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Prognostic Significance of Precordial ST Segment Depression During Inferior Myocardial Infarction in the Thrombolytic Era: Results in 16,521 Patients

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Objectives. **We examined the prognostic significance of precordial ST segment depression among patients with an acute inferior myocardial infarction.**

Background. **Although precordial ST segment depression has been associated with a poor prognosis, this correlation has not been adequately quantified, partly because of small sample sizes and methodologic limitations in previous studies.**

Methods. **We examined the clinical and angiographic outcomes of 16,521 patients with an acute inferior myocardial infarction who underwent thrombolysis in the Global Utilization of Streptokinase and t-PA for Occluded Coronary Arteries (GUSTO-I) study. Patients were classified into those without precordial ST segment depression (n = 6,422 [38.9%]), those with ST segment depression in leads V_1 to V_3 only (n = 5,850 [35.4%]), those with ST segment depression in leads V_4 to V_6 only (n = 876 [5.3%]) and those with ST segment depression in both leads V_1 to V_3 and leads V_4 to V_6 (n = 3,373 [20.4%]) on initial electrocardiography. Outcome measures included postinfarction complications (second- or third-degree heart block, congestive heart failure or shock) and 30-day and 1-year mortality.**

Results. **Patients with precordial ST segment depression had larger infarctions, more postinfarction complications and a higher mortality rate than those without precordial ST segment depression (4.7% vs. 3.2% at 30 days; 5.0% vs. 3.4% at 1 year; both $p < 0.001$), regardless of whether ST segment depression was noted in leads V_1 to V_6 or in leads V_4 to V_6. The magnitude of precordial ST segment depression (sum of leads V_1 to V_6) added significant independent prognostic information after adjustment for clinical risk factors; the risk of 30-day mortality increased by 36% for every 0.5 mV of precordial ST segment depression.**

Conclusions. **Assessment of the magnitude of precordial ST segment depression is useful for acute risk stratification in patients with an inferior myocardial infarction.**

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In 1980, Shah et al. (1) first reported that precordial ST segment depression was a marker for increased risk in patients with an inferior myocardial infarction. Since then, its pathogenesis and prognostic importance have been heavily debated (2–39). Three potential etiologies for precordial ST segment depression have been proposed: 1) that it represents purely "reciprocal changes" resulting from inferior ST segment elevation; 2) that it results from anterior myocardial ischemia during an inferior infarction, and thus is a marker for multivessel coronary artery disease; or 3) that it results from a more extensive inferior infarction involving the posterolateral wall or the right ventricle, or both.

The prognostic importance of precordial ST segment depression also remains unclear. Although many studies have reported that patients with precordial ST segment depression appear to have larger infarctions, few studies have found any significant difference in short- or long-term survival between those with and without this marker (40). There are several potential explanations for this contradiction: 1) Many of these previous series had a limited number of patients—33 of 36 studies included <100 patients—thus increasing the potential to miss a significant outcome difference. 2) Most studies classified patients into those with or without ST segment depression without considering the magnitude of the ST segment depression. 3) The pattern and lead distribution of ST segment depression may influence its prognostic significance. For example, Hsadia et al. (36) have reported that patients with ST segment depression in leads V_4 to V_6 have a poorer prognosis than those whose ST segment depression is limited to leads V_1 to V_3 (36).

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The purpose of our study was to qualitatively analyze the pathogenesis and prognostic significance of precordial ST segment depression in a large population of patients with inferior myocardial infarction treated in the thrombolytic era. Through the Global Utilization of Streptokinase and t-PA (tissue-type plasminogen activator) for Occluded Coronary Arteries (GUSTO-I) clinical data base (41), we had access to detailed clinical, electrocardiographic (ECG) and angiographic information for >16,000 patients with an acute inferior infarction.

Methods

Patient population. The study population was drawn from patients who had an inferior myocardial infarction and who were enrolled in the GUSTO-I study. Patients were eligible for GUSTO-I if they presented within 6 h of the onset of chest pain and were found to have ≥0.1-mV ST segment elevation in two or more limb leads or ≥0.2 mV-elevation in two or more precordial leads on their initial ECG. Exclusion criteria were limited to known contraindications to thrombolytic therapy. A complete description of the organization and conduct of the GUSTO-I study has been reported elsewhere (41).

