td>
</tr>
<tr>
<td>Leukemia</td>
<td>6</td>
</tr>
<tr>
<td>Connective tissue disease</td>
<td></td>
</tr>
<tr>
<td>SLE</td>
<td>6</td>
</tr>
<tr>
<td>Dermatomyositis</td>
<td>2</td>
</tr>
<tr>
<td>PSS</td>
<td>1</td>
</tr>
<tr>
<td>RA</td>
<td>2</td>
</tr>
<tr>
<td>Overlap syndrome</td>
<td>2</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>10</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>3</td>
</tr>
<tr>
<td>Nephrotic syndrome</td>
<td>4</td>
</tr>
</tbody>
</table>

PSS = progressive systemic sclerosis; RA = rheumatoid arthritis; SLE = systemic lupus erythematosus.
thyroidism had ST-T waves changes suggestive of acute pericarditis.

DISCUSSION

Echocardiography is the most accurate noninvasive tool to detect PE; however, to date, echocardiographic reports have concentrated on describing the sensitivity of quantification of PE, and surprisingly few studies have considered the prevalence of diagnostic ECG changes in patients with PE. Among clinically stable patients referred to our echocardiography laboratory for cardiac assessment, we found that 23% of patients with silent PE had PR-segment depression, in contrast to the low incidence of widespread ST-segment elevation (5%). These data indicate that the incidence of PR-segment depression is not rare in patients with clinically silent PE.

Pericardial fluid. Myocardial interstitial fluid is reported to be the source of pericardial fluid that drains to the subepicardium, and pericardial fluid, regardless of the cause, arises primarily from the epicardial surface of the heart (7). Two major pathophysiologic bases for the accumulation of excessive pericardial fluid have been reported: pericardial inflammation and fluid retention due to hemodynamic factors (hydropericardium) (1). In this study, 54 patients had PE primarily associated with the diagnosis of heart disease; 45 patients had PE associated with pericardiotomy; and the primary disease was noncardiac in 77 patients. The patients with PE associated with chronic heart disease, hypothyroidism or renal disease had neither widespread PR-segment depression nor ST-segment elevation suggestive of pericarditis. Fluid flux at the level of the microvascular membrane into the interstitium is governed by hydrostatic and osmotic pressures generated in the microvessels and interstitium. Therefore, the factors related to the occurrence of noninflammatory PE are hemodynamic, as well as a combination of increased capillary permeability, lymphatic obstruction, lower colloid osmotic pressure and/or sodium and water retention. Most of the PE in hypothyroidism is caused by transudates, whereas uremic pericardial inflammation is caused by uremic exudates;

Figure 1. Electrocardiogram of a patient judged to have PR-segment depression with ST-segment elevation. Note the downward displacement of the PR segment in both the limb and precordial leads.
however, uremic pericarditis is unique in that inflammatory cells do not penetrate the myocardium (8). Thus, it is not surprising to find an absence of customary widespread ST-T-wave changes or PR-segment depression of subepicardial myocarditis in patients with chronic renal failure and hypothyroidism.

**PR-segment deviations.** The diagnosis of acute pericarditis requires typical widespread J-ST-segment elevation (stage I ECG changes), but stage I ECG changes are frequently not recorded, and nearly half of the patients with acute pericarditis of mixed causes have a variation in the typical ECG evolution of acute pericarditis (8,9). PR-segment depression is also known to be one of the typical ECG changes associated with acute pericarditis (3,4). Pericarditis, sympathetic stimulation and left atrial overloading due to LV failure are some of the geneses of PR-segment

![Electrocardiogram of a patient judged to have PR-segment depression with low to inverted T waves. Note the downward displacement of the PR segment in both the limb and precordial leads.](image)

