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The Electrocardiogram Predicts One-Year Outcome of Patients With Unstable Angina and Non–Q Wave Myocardial Infarction: Results of the TIMI III Registry ECG Ancillary Study

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Objectives. **We sought to determine the prognostic value of the admission electrocardiogram (ECG) in patients with unstable angina and non–Q wave myocardial infarction (MI).**

Background. **Although the ECG is the most widely used test for evaluating patients with unstable angina and non–Q wave MI, little prospective information is available on its value in predicting outcome in the current era of aggressive medical and interventional therapy.**

Methods. **ECGs with the qualifying episode of pain were analyzed in patients enrolled in the Thrombolysis in Myocardial Ischemia (TIMI) III Registry, a prospective study of patients admitted to the hospital with unstable angina or non–Q wave MI.**

Results. **New ST segment deviation ≥1 mm was present in 14.3% of 1,416 enrolled patients, isolated T wave inversion in 21.9% and left bundle branch block (LBBB) in 9.0%. By 1-year follow-up, death or MI occurred in 11% of patients with ≥1 mm ST segment deviation compared with 6.8% of patients with new, isolated T wave inversion and 8.2% of those with no ECG changes ($p < 0.001$ when comparing ST with no ST segment deviation). Two other high risk groups were identified: those with only 0.5-mm ST segment deviation and those with LBBB, whose rates of death or MI by 1 year were 16.3% and 22.9%, respectively. On multivariate analysis, ST segment deviation of either ≥1 mm or ≥0.5 mm remained independent predictors of death or MI by 1 year.**

Conclusions. **The admission ECG is very useful in risk stratifying patients with non–Q wave MI. The new criteria of not only ≥1-mm ST segment deviation but also ≥0.5-mm ST segment deviation or LBBB identify high risk patients, whereas T wave inversion does not add to the clinical history in predicting outcome.**

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Unstable angina is a diagnosis applied to a heterogeneous group of patients (1–3). The diagnosis is typically made by the patient's description of the character and circumstances of the chest pain, with some patients developing myocardial necrosis (i.e., non–Q wave myocardial infarction [MI]) (4). Across this broad group of patients, usually referred to as having "acute coronary syndromes," the risk of subsequent adverse outcome varies widely (5,6). Accordingly, efforts have been focused on better identification of high risk patients who need more aggressive medical and interventional treatment (2). Because of its universal availability, low cost and simplicity, electrocardiography is an attractive method to risk stratify patients. However, little prospective information is available on its value in predicting outcome in the current era of aggressive medical and interventional therapy.

The Thrombolysis in Myocardial Ischemia (TIMI) III Reg-

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Abbreviations and Acronyms

ECG = electrocardiogram, electrocardiographic
LBBB = left bundle branch block
MI = myocardial infarction
TIMI = Thrombolysis in Myocardial Ischemia

istry was a prospective, observational study collecting a wide variety of data to characterize the various types of patients with unstable angina and non–Q wave MI and their outcomes (7). To extend these observations, serial electrocardiograms (ECGs) were obtained from all patients enrolled in the TIMI III Registry at nine hospitals participating in the ECG Ancillary Study. The major goal of this ancillary study was to determine the value of ST segment or T wave changes on a 12-lead ECG in characterizing the outcome of patients with unstable angina. In addition, the outcomes of two poorly characterized groups of patients with unstable angina and non–Q wave MI were prospectively examined—those with 0.5-mm ST segment deviation and those with left bundle branch block (LBBB). It was hypothesized that these two groups would constitute high risk groups.