Treatment strategies. Patients were randomized to one of four thrombolytic/heparin regimens: streptokinase with either subcutaneous or intravenous heparin, accelerated recombinant tissue-type plasminogen activator (rt-PA) with intravenous heparin or both streptokinase and rt-PA with intravenous heparin. Additional treatment—chewable aspirin (≥160 mg/day) and beta-adrenergic blockade (intravenous atenolol, two 5-mg doses, followed by 50 to 100 mg orally per day)—was administered to patients who had no contraindications. All other pharmacologic and interventional treatments were administered at the discretion of the attending physician.

Electrocardiographic criteria. Enrollment ECGs were interpreted by a central Core Laboratory (Duke University, Durham, North Carolina) without knowledge of patient outcomes. For the current study, an inferior myocardial infarction was defined as ≥0.1-mV ST segment elevation in at least two of the three inferiorly oriented leads: II, III and aVF. Patients who had left or right bundle branch block, ventricular paced rhythm, evidence of a prior infarction (significant Q waves in leads that had no ST segment elevation) or uninterpretable ECG results were excluded from this analysis because these conditions may interfere with the classification of ST segment deviations. Finally, a small percentage of patients had both anterior (leads V_1 to V_3) and inferior ST segment elevation. Those patients in whom the sum (Σ) of anterior ST segment elevation (Σ leads V_1 to V_3) exceeded the sum of inferior ST segment elevation (Σ leads II, III and aVF) were considered to have had an anterior infarction and were excluded from the analysis.

The degree of ST segment deviation was determined for all leads (measured at 60 ms after the J point relative to the TP segment). Patients who had ≥0.1-mV ST segment depression in at least two precordial leads were considered to have precordial ST segment depression. For the primary analyses, patients were classified into one of four categories based on the distribution of precordial ST segment depression—group 1 = those with no significant precordial ST segment depression; group 2 = those with ST segment depression in leads V_1 to V_3 only; group 3 = those with ST segment depression in leads V_4 to V_6 only; and group 4 = those with widespread ST segment depression in both leads V_1 to V_3 and leads V_4 to V_6. This lead distribution classification pattern was chosen to be consistent with previous studies. Other patterns of ECG classification (e.g., defining group 2 as those with ST segment depression in leads V_1 to V_4 and group 3 as those with ST segment depression in leads V_5 to V_6 and leads I and aVL) were also examined; however, they were less capable of discriminating patient outcomes than our primary classification scheme.

Data collection. Baseline clinical and demographic data were collected for all patients enrolled in the GUSTO-I study. In-hospital clinical events were also reported prospectively by the site investigators according to standardized definitions and included congestive heart failure, cardiogenic shock, second- or third-degree heart block, sustained ventricular tachycardia or fibrillation requiring cardioversion, reinfarction and stroke. Angiographic data were available for 57.5% of patients who underwent diagnostic cardiac catheterization before hospital discharge. Angiograms were analyzed for infarct location, degree of stenosis, number of diseased vessels, Thrombolysis in Myocardial Infarction (TIMI) flow grade (42) in the infarct-related artery and left ventricular ejection fraction. One-year survival data were available for 99% of the patients.

Statistical analysis. Continuous data are summarized as medians with 25th and 75th percentiles, and categorical variables as percentages, unless otherwise indicated. Selected baseline characteristics and clinical outcomes were compared among the four groups by chi-square tests for discrete variables and by nonparametric analysis of variance (Kruskal-Wallis) for continuous variables. The Spearman correlation coefficient was used to summarize the relation between measurement of inferior ST segment elevation (Σ leads II, III and aVF) and precordial ST segment depression. One-year survival was displayed for each ST segment depression classification with Kaplan-Meier survival curves.

Logistic regression modeling was used to test whether the distribution and magnitude of ST segment elevation or depression were predictive of 30-day mortality. Logistic regression models were also used to examine whether these predictors added independent prognostic information after adjustment for other baseline clinical risk factors. The clinical risk factors examined in these models were those previously identified by Lee et al. (43): age, systolic blood pressure, admission Killip class, heart rate, prior infarction, height, weight, time to thrombolytic treatment, type of thrombolytic agent, diabetes, hypertension, current smoking, prior bypass surgery and known cerebrovascular disease (43).