**Figure 2.**

**Table 3.** PR-segment Deviation and ST-T-Wave Changes

<table>
<thead>
<tr>
<th>ST Segment</th>
<th>T Waves</th>
<th>PR Segment</th>
<th>Post-Pericardiotomy (n)</th>
<th>Malignancy (n)</th>
<th>Connective Tissue Disease (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated</td>
<td>upright</td>
<td>depressed</td>
<td>1</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Isoelectric</td>
<td>upright</td>
<td>depressed</td>
<td>3</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
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<td>low to flat</td>
<td>depressed</td>
<td>9</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>Isoelectric</td>
<td>inverted</td>
<td>isoelectric</td>
<td>4</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Isoelectric</td>
<td>upright</td>
<td>isoelectric</td>
<td>8</td>
<td>13</td>
<td>5</td>
</tr>
<tr>
<td>undetermined†</td>
<td>depressed</td>
<td></td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>undetermined†</td>
<td>isoelectric</td>
<td></td>
<td>14</td>
<td>8</td>
<td>1</td>
</tr>
</tbody>
</table>

*Leads of epicardial derivation: leads I, II, aVL, aVF and V3–6. †Undetermined: ST-T-wave changes due to bundle branch block, old myocardial infarction or left ventricular hypertrophy.
depression (10,11). The ECG changes produced by hyper-
sympathetic activity are characterized by concordant PR-
and ST-segment depressions (the PR and ST-segments are
in the arcs of circumference with the same radius) (10).
However, none of our patients had concordant PR- and
ST-segment deviations, and there was no significant dif-
ference in the heart rate between patients with and without
PR-segment depression. Considering the fact that all of the
patients with widespread PR-segment depression were at
three to six weeks post-pericardiotomy or had malignant
disease or connective tissue disease indicates that PR-
segment depression in our patients reflects abnormal atrial
repolarization due to atrial inflammation.

Diagnostic considerations. The diagnostic significance of
PR-segment depression in patients with pericardial involve-
ment is that PR-segment depression is detected longer after
the ST-segments return to baseline and could be diagnosed
in patients with ST-segment changes due to bundle branch
block, MI or LV hypertrophy. Post-pericardiotomy syn-
drome develops within days to a month after the operation.
The effect of anti-heart antibody in producing pericardial
inflammation is proportional to the extent of surgical repair,
but the anti-heart antibody appears to be pathogenetic in
the presence of a viral infection (2,8). Although a small to
moderate amount of PE is often observed in post-
pericardiotomy syndrome, widespread ST-segment eleva-
tion suggestive of pericarditis is rarely seen (8). Our study
is consistent with the observation that widespread ST-
segment elevation was detected in only one patient (2%).
However, pericardial inflammation could be diagnosed
more frequently by PR-segment depression in post-
pericardiotomy patients.

Pericarditis is a common cardiac manifestation of auto-
immune disease. The inflammatory process associated with
epicardial microvasculitis may increase the production of
pericardial fluid by a loss of interstitial fluid from the
myocardium to the pericardial space. Metastatic and mul-
ticentric malignancy can also affect the pericardium and
pericardium is reported to be involved in 5% to 15% of
patients with malignant neoplasm at autopsy (12,13).
Asymptomatic pericardial effusions in patients with malign-
ant neoplasm could be due to malignant pericardial in-
volvement, impaired lymphatic drainage or nonmalignant
causes, such as previous radiation, chemotherapy and infec-
tion. In contrast to the 12% incidence of widespread
ST-segment elevation in patients with PE due to connective
tissue disease or malignant disease, 42% had PR-segment
depression. Moreover, 20 of 32 patients with an isoelectric
ST-segment and low to inverted T-waves (late stage II
ECG change of acute pericarditis) had PR-segment depres-
sion, indicating that patients whose ECG was recorded first
in late stage II may only show widespread PR-segment
depression due to subepicardial atrial inflammation associ-
ated with inflammatory pericardial fluid retention.

Conclusions. PR-segment depression was a relatively
common ECG sign associated with clinically silent PE, and
it was an ECG indicator of inflammatory pericardial in-
volvement.

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