Methods

Patient group. The details of the TIMI III Registry have been previously reported (7). The study was conducted between October 1990 and April 1993 at 18 clinical centers in the United States and Canada, nine of which participated in the prospective ECG Ancillary Study (see Appendix). The Registry was composed of two parts: The "enumeration roster" included all consecutive patients admitted with unstable angina or non–Q wave MI who met the following criteria: *Inclusion criteria* = the presence of typical chest discomfort (or equivalent) believed to be ischemic in nature, lasting at least 5 min and occurring within 96 h of (or during) hospital admission, and having an unstable pattern of pain, consisting of either rest pain, new onset, severe or frequent angina, accelerating angina or angina occurring within 21 days after an acute MI. *Exclusion criteria* = nonischemic or atypical pain, persistent new ST segment elevation or Q wave MI on presentation or admission directly for a revascularization procedure.

From the enumeration roster, 404 patients were enrolled in the concurrent TIMI IIIB trial (5). From the remaining patients, specific subgroups, characterized by age, gender and race, were randomly selected for inclusion in the "prospective study" using a sampling ratio that sought to enroll a larger proportion of elderly, women and blacks (7). After written informed consent was obtained, more detailed clinical information was collected, including 1-year telephone follow-up for vital status, which was complete in 96% of patients. The study was approved by each participating hospital's Institutional Review Board.

ECG Ancillary Study. For patients in the "prospective study," ECGs were collected in association with the qualifying episode of ischemic pain, and the most recent ECG before the qualifying episode of pain (or one 12 to 24 h after if not available). Each ECG was evaluated in the central ECG core laboratory by a single electrophysiologist (L.I.G.) who had no knowledge of the patients' outcome. The rate, rhythm and presence of conduction defects, including LBBB (either new or old), were recorded. In addition, each lead was evaluated separately for the presence or absence of 1) Q waves >0.03 s in width and >0.3 mm in depth; 2) the presence and degree of ST segment deviation (depression or elevation), categorized as none, 0.5 mm, 1.0 mm, 2.0 mm or >2.0 mm; 3) T wave deviation, categorized as positive (≥1.0 mm), biphasic or with amplitude <1.0 mm or negative (inversion ≥1.0 mm).

Data from the qualifying ECG were compared with the prequalifying ECG, if available, to categorize the presence on the qualifying ECG of "new or presumably new" ST segment deviation or T wave inversion in two or more contiguous leads. As in TIMI IIIB, the definition of ST segment deviation was transient or persistent ST segment depression or transient ST segment elevation (5). Accordingly, in patients with ST segment elevation on the qualifying ECG, a comparison ECG was required for inclusion in the analysis.

Of 1,565 patients enrolled in the prospective study at the participating hospitals, the qualifying ECG was not available in 126, most frequently because it was obtained at a nonparticipating hospital before transfer of the patient to the TIMI III Registry hospital. In addition, two other groups were prospectively excluded from the ECG analysis: those who began taking digoxin between the prequalifying and qualifying ECG (n = 4); those with apparent ST segment elevation on the qualifying ECG in whom a comparison baseline ECG was not available (n = 16); in addition, three patients were not enrolled in the ancillary study.

End points. The following end points were evaluated: 1) death; 2) post-enrollment MI as confirmed by a creatine kinase MB fraction greater than the upper limit of normal (i.e., a recurrent MI in patients with evolving non–Q wave MI on admission) and recurrent ischemia, defined as either in-hospital ischemic pain at rest associated with ST segment or T wave changes as assessed by the local investigator; or 3) post–hospital discharge recurrent ischemic pain requiring readmission to the hospital.

Statistical analyses. To evaluate the relation between ECG findings on the qualifying ECG and clinical outcomes, patients were divided into four mutually exclusive groups: those with LBBB; new or presumably new ST segment deviation ≥1 mm (in the absence of LBBB); isolated T wave inversion or pseudonormalization (and no ST segment deviation); or none of these ECG changes. These groups were compared for their baseline characteristics, in-hospital treatment and outcome. Both the four-way and pairwise comparisons were accomplished using the Mantel-Haenszel statistic. In addition, analysis by a Cox proportional hazards model using age, gender and race as covariates was performed for clinical