Table 1. Baseline Clinical Characteristics by Precordial ST Segment Depression Classification

Characteristic	No ST Segment Depression (n = 6,422)	ST Segment Depression		
		Leads V_1–V_3 (n = 5,850)	Leads V_4–V_6 (n = 876)	Leads V_1–V_3 + V_4–V_6 (n = 3,373)
Age (yr)	60 (50, 68)	61 (52, 69)	61 (53, 69)	61 (52, 69)*
Systolic BP (mm Hg)	128 (110, 142)	128 (111, 142)	128 (110, 144)	127 (111, 142)
Heart rate (beats/min)	70 (60, 80)	72 (61, 84)*	71 (60, 82)	72 (62, 85)*
Male gender	73.0%	73.8%	78.3%*	79.5%*
Hypertension	39.9%	35.7%*	34.9%*	34.0%*
Diabetes mellitus	16.5%	11.6%*	13.1%*	9.2%*
Current smoking	43.2%	46.9%*	50.3%*	54.0%*
Hyperlipidemia	37.7%	37.3%	32.1%*	32.4%*
Previous angina	33.4%	33.9%	38.5%	34.8%

*$p < 0.001$ versus patients with no ST segment depression. Data are expressed as median values (25th, 75th percentiles) or percent of patients. BP = blood pressure.

Results

Study group. Baseline ECGs were available for analysis in 38,006 (92.7%) of the 41,021 GUSTO-I patients. Of these, 18,773 (49.4%) met our definition for an acute inferior infarction. From this cohort, we excluded 567 patients (3.0%) with left bundle branch block, 444 (2.4%) with a paced rhythm or uninterpretable ECG and 1,241 (6.6%) with a prior Q wave infarction, leaving 16,521 patients in our final inferior infarction cohort.

Precordial ST segment depression was present in 10,099 of the patients (61.1%) with inferior infarction. Patients were classified into four exclusive groups on the basis of the presence and distribution of precordial ST segment depression: group 1 = patients without precordial ST segment depression (n = 6,422 [38.9%]), group 2 = those with ST segment depression in leads V_1 to V_3 only (n = 5,850 [35.4%]), group 3 = those with ST segment depression in leads V_4 to V_6 only (n = 876 [5.3%]) and group 4 = those with widespread ST segment depression in both leads V_1 to V_3 and leads V_4 to V_6 (n = 3,373 [20.4%]). Baseline clinical characteristics for each group are displayed in Table 1. Patients without precordial ST segment depression (group 1) were less likely to be smokers and more likely to have hypertension or diabetes than patients with precordial ST segment depression (groups 2 to 4). Cardiac catheterization results are displayed in Table 2. The overall rate of in-hospital cardiac catheterization was 57.5%, with no significant difference in frequency among the four groups. The median time from thrombolysis to diagnostic cardiac catheterization was 4 days for each subgroup. The proportion of patients with significant (≥70%) stenosis in the left anterior descending coronary artery was similar for those with and without precordial ST segment depression (25% vs. 24%, $p > 0.1$). Similarly, the percentage of patients with multivessel coronary artery disease did not vary by the presence or distribution of precordial ST segment depression. However, patients who had ST segment depression in leads V_1 to V_3 were more likely to have involvement of the left circumflex artery compared with patients in the other groups. Left ventricular ejection fraction was significantly lower in patients who had ST segment depression in leads V_1 to V_3 (group 2) or widespread ST segment depression (group 4)

Table 2. Catheterization Results by Precordial ST Segment Depression Classification

	No ST Segment Depression (n = 3,817)	ST Segment Depression		
		Leads V_1–V_3 (n = 3,351)	Leads V_4–V_6 (n = 497)	Leads V_1–V_3 + V_4–V_6 (n = 1,851)
Catheterization performed	59%	57%	57%	55%
≥70% stenosis				
LAD	25%	24%	26%	24%
LCx	28%	40%*	28%	34%*
RCA	74%	66%*	77%	75%*
Multivessel disease	29%	30%	32%	32%
TIMI grade 3 flow	46%	51%	53%	48%
LVEF (%)	56 (50, 65)	54 (47, 61)*	56 (50, 64)	54 (45, 60)*

*$p < 0.001$ versus patients with no ST segment depression. Data presented are medians (25th, 75th percentiles) or percent of patients. LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; LVEF = left ventricular ejection fraction; RCA = right coronary artery; TIMI grade 3 flow = Thombolysis in Myocardial Infarction grade 3 flow (42) in the infarct-related artery 90 min after start of thrombolysis for patients in the GUSTO-I angiographic substudy (n = 953) (45).

Table 3. Therapy Received by Precordial ST Segment Depression Classification

Post-MI Treatment	No ST Segment Depression (n = 6,422)	ST Segment Depression		
		Leads V_1–V_3 (n = 5,850)	Leads V_4–V_6 (n = 876)	Leads V_1–V_3 + V_4–V_6 (n = 3,373)
Thrombolytic therapy				
Accelerated rt-PA	24.8	26.1	24.8	25.5
SK-IV heparin	24.7	25.6	25.9	25.3
Combination	25.6	25.0	25.2	26.2
SK-SQ heparin	24.9	23.3	24.1	23.1
Aspirin	97.5	97.7	96.8	97.9
Nitrates	87.5	86.2	83.5*	84.6*
Beta-blockers	76.8	75.8	73.0	72.9*
Calcium channel blockers	33.9	30.6*	32.8	28.4*
ACE inhibitors	11.6	13.3	13.9	13.4*
Digitalis	8.7	10.2	8.8	11.5*
Coronary angioplasty	28.2	27.9	27.5	28.7
Bypass surgery	8.5	7.9	8.7	8.2

*$p < 0.001$ versus patients with no ST segment depression. Data are expressed as percent of patients. ACE = angiotensin-converting enzyme; Combination = recombinant tissue-type plasminogen activator (rt-PA) and streptokinase (SK) with intravenous (IV) heparin; SC = subcutaneous.

than in those who had no ST segment depression (group 1) or ST segment depression in leads V_4 to V_6 only (group 3).

In-hospital treatment. All patients in this study received thrombolytic therapy according to the GUSTO-I protocol (Table 3). The use of aspirin and nitrates was similarly high (overall averages 98% and 86%, respectively) in all subgroups. Patients without precordial ST segment depression (group 1) were more likely than those with ST segment depression to receive beta-blockers and calcium channel blockers and were less likely to receive digitalis or an angiotensin-converting enzyme inhibitor, partly reflecting a greater preservation of left ventricular function in these patients. The in-hospital use of coronary angioplasty and bypass surgery were similar in the four subgroups.

Outcomes. Acute clinical outcomes by precordial ST segment depression classification are displayed in Table 4. In general, patients with inferior infarction treated with thrombolytic therapy had an excellent prognosis. Stroke occurred in 1.3% of the patients, reinfarction in 4.2% and congestive heart failure in 11.6%; the 30-day mortality rate was 4.4%. Despite this low overall event rate, precordial ST segment depression remained an important predictor of poor outcomes among patients who had inferior infarction. Inferior infarction patients who had no precordial ST segment depression (group 1) had significantly less myocardial damage as assessed by peak serum creatine kinase (CK) and had fewer postinfarction complications, including second- and third-degree atrioventricular block, ventricular tachycardia or fibrillation, congestive heart failure and cardiogenic shock, than those who had precordial ST segment depression (groups 2 to 4). Patients who had no precordial ST segment depression also had significantly lower in-hospital (3.2% vs. 4.7%, $p < 0.001$)

Table 4. Clinical Outcomes by Precordial ST Segment Depression Classification

	No ST Segment Depresssion (n = 6,422)	ST Segment Depression		
		Leads V_1–V_3 (n = 5,850)	Leads V_4–V_6 (n = 876)	Leads V_1–V_3 + V_4–V_6 (n = 3,373)
Peak CK (IU/liter)	1,042 (523, 1,884)	1,708* (925, 2,811)	1,131* (552, 1,933)	1,506* (810, 2,597)
Congestive heart failure	9.6%	12.6%*	10.1%	13.9%*
Cardiogenic shock	4.1%	4.3%	4.1%	6.8%*
2°–3° AV block	10.9%	11.3%	10.5%	14.6%*
VT/VF	7.5%	9.4%*	9.8%*	11.6%*
Stroke	1.1%	1.3%	1.7%	1.8%
Reinfarction	4.1%	4.3%	3.8%	4.2%
Mortality rate				
30 days	3.4%	4.3%*	4.9%*	6.3%*
1 yr	4.6%	6.1%*	6.5%*	8.9%*

*$p < 0.05$ versus patients with no ST segment depression. Data are expressed as medians (25th, 75th percentiles) or percent of patients. AV = atrioventricular; CK = creatine kinase; VT/VF = ventricular tachycardia/ventricular fibrillation.

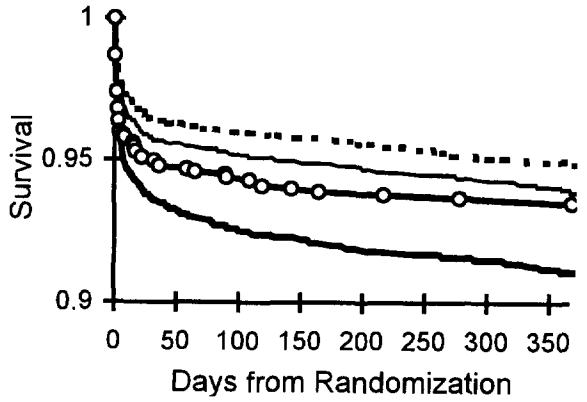

Figure 1. One-year survival in patients with inferior myocardial infarction and no ST segment depression (**dashed line**), ST segment depression in leads V_1 to V_3 (**thin solid line**), ST segment depression in leads V_4 to V_6 (**solid line with circles**) or ST segment depression in both leads V_1 to V_3 and leads V_4 to V_6 (**thick solid line**).

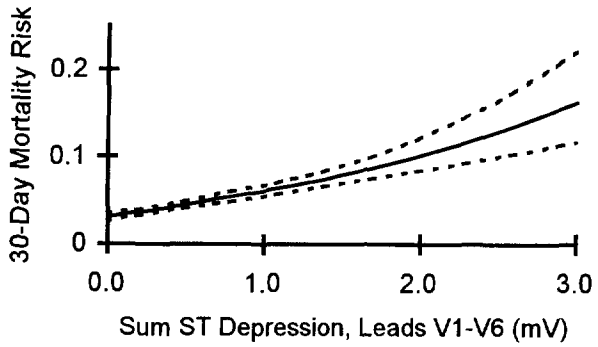

Figure 2. Relation between the magnitude of precordial ST segment depression and 30-day mortality. The probability curve is displayed with 95% confidence limits.

30-day (3.4% vs. 5.0%, $p < 0.001$) and 1-year mortality (4.6% vs. 7.0%, $p < 0.001$) than patients who had precordial ST segments depression.

Among patients who had precordial ST segment depression, those with depression in leads V_1 to V_3 or both V_1 to V_3 and V_4 to V_6 (groups 2 and 4) had higher peak CK levels than those with ST segment depression limited to leads V_4 to V_6 (group 3)—median 1,708 IU/liter and 1,506 IU/liter versus 1,131 IU/liter, respectively ($p < 0.001$). Postinfarction left ventricular function was also slightly worse in groups 2 and 4 than in group 3—median ejection fraction 54% versus 56%, $p < 0.001$. The difference in myocardial damage was also demonstrated clinically by the more frequent congestive heart failure and shock in groups 2 and 4 than in group 3. Patients who had widespread ST segment depression (group 4) had the highest 30-day mortality rate (6.3%) compared with those with ST segment depression limited to leads V_1 to V_3 (4.3%) or leads V_4 to V_6 (4.9%) and those with no ST segment depression (3.2%). This trend toward a poorer prognosis for patients with widespread ST segment depression continued throughout 1 year, as shown in Figure 1.

ST-segment depression versus outcomes. Table 5 and Figure 2 examine the relation between the magnitude of precordial ST segment depression and patient outcomes. The 30-day mortality rate rose nonlinearly with the increasing degree of precordial ST segment depression (Σ leads V_1 to V_6). The sum of precordial ST segment depression also correlated with the amount of myocardial damage (higher peak CK measurements and more congestive heart failure and cardiogenic shock). For example, 19% of patients with inferior infarction in our data set had cumulative precordial ST segment depression of ≥0.8 mV. These patients had significantly higher peak CK levels (1,934 vs. 987 IU/liter, $p < 0.001$) and more frequently developed congestive heart failure (16.9% vs. 9.1%, $p < 0.001$) and cardiogenic shock (7.7% vs. 3.0%, $p < 0.001$) than those with little or no precordial ST segment depression. The frequency of significant heart block and life-threatening arrhythmias also increased with the increasing degree of precordial ST segment depression. In contrast, the sum of precordial

Table 5. Clinical Outcomes by Sum of Precordial ST Segment Depression

	Sum of Precordial ST Segment Depression (mV)			
	<0.2 (n = 5,633)	0.2 to <0.5 (n = 4,716)	0.5 to <0.8 (n = 3,005)	≥0.8 (n = 3,167)
Median peak CK (IU/liter)	987	1,402*	1,578*	1,934*
Congestive heart failure	9.1%	10.8%*	11.8%*	16.9%*
Cardiogenic shock	3.9%	3.8%	4.7%	7.7%*
2°–3° AV block	10.1%	11.0%	12.7%*	15.0%*
VT/VF	7.0%	7.6%	10.1%*	14.1%*
Stroke	1.1%	1.3%	1.4%	1.8%
Reinfarction	3.9%	4.3%	4.6%	4.0%
Mortality rate				
30 days	3.2%	3.9%	4.2%*	7.5%*
1 yr	4.8%	5.4%	6.4%*	10.0%*

*$p < 0.01$ versus those with <0.2 mV. Data are expressed as medians (25th, 75th percentiles). Abbreviations as in Table 4.

Table 6. Thirty-Day Mortality Predictive Models

	Univariate Chi-Square	Chi-Square Adjusted for Clinical Variables*
Σ inferior ST elevation (leads II, III, aVF)	16.6	13.9
No. of leads with precordial ST depression	46.2	24.8
Σ ST depression		
Leads V_1–V_3	64.3	34.8
Leads V_4–V_6	67.7	30.9
Leads V_1–V_6	87.1	44.8
Leads V_1–V_6+Σ inferior ST elevation	71.2	40.8

*Age, systolic blood pressure, admission Killip class, heart rate, previous infarction, height, weight, time to thrombolytic treatment, type of thrombolytic agent, diabetes, hypertension, current smoking, prior bypass surgery and history of cerebrovascular disease. Σ = sum of.

ST segment depression did not correlate with reinfarction or stroke rates ($p > 0.1$).

Table 6 displays the relations of selected ECG variables and 30-day mortality before and after adjustment for baseline clinical prognostic factors. The sum of inferior ST segment elevation (Σ leads II, III and aVF) was the least significant ECG prognostic measure tested (univariable and adjusted chi-squares of 16.6 and 13.9, respectively). The prognostic significance of precordial ST segment depression in leads V_1 to V_3 was similar to that in leads V_4 to V_6. The sum of precordial ST segment depression (Σ leads V_1 to V_6) was the most significant ECG predictor of 30-day mortality tested (univariable and adjusted chi-squares of 87.1 and 44.8, respectively). In fact, in a multivariable ECG and clinical analysis, no other ECG predictor was significant after accounting for this factor.

Discussion

The prognostic significance of precordial ST segment depression in patients with an inferior myocardial infarction has been controversial, in part because of the limited size of previous studies. On examining data from 16,521 such patients from the GUSTO-I trial, we confirmed that those who had precordial ST segment depression had significantly larger infarctions, more postinfarction complications and higher mortality than those without precordial ST segment depression. Furthermore, the degree of precordial ST segment depression was a more powerful ECG predictor of outcome than the amount of inferior ST segment elevation. Poorer 30-day and 1-year prognoses were found in all patients who had precordial ST segment depression, whether the changes were in leads V_1 to V_3 or leads V_4 to V_6. The best independent ECG predictor of patient outcomes after inferior infarction was the cumulative sum of precordial ST segment depression (leads V_1 to V_6).

Pathophysiology of precordial ST segment depression. Previous investigators have put forth a number of explanations for precordial ST segment depression during an inferior infarction. Researchers have proposed that precordial ST segment depression is purely an ECG consequence of ST segment elevation in the inferior limb leads, without physiologic importance (4,9,13,16,31–33). In contrast, we found that the magnitude of inferior ST segment deviation correlated only marginally with precordial ST segment depression in leads V_1 to V_3 ($r = -0.44$) and was not correlated with ST segment depression in leads V_4 to V_6 ($r = -0.09$). We also demonstrated that precordial ST segment depression had considerable prognostic importance, exceeding that gained from examining the degree of inferior ST segment elevations.

Others have proposed that precordial ST segment depression during an inferior infarction signifies anterior wall ischemia and thus is a marker for left anterior descending coronary artery or multivessel disease (3,10,19,20,23,27). In contrast, we found that the frequency of left anterior descending coronary artery disease did not vary by the presence or distribution of precordial ST segment depression, nor did the frequency of multivessel coronary artery disease.

Still others have hypothesized that precordial ST segment depression is caused by posterolateral wall involvement during an inferior infarction (1,2,6,11,29,30,35). Indeed, we found that patients who had ST segment depression in leads V_1 to V_3 had larger infarctions, as shown by higher peak CK levels, more congestive heart failure symptoms and worse left ventricular ejection fractions. Likewise, we found that the circumflex artery, which often supplies blood to the posterior and lateral myocardium, was more often the infarct-related artery among patients with precordial ST segment depression in leads V_1 to V_3. Thus, we conclude that precordial ST segment depression in leads V_1 to V_3 is a marker for larger inferior wall infarctions usually with extension to the posterolateral wall.

This explanation, however, does not appear to explain ST segment depression in leads V_4 to V_6. Despite having lower peak CK levels and less severe left ventricular dysfunction than patients with ST segment depression in leads V_1 to V_3, patients with ST segment depression in leads V_4 to V_6 had similar 30-day and 1-year mortality. This apparently paradoxical result (smaller infarctions yet poorer prognoses for inferior infarction patients with ST segment depression in the lateral precordium) is consistent with the findings of others and deserves further investigation (36).

Prognostic significance of precordial ST segment depression. Patients who have an inferior infarction generally have a more favorable prognosis than those who have anterior infarction. In the GUSTO-I trial, the unadjusted 30-day mortality rate for inferior infarction patients was 5.0% compared with 9.9% for those who had an anterior infarction (43). It is clear, however, that patients with inferior infarction are a heterogeneous group (34,40). From this large clinical series, we show that the magnitude of precordial ST segment depression is useful for the stratification of patients with inferior infarction into low and high risk categories.

Few studies have been able to show that precordial ST segment depression can predict patient outcomes (21). Our study found that patients without precordial ST segment depression treated with acute thrombolytic therapy were at low risk with a 30-day mortality rate of 3.4%. In contrast, patients with ≥ 0.8 mV of ST segment depression, despite receiving aggressive therapy, had a mortality rate of 7.5%, approaching that seen in patients with anterior infarction. We also found that a patient's risk for mortality increased in a near linear fashion with increasing precordial ST segment depression, whether the ST segment depression was in the anterior (V_1 to V_3) or lateral precordial (V_4 to V_6) leads. Finally, the sum of precordial ST segment depression was a strong independent prognostic factor even after adjustment for the magnitude of inferior ST segment elevation and known clinical risk factors (see previous discussion). Even after considering baseline clinical risk factors, a patient's risk of 30-day mortality increased by 36% with every 0.5-mV increment of cumulative precordial ST segment depression (Σ leads V_1 to V_6).

Study limitations. Although the present study is the largest report on outcomes after inferior myocardial infarction, certain limitations need to be acknowledged. First, our study patients included those eligible for thrombolytic therapy who were selected for enrollment in a randomized clinical trial. In general, these patients tend to be somewhat healthier and have better outcomes than community-based populations (44). Thus, these results should ideally be confirmed in a large, unselected population with infarction. Second, our angiographic data were also selective, representing only patients who underwent catheterization at the discretion of the physician. However, nearly 60% of our patients with inferior infarction underwent catheterization without significant variation among our ECG classifications. Furthermore, these catheterization findings were similar when we limited our analysis to those who underwent catheterization as part of the GUSTO-I angiographic substudy (n = 953) (45).

Finally, other investigators have reported that the prognostic significance of precordial ST segment depression may change over time, with persistent ECG changes being more predictive (28). We analyzed the tracings available to the clinician when acute treatment decisions were being made. Although we may have underestimated the predictive power of precordial ST segment depression by analyzing ECG changes at presentation, we believe that the results reflect its prognostic use in the emergency room setting.

Clinical implications. In conclusion, when assessing risk in patients with acute inferior myocardial infarction, the clinician should consider the cumulative sum of ST segment depression in all precordial leads. Those without precordial ST segment depression are generally at low risk for postinfarction complications or death; however, the risk for adverse outcomes increases significantly as the magnitude of precordial ST segment depression increases (increasing 30-day mortality by a third with every 0.5 mV of ST segment depression).

Because the benefits from many interventions are directly related to a patient's underlying risk for adverse outcomes, clinicians should consider a more aggressive diagnostic and therapeutic approach for inferior infarction patients with significant precordial ST segment depression, and a more conservative approach for those without precordial ST segment depression. Thus, the clinician can use this easily obtainable prognostic information from the initial ECG to help tailor therapeutic decisions in the management of patients with inferior myocardial infarction (46).

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