Clinical and prognostic importance of persistent precordial (V₁-V₄) electrocardiographic ST segment depression in patients with inferior transmural myocardial infarction

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ABSTRACT Forty-three consecutive patients with acute inferior transmural myocardial infarction but no history or electrocardiographic evidence of prior myocardial infarction were evaluated prospectively to assess the clinical and prognostic importance of persistent precordial (V₁-V₄) ST segment depression. Patients were evaluated within 24 hr of admission by history, physical examination, cardiac enzyme levels, right heart catheterization, and radionuclide angiography; all were followed for 1 year. Ten of the 43 patients (group I) had persistent anterior precordial ST segment depression, defined as 1 mm or greater in one or more precordial leads (V₁-V₄) 24 hr after admission to the coronary care unit, and 33 patients (group II) did not. Clinical variables that differed between groups I and II, respectively, included mean age (67 ± 9 [± 1 SD] vs 59 ± 8 years; p < .01), incidence of Killip class II to IV (100% vs 33%; p < .001), and average peak creatine kinase concentration (2878 ± 1139 vs 1511 ± 1034 IU/liter; p < .001). Hemodynamic differences between groups I and II included a higher pulmonary arterial wedge pressure (19 ± 4 vs 11 ± 5 mm Hg; p < .001) and a lower cardiac index (2.0 ± 0.5 vs 2.6 ± 0.7 liters/min/m²; p < .05). An evaluation of left ventricular ejection fraction and wall motion index by radionuclide angiography showed that group I had a lower ejection fraction (44 ± 11% vs 53 ± 10%; p < .05) and higher wall motion index (1.7 ± 0.4 vs 1.4 ± 0.3; p < .05) compared with group II. Prognostically, group I had a higher incidence of recurrent myocardial infarction (30% vs 0%; p < .01) and a higher 1 year mortality (60% vs 0%; p < .001). Univariate analysis revealed that several clinical, electrocardiographic, hemodynamic, and radionuclide angiographic variables were predictive of 1 year mortality, with persistent precordial ST segment depression being the most powerful (r = .73). Multivariate analysis was used to determine which variables had independent value for predicting death within 1 year. The most important variables were persistent precordial ST depression followed by elevated heart rate. No other variables added to this combination improved their predictive value (r = .82). We conclude that patients with their first acute inferior transmural myocardial infarction who have persistent precordial (V₁-V₄) ST segment depression have clinical, hemodynamic, and noninvasive evidence of decreased left ventricular performance and a high 1 year mortality.


THE PATHOGENETIC, clinical, and prognostic implications of precordial electrocardiographic ST segment depression during an acute inferior transmural myocardial infarction are controversial.¹,² The report-
The high incidence of precordial ST segment depression early during an acute inferior myocardial infarction may explain some of the controversy concerning its usefulness for identifying high-risk subgroups. We have also noted a variable time course in the resolution of this electrocardiographic abnormality. No prior study has used early clinical, hemodynamic, and noninvasive assessment of left ventricular function to evaluate prospectively whether this electrocardiographic finding also is of prognostic value in patients with inferior myocardial infarction. The purpose of this investigation was to test the hypothesis that precordial (V₃₋V₄) ST segment depression, which persists for 24 hr or longer in patients with their first acute inferior transmural myocardial infarction, identifies a high-risk subgroup.

Methods

Patient selection. The study population consisted of patients admitted consecutively to the Coronary Care Unit of the Veterans Administration Hospital in San Antonio, who were studied prospectively if they satisfied the following criteria: (1) acute inferior transmural myocardial infarction diagnosed by chest pain lasting 30 min or longer with evolution of diagnostic Q waves and a characteristic rise and fall of serum creatine kinase (CK) and CK-MB isoenzyme levels, (2) no history or electrocardiographic evidence of prior myocardial infarction, (3) absence of valvular, congenital, or cardiomyopathic heart disease or history of coronary artery bypass surgery, (4) absence of bundle branch block, (5) absence of left or right ventricular hypertrophy by standard electrocardiographic criteria, and (6) absence of a permanent pacemaker.

Over a 2 year period a total of 43 patients met these criteria and were studied after written informed consent was obtained according to a protocol approved by our institutional review board. These patients represent a subgroup of 53 patients previously reported from a study designed to evaluate the detection of right ventricular infarction.24-25 The patients were all men with a mean age of 61 years (range 46 to 86). The therapeutic regimen at the time of study included β-adrenergic blocking drugs in five patients and nitrates in two patients. No patients were receiving digitalis or other drugs that are known to alter ST segments, and none received thrombolytic therapy. All clinical, hemodynamic, and noninvasive studies were completed between the initial ECG and the ECG obtained 24 hr after admission and within 36 hr of the onset of symptoms.

Clinical evaluation. A detailed clinical history and physical examination were obtained from each patient by one or more staff cardiologists after admission to the coronary intensive care unit. The following variables were evaluated: age, previous history of angina pectoris, jugular venous distension, presence of a left-sided third heart sound (S₃), and rales. Patients were assigned by clinical criteria to Killip classes I to IV.29 In each patient, serial blood samples were obtained for serum CK determination and fractionated for CK-MB isoenzyme.30

Electrocardiographic evaluation. The ECGs obtained on admission and 24 hr after admission to the coronary care unit were evaluated by an investigator with no knowledge of the patient’s clinical or laboratory data. ECGs were recorded at a paper speed of 25 mm/sec and a sensitivity of 1 mm = 0.1 mV. ST segment elevation and depression were measured 80 msec after the J point. Measurements from 3 consecutive beats were averaged for each lead studied, and an abnormal ST shift was considered present if the lead demonstrated 1 mm or greater elevation or depression. The ST segment changes for each lead were then grouped and totaled into summed inferior (II, III, aVF) ST segment elevation and summed anterior precordial (V₁₋V₄) ST segment depression. These measurements were performed on the admission ECG and on the ECG taken routinely 24 hr after admission.

Hemodynamics. Right heart catheterization was performed in all 43 patients with a balloon-tipped, flow-directed thermodilution catheter. With a Statham P23Db transducer leveled at the midchest, calibrated recordings of mean right atrial (RA), mean pulmonary arterial pressure (PA), and mean pulmonary arterial wedge pressures (PAWP) were recorded. Systolic and diastolic blood pressures (SBP and DBP) were measured with a cuff sphygmomanometer. Heart rate was determined from a simultaneously recorded ECG. Cardiac output (CO, liters/min) was determined in triplicate by the thermodilution technique. From these data, cardiac index (CI, liters/min/m²), stroke volume index (SVI, ml/m²), mean arterial pressure (MAP, mm Hg), left ventricular stroke work index (LWVI, g-m/m²), systemic and pulmonary vascular resistance (SVR and PVR, dyne-sec-cm⁻⁵) were calculated:

\[ CI = \frac{CO}{BSA} \]
\[ SVI = \left(\frac{CL}{HR}\right) \times 1000 \]
\[ MAP = \left(\frac{SBP + 2 \times DBP}{3}\right) \]
\[ LVSVI = \frac{SVI \times (MAP - PAWP)}{0.0136} \]
\[ SVR = \left[\frac{(MAP - RA)}{CO}\right] \times 80 \]
\[ PVR = \left[\frac{(PA - PAWP)}{CO}\right] \times 80 \]

where BSA is the body surface area (m²).

Radionuclide angiography. Good-quality gated equilibrium radionuclide angiographic images were obtained in the anterior and 45 degree left anterior oblique projections in 41 of the 43 patients (95%) after injection of 20 mCi of technetium-99m-labeled human serum albumin. Two patients died before radionuclide studies were performed. Images were acquired under electrocardiographic control with a single-crystal gamma scintillation camera (Ohio Nuclear 420). Count information in consecutive corresponding 40 msec segments of each cardiac cycle was summed and stored as images until each frame contained at least 300,000 counts. Nine-point spatial smoothing was performed on each image. A semiautomated edge detection program defined a left ventricular region of interest for each left anterior oblique image. From these left ventricular regions of interest, a left ventricular time-activity curve was generated after background (obtained manually from a left ventricular end-diastolic paraventricular region of interest) was subtracted. The left ventricular ejection fraction was calculated by subtracting end-systolic from end-diastolic counts and dividing by end-diastolic counts × 100. This radionuclide angiographic method of obtaining left ventricular ejection fraction has been previously validated in our laboratory in comparison with biplane cineangiography (correlation coefficient \( r = 0.93 \)).31 Right ventricular ejection fraction was calculated according to the method of Maddahi et al.32

Left ventricular wall motion was analyzed by an independent observer with no knowledge of the patient’s clinical status. Seven corresponding segments were identified and each was evaluated for the degree of dysynergy. The seven left ventricular regions for wall motion analysis were anterobasilar, anterior, apical, inferior, inferobasilar, septal, and posterolateral. Wall motion was scored from 1 to 4 as follows: 1 = normal, 2 = hypokinesis, 3 = akinesia, 4 = dyskinesis. The scores of all identified segments for each patient were then added, and the total score was divided by the total number of segments visualized to obtain a left ventricular wall motion index.33 In the 41
patients in whom high-quality radionuclide angiograms were obtained, 274 (95%) of the possible 287 left ventricular segments were analyzed.

Clinical follow-up. All patients were followed regularly for 1 year. The clinical variables evaluated during follow-up included angina pectoris, cardiac catheterization, coronary artery bypass surgery, recurrent myocardial infarction, and cardiac death.

Statistical analysis. Continuous data are presented as the mean ± 1 SD and were compared between patient groups by unpaired t tests. Dichotomous data were analyzed by chi-square tests with Yate's correction or Fischer's exact tests. The survival distribution between patient groups was given by the Kaplan-Meier product-limit estimate and was compared by the Mantel-Cox statistic.4 Differences between groups were considered significant when a p value of .05 or less was observed. All clinical, electrocardiographic, hemodynamic, and radionuclide angiographic variables evaluated were considered individually by univariate analysis to determine their association with 1 year mortality by computing a Pearson's correlation matrix. Then a stepwise multivariate analysis was performed to determine the optimal ordering of variables for predicting 1 year mortality.4

Results

Patient groups. Group I patients (n = 10) had summed anterior precordial (V₁-V₄) ST segment depression of 1 mm or greater that persisted for at least 24 hr, whereas group II (n = 33) did not. The typical electrocardiographic patterns from the two groups are shown in figure 1. The mean summed anterior precordial ST segment depression on the initial ECG was higher in group I (8.6 ± 2.4 mm) compared with that in group II (1.3 ± 2.5 mm; p < .001). All patients in group I had 4 mm or greater summed anterior precordial ST segment depression on their initial ECG compared with only four of the 33 patients (12%) in group II (p < .01). The mean summed anterior precordial ST segment depression on the 24 hr ECG in group I was 6.4 ± 2.6 mm and by definition it was 0 mm in group II.

There was only a weak linear correlation between the summed inferior (II, III, aVF) ST segment elevation and the summed anterior precordial ST segment depression on the initial ECG (r = .53, p = .05). There was no significant correlation when the 24 hr ECGs were evaluated in a similar manner.

Clinical variables. The clinical variables that differed between the groups are shown in figure 2. Group I patients were older than group II patients (67 ± 9 vs 59 ± 8 years; p < .01). Rales on physical examination were more frequent in group I as compared with group II (80% vs 33%; p < .05). In addition, the presence of a left ventricular third heart sound (S₃) was more com-
mon in group I (90% vs 36%; p < .01). As a result, all patients in group I were classified in Killip class II or higher as compared with only 33% of patients in group II (p < .001). Furthermore, peak CK level was higher in group I (2878 ± 1139 vs 1511 ± 1034 IU/liter; p < .001). There was no difference between the two groups with regard to a history of prior angina pectoris or jugular venous distension.

**Hemodynamic variables.** Selected hemodynamic variables are shown in figure 3. Systolic blood pressure was lower in group I compared with group II (117 ± 11 vs 130 ± 16 mm Hg; p < .05). Pulmonary arterial wedge pressure was higher in group I (19 ± 4 vs 11 ± 5 mm Hg; p < .001). Cardiac index was lower in group I (2.0 ± 0.5 vs 2.6 ± 0.7 liters/min/m²; p < .05), as were the stroke volume index (23 ± 8 vs 35 ± 9 ml/m²; p < .001) and left ventricular stroke work index (25 ± 9 vs 43 ± 12 g-m/m²; p < .001). There was no significant difference between the two groups with regard to mean heart rate, systemic vascular resistance, or pulmonary vascular resistance.

**Radionuclide angiographic variables.** The radionuclide angiographic variables are displayed in figure 4. Group I patients had a lower left ventricular ejection fraction compared with group II patients (44 ± 11% vs 53 ± 10%; p < .05). Group I patients had a higher left ventricular wall motion index (1.7 ± 0.4 vs 1.4 ± 0.3; p < .05). When regional wall motion was analyzed, group I tended to have a higher incidence of posterolateral wall motion abnormalities compared with group II (63% vs 27%), although this did not reach statistical significance (p = .07). There were no differences in individual wall motion abnormalities in any of the other segments. There was no significant difference in right ventricular ejection fraction between the groups.

**Follow-up data.** Group I had a higher recurrent myocardial infarction rate compared with group II (30% vs 0%; p < .01) and a higher 1 year mortality rate (60% vs 0%; p < .001). All deaths in group I occurred within 3 months of acute myocardial infarction. These data are displayed in figure 5. There were no significant differences between the two groups with regard to postinfarction angina pectoris, cardiac catheterization, or coronary artery bypass surgery.

To further define which variables were most useful prognostically, univariate and multivariate analysis was performed. The univariate correlation of each variable evaluated in this study with 1 year mortality is displayed in table 1. There were several clinical, elec-

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**FIGURE 2.** Clinical variables that differed between patients in groups I and II.

**FIGURE 3.** Hemodynamic variables for patients in groups I and II. BP = blood pressure; PAWP = pulmonary arterial wedge pressure; LV = left ventricular.
trocardiographic, hemodynamic, and radionuclide angiographic variables that were individually predictive of death within 1 year. The optimal ordering of these variables by stepwise multivariate analysis revealed that persistent precordial ST segment depression followed by an elevated heart rate were the only independent predictors of cumulative 1 year mortality ($r = .82$). No other clinical, electrocardiographic, hemodynamic, or radionuclide angiographic variables added to this combination to improve their predictive value.

Discussion

Patients without a prior history of myocardial infarction who sustain an acute inferior transmural myocardial infarction in general represent a group of patients with a favorable prognosis compared with patients who sustain an acute anterior transmural myocardial infarction. However, there are subgroups of patients with acute inferior wall myocardial infarction who do not have such a good prognosis. It would be clinically useful to identify such a high-risk subgroup of patients.

![FIGURE 4](image-url) Noninvasive assessment of ventricular function and left ventricular wall motion index (LVWMI) for patients in groups I and II. LVEF = left ventricular ejection fraction; RVEF = right ventricular ejection fraction.

![FIGURE 5](image-url) Follow-up data between the patients in groups I and II. Left, Incidence of recurrent myocardial infarction ≤ 90 days and 90 day mortality. Right, Cumulative survival of patients through 1 year in groups I and II.

### TABLE 1

Univariate analysis of variables for predicting 1 year mortality

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<tr>
<th>Variable</th>
<th>Correlation coefficient for death</th>
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<td>Clinical</td>
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<td>≥1 mm 24 hr after admission</td>
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<tr>
<td>≥4 mm at admission</td>
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<td>≥1 mm at admission</td>
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<td>Hemodynamic</td>
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<td>Left ventricular stroke work index</td>
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<td>Stroke volume index</td>
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<td>Pulmonary vascular resistance</td>
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<td>Mean pulmonary arterial wedge pressure</td>
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<tr>
<td>Cardiac index</td>
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<td>Systemic vascular resistance</td>
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<td>Systolic blood pressure</td>
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<td>Radionuclide angiographic</td>
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<tr>
<td>Left ventricular ejection fraction</td>
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<td>.033</td>
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<tr>
<td>Left ventricular wall motion index</td>
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<td>.036</td>
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<tr>
<td>Right ventricular ejection fraction</td>
<td>-.18</td>
<td>.262</td>
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with their first inferior myocardial infarction for possible early intervention.

**Initial precordial ST segment depression.** Shah et al.\(^1\) first described the clinical and prognostic implications of precordial ST segment depression during acute inferior transmural myocardial infarction. They reported that this abnormality on the admission ECG identified a high-risk subgroup of patients with inferior infarction. Since that study, there has been much controversy over the pathogenesis and prognostic significance of this electrocardiographic finding.\(^1\)-\(^25\) Some studies have shown that this abnormality identifies a high-risk subgroup of patients with inferior transmural myocardial infarction who have a worse clinical course,\(^1\)-\(^18\) whereas others have failed to confirm these findings and suggest that it represents a transient event commonly seen with inferior infarction.\(^19\)-\(^23\) Three different mechanisms have been proposed for this acute electrocardiographic abnormality: (1) extensive inferior or additional posterior wall infarction,\(^1\)-\(^13\) (2) concomitant anterior wall ischemia,\(^14\)-\(^18\) or (3) reciprocal changes secondary to inferior infarction.\(^19\)-\(^23\) Thus the clinical significance as well as the mechanism for this finding remain highly debated.

The controversy in the literature may be attributable to differences in study design, including patient inclusion criteria, the leads used to define precordial ST segment depression, and the magnitude of these changes. With regard to patient inclusion criteria, not all studies excluded patients with prior myocardial infarction,\(^14\),\(^15\),\(^21\) and some were retrospective.\(^14\)-\(^16\) Moreover, there was a wide variability in the ECG leads used to define precordial ST segment depression. Some studies used \(V_1-V_9\),\(^10\) \(V_2-V_4\),\(^2\) \(V_6-V_{10}\),\(^3\),\(^5\)-\(^7\),\(^9\),\(^11\),\(^21\),\(^23\),\(^24\) or \(V_1-V_{12}\),\(^1\),\(^4\),\(^8\),\(^18\) while others included leads I and/or aVL.\(^12\),\(^14\),\(^15\)-\(^17\),\(^19\),\(^20\),\(^22\),\(^25\)

Lew et al.\(^9\) have recently shown that there is a strong linear correlation between the magnitude of inferior ST segment elevation to ST segment depression in aVL (\(r = .88\)) during inferior myocardial infarction. This suggests that ST segment depression in aVL is predominantly a reciprocal phenomenon and may weaken data when included with the precordial leads. One final difference in study design was that the magnitude of the summed ST segment depression defined as being abnormal varied widely from one study to the next, ranging from 1 to 4.5 mm or greater.

Another factor that differed among various studies was the reported incidence of ST segment depression, which ranged from 50%\(^22\) to 100%.\(^20\) This variable incidence may have been due to the electrocardiographic criteria used as well as to the variable time course for resolution of this abnormality, since studies in which the ECG was available early after the onset of chest pain reported a much higher incidence of precordial ST segment depression than those in which the ECG was obtained at a later time. Thus, considering the marked differences in study design, it is not surprising that there has been controversy concerning the incidence and significance of precordial ECG ST segment depression during acute inferior myocardial infarction.

**Persistent precordial ST segment depression.** Precordial ST segment depression frequently is present on the admission ECG in patients with acute inferior myocardial infarction; it resolves in some patients within 24 hr after admission but persists in others. Our data have shown that patients with persistent precordial (\(V_1-V_4\)) ST segment depression have a greater magnitude of initial summed precordial ST segment depression compared with those without persistent precordial ST segment depression. Moreover, patients with persistent precordial ST segment depression during a first inferior transmural myocardial infarction frequently had clinical evidence of decreased left ventricular function manifest by a significantly higher incidence of pulmonary rales, a third heart sound, a higher Killip class, and a higher peak serum CK level. These clinical findings correlated with hemodynamic evidence of decreased left ventricular function, manifest by a higher pulmonary arterial wedge pressure and a lower cardiac index. Worse left ventricular performance was also manifest in these patients by a lower left ventricular ejection fraction and a higher left ventricular wall motion index.

The prognosis after a first acute inferior transmural myocardial infarction was related to the persistence of this electrocardiographic abnormality. There was a higher incidence of reinfarction, and six of the 10 patients with persistent precordial ST segment depression died within 1 year. By contrast, all 33 patients who did not have persistent precordial ST segment depression were alive at 1 year. In addition, when all clinical, electrocardiographic, hemodynamic, and radionuclide angiographic variables were considered, persistent precordial ST segment depression had the highest univariate correlation with death within 1 year. Furthermore, multivariate analysis revealed that only this electrocardiographic finding and the initial heart rate had independent predictive power in identifying patients at risk for 1 year mortality.

**Conclusions.** We conclude that precordial (\(V_1-V_4\)) ST segment depression, persisting for at least 24 hr, identifies a high-risk subgroup of patients with acute inferior or transmural myocardial infarction. There is clinical,
hemodynamic, and noninvasive evidence that this electrocardiographic abnormality is associated with more extensive myocardial damage. In addition, there is a significantly higher incidence of recurrent myocardial infarction and a 60% mortality rate within 90 days in this subgroup. This high-risk subgroup of patients has a significantly higher magnitude of summed precordial (V1-V4) ST segment depression on their initial ECG compared with those patients who did not have these persistent electrocardiographic changes. Thus the initial magnitude of the precordial (V1-V4) ST segment depression helps to identify a high-risk subgroup of patients with inferior myocardial infarction at the time of admission, and the persistence of these changes at 24 hr subselects those patients at highest risk for further cardiac events.

References

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