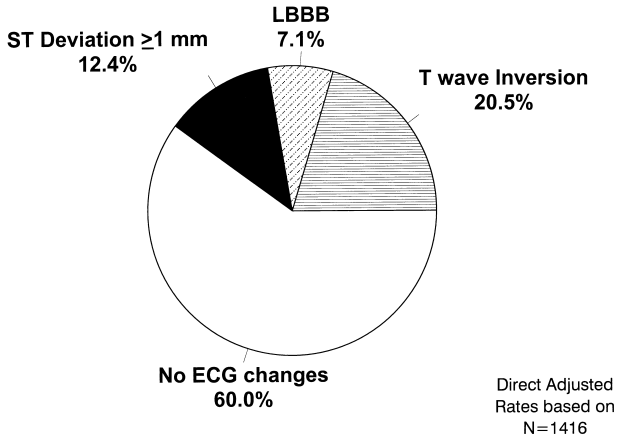


Figure 1. Distribution of ECG changes with the qualifying episode of pain. Rates are the direct-adjusted rates to match the age-gender-race distribution in the enumeration roster of all consecutive patients admitted with unstable angina and non–Q wave MI.

outcomes at 42 days and 1 year to identify multivariate predictors of outcome.

Kaplan-Meier event rates, percentages and means of baseline characteristics and outcome data for the patients in the ECG Ancillary Study were directly adjusted to the age-gender-race distribution from the enumeration roster (8). That is, the event rates and proportions were calculated for each age-gender-race category, and a weighted average of these estimates was calculated. The weights used were proportional to the number of patients enumerated in each age-gender-race category. For comparisons of subgroups, chi-square analysis was used. To adjust for the effects of multiple testing, p values of 0.01 to 0.001 were considered as providing some evidence of group differences, and $p < 0.001$ was considered as providing strong evidence of group differences.

Results

Distribution of ECG findings. Among the 1,416 patients with unstable angina or non–Q wave MI in the study, 14.3% demonstrated new or presumably new ST segment deviation ≥1 mm on the qualifying ECG, 9% demonstrated LBBB, 21.9% had T wave changes and 54.9% did not have these ECG changes. Among patients with ST segment deviation, 23 (1.6% of the total group) had transient ST segment elevation, whereas 179 (12.6%) had ST segment depression. Of the patients with LBBB, only 6 (0.4% of the total group) had developed a new LBBB at the time of presentation. Using the sampling ratios in the age-gender-race subgroups of patients in the prospective study, direct adjusted rates were calculated to estimate the prevalence of ECG findings in the entire group of patients admitted to the hospital with unstable angina and non–Q wave MI (Fig. 1). As shown, a total of 40% of the total group of patients with unstable angina and non–Q wave MI demonstrated one of these changes on the qualifying ECG.

Baseline characteristics. Patients with new ST segment deviation ≥1 mm were older, but other baseline characteristics were similar, including gender, race, coronary risk factors, pattern of angina, history of angina or previous revascularization (Table 1). Patients with isolated T wave inversion were similar in terms of baseline characteristics to those without ECG changes. Patients in Canada and the United States had a similar distribution of ECG findings. Two-thirds of patients had previously been admitted to the hospital for unstable angina, indicating the recurrent nature of unstable angina. Previous angina was present in 79% of patients, and nearly one-quarter had undergone previous coronary artery bypass graft surgery (Table 1).

Despite the high prevalence of previous coronary artery disease, only 45% of patients were taking aspirin at the time of enrollment. Only 27% were receiving beta-blockers, in contrast to calcium antagonists and nitrates, which were being used in nearly 50% of patients (Table 1). Rales over more than one-third of the lung fields ranged from 3% in patients without ECG changes to 21% in patients with LBBB ($p < 0.001$). Rest pain was present in 78% of patients. The rate of non–Q wave MI on presentation ranged from 19% in patients without ECG changes to 39% in patients with ST segment deviation ≥1 mm ($p < 0.001$).

In-hospital treatment. Intravenous nitroglycerin and beta-blockers tended to be prescribed more often in patients with ST segment deviation. Heparin was used in only 55% of patients with ST segment deviation (Table 2). Aspirin treatment did not differ by presenting ECG findings, but was used in only 82% of patients, even in those with ST segment deviation (79%). Calcium antagonists were used in the majority of patients, more so than beta-blockers.

Cardiac procedures. Cardiac catheterization was performed in two-thirds of patients with ST segment, T wave or no ECG changes, but in less than half of patients with LBBB (Table 2). In patients undergoing catheterization, multivessel disease was found in 66% of patients with ST segment deviation, compared with 40% of patients without ECG changes ($p < 0.001$). The absence of significant coronary stenosis ranged from only 10% of patients with ST segment deviation to 29% of patients without ECG changes to 34% of patients with LBBB (Table 2).

Revascularization in the hospital was more frequent in patients with ST segment deviation at presentation, primarily because of the increased rate of bypass surgery performed in 22% of these patients compared with 9% of patients without ECG changes ($p < 0.001$) (Table 2). Interestingly, percutaneous transluminal coronary angioplasty was performed at a similar rate, regardless of the presence or absence of ST segment or T wave changes, although only 6% of patients with LBBB underwent coronary angioplasty. After the initial hospital period, only 2% to 3% more patients underwent revascularization through 1 year, indicating that the initial clinical presentation and ECG findings allowed for accurate triage to the ultimate treatment strategy. Hospital length of stay for all patients was relatively long, >1 week on average.

Clinical outcome. Mortality was low overall, ~1% in the hospital and 2% to 5% by 42 days (Table 2 and 3). By 1-year

Table 1. Baseline Characteristics by Electrocardiographic Findings

	All Pts (n = 1,416)	LBBB (n = 127)	ST Dev ≥1 mm (n = 202)	Isolated T Wave Changes (n = 310)	No ECG Changes (n = 777)	p Value Four Way*	p Value ST vs. No ST Dev
Mean age (yr)	62.5	65.7	63.9	61.1	59.4	< 0.001	< 0.001
>75 yr (%)	13.8	29.0	23.6	13.7	10.0	< 0.001	< 0.001
% male	58.3	44.6	57.6	57.6	60.4	0.176	0.448
% black	13.2	13.4	12.0	17.6†	11.9	0.03	0.554
Prior hosp for unstable angina	66.3	84.8	72.0	66.7	62.9	0.002	0.04
Prior MI	41.0	55.0	46.3	45.9	36.6	0.001	0.042
Medication in prior week							
Aspirin <24 h	44.6	47.9	47.1	48.9	42.3	0.541	0.191
Heparin	5.2	4.1	9.2	3.6	5.1	0.274	0.077
Warfarin	5.7	12.5	7.9	6.3	4.2	0.033	0.522
Thrombolysis	0.7	0	1.1	0	0.9	0.556	0.872
Nitrates	42.5	54.0	48.6	43.6	39.5	0.001	0.007
Beta-blockers	27.1	14.6	36.0	25.7	27.3	0.008	0.137
Ca-blockers	46.4	36.7	46.0	49.6	46.5	0.248	0.461
ACE inhibitors	17.4	33.9	21.0	19.7	14.0	0.004	0.289
Rales >1/3 lungs	5.8	21.4	9.4	6.6*	2.9	< 0.001	0.02
Acute pulmonary edema	2.4	11.8	5.5	2.1	0.8	< 0.001	0.023
Cardiogenic shock	1.1	0.8	0.2	1.6	1.1	0.743	0.354
Other major illness	9.3	19.5	9.6	10.6	7.5	0.255	0.861
Non-Q wave MI at entry	24.8	31.8	38.8	31.3‡	18.8	< 0.001	< 0.001

*Mantel-Haenzel statistic comparing all four electrocardiographic (ECG) groups. †p < 0.01, ‡p < 0.001, T wave inversion group versus no ECG changes group; all other comparisons between these two groups were p = NS. Direct adjusted rates controlling for sampling in age, gender and race strata (see Methods). Data presented are percent of patients (Pts), unless otherwise indicated. ACE = angiotensin-converting enzyme; Dev = deviation; hosp = hospital admission; LBBB = left bundle branch block; MI = myocardial infarction.

follow-up, the mortality rate had risen to 9.8% in patients with ST segment deviation ≥1 mm, compared with 5.5% for patients with T wave or no ECG changes (p < 0.001) (Table 3). Death or MI occurred in 11% of patients with ST segment deviation ≥1 mm, compared with 7% for those with new, isolated T wave inversion and 8% for those with no ECG changes (p < 0.001). The rate of death or MI was not statistically different between those with T wave inversion and those with no ECG changes. Patients with LBBB had a very low rate of death or MI in the hospital (<1%), but by 1-year follow-up they had the highest rate of death or MI (23%).

Recurrent ischemia (rest pain with ST segment or T wave changes) occurred in the hospital more frequently (19%) in patients with ST segment deviation at presentation, compared with 11% of patients with initial T wave changes and 7.5% of patients without ECG changes (p < 0.001) (Table 2). Recurrent rest pain without ECG changes was common, occurring in approximately one-third of patients in all groups. Through 1-year follow-up, recurrent angina requiring readmission to the hospital occurred in ~15% of patients (Table 3). The 1-year rate of death, MI or recurrent ischemia (with ECG changes or requiring readmission to the hospital) ranged from 25.5% of patients without ECG changes on the initial ECG to 36% of patients with ST segment deviation (p < 0.001).

Location and severity of ECG changes. The difference in outcome by location of ECG changes is shown in Figure 2. Among patients with ST segment deviation ≥1 mm, anterior changes carried the worst prognosis, with a rate of death or MI of 12.4% by 1 year, compared with 7% to 8% for other locations or no ST segment deviation (p = 0.002). In contrast, the location of isolated T wave changes was not correlated with outcome (Fig. 2).

Degree of ST segment deviation and outcome. The prognostic significance of different degrees of ST segment deviation is shown in Table 4. A total of 187 patients (13% of the total group) demonstrated 0.5-mm ST segment deviation. The clinical outcome at follow-up was similar or worse for patients with 0.5-mm ST segment deviation than for those with ≥1 mm: Death or MI by 1 year occurred in 16% of patients with ST segment deviation 0.5 mm, compared with 6% of patients without ST segment deviation and 10% to 15% of patients with ST segment deviation ≥1 mm (p < 0.001).

Multivariate predictors of long-term outcome. On multivariate analysis, seven variables were identified as independent predictors of death or MI by 1 year (Table 5). The two ECG variables were LBBB and ST segment deviation ≥0.5 mm, which were each associated with a risk ratio of death or MI at 1 year of 2.80 and 2.45, respectively (each p < 0.001). In another model, ST segment deviation ≥1 mm was an independent predictor (p < 0.001), but it had a lower risk ratio (1.85) than ST segment deviation ≥0.5 mm.

Discussion

In this prospective study of unstable angina and non–Q wave MI, the admission ECG was a valuable tool in predicting

Table 2. In-Hospital Treatment and Outcome

	All Pts (n = 1,416)	LBBB (n = 127)	ST Dev ≥1 mm (n = 202)	Isolated T Wave Changes (n = 310)	No ECG Changes (n = 777)	p Value	
						Four Way*	ST vs. No ST Dev
Meds for qualifying event							
Aspirin	82.3	82.5	79.0	83.1	82.6	0.776	0.587
Heparin	52.5	51.2	55.4	55.9	51.0	0.062	0.025
IV nitroglycerin	32.6	35.9	44.6	32.2	29.9	< 0.001	< 0.001
Nitrates	72.4	67.2	69.8	70.0	74.4	0.312	0.452
Beta-blockers	38.0	19.2	47.9	38.0	38.2	< 0.001	0.083
Ca-blockers	54.4	38.4	62.1	56.1	54.1	0.013	0.052
ACE inhibitors	17.1	38.4	22.8	16.1	13.8	< 0.001	0.158
Cath performed	62.4	45.4	66.6	65.6	62.5	0.003	0.03
0 VD	24.0	33.5	10.4	16.7	29.1		
1 VD	30.1	29.6	23.3	32.9	30.7	< 0.001	< 0.001
2 VD	22.2	14.7	32.7	25.8	19.1		
3 VD	23.7	22.2	33.9	24.6	21.1		
LMCA stenosis	7.4	4.7	15.3	7.6	5.7	0.016	0.019
PTCA	20.3	5.8	23.5	22.4	20.6	0.095	0.582
CABG	11.5	7.6	21.8	14.6	8.7	< 0.001	< 0.001
PTCA or CABG	31.1	11.9	45.3	36.1	28.7	< 0.001	0.001
In-hospital event							
Death	0.6	0.3	1.4	1.0	0.4	0.112	0.033
MI	1.4	0.4	1.7	1.3	1.5	0.477	0.391
Death or MI	1.8	0.8	2.6	1.6	1.6	0.203	0.091
Ischemia with ECG changes	9.5	5.6	18.2	11.4	7.5	< 0.001	< 0.001
Death/MI/ischemia with ECG changes	10.5	6.4	20.2	12.6	8.3	< 0.001	< 0.001
Ischemia without ECG changes	31.6	37.0	31.2	31.6	31.0	0.399	0.937
Length of stay (days)	8.9	8.5	9.9	9.6†	7.5	< 0.001‡	< 0.001

*Mantel-Haenzel statistic comparing all four electrocardiographic (ECG) groups. †$p < 0.001$ comparing T wave inversion group versus no ECG changes; all other comparisons of these two groups were p = NS. ‡For length of stay, the four-way p value was obtained from an F test statistic comparing the mean values among four groups, controlling for age, gender and race. Direct adjusted rates controlling for sampling in age, gender and race strata (see Methods). Data are percent of patients. Two-way p value obtained from a *t* test statistic comparing the mean values between the two groups, controlling for age, gender and race. CABG = coronary artery bypass grafting; Cath = catheterization, IV = intravenous; LMCA = left main coronary artery; Meds = medications; PTCA = percutaneous transluminal coronary angioplasty; VD = vessel disease; other abbreviations as in Table 1.

outcome. Several groups of patients could be identified as high risk: patients with ST segment deviation ≥1 mm, those with ≥0.5 mm ST segment deviation and those with LBBB. Interestingly, the presence of isolated T wave changes, even in the anterior leads, did not appear to influence short- or long-term prognosis, and thus appears to add little to the clinical assessment. In contrast, using the new ECG criteria of ST segment deviation ≥0.5 mm or LBBB, which identify as "high risk" nearly one-third of all patients with unstable angina and non–Q wave MI, the long-term prognosis was poor, with a 15.8% rate of death or MI by 1 year. This highlights the chronic and recurrent nature of unstable angina and suggests that attention should be focused on maximizing current medical therapy for these high risk patients, and should strengthen the resolve of clinical investigators to find new medical and interventional treatments for these patients.

ST segment deviation. The presence of transient ST segment depression or elevation ≥1 mm has previously been recognized as a marker of adverse outcome in patients with unstable angina (9–14). However, prospective, multicenter data have been sparse in the current era of aggressive management and combination antithrombotic therapy. In this large, prospective study, we observed that ST segment deviation remains one of the adverse predictors of subsequent death or MI by 1-year follow-up. In this cohort, ST segment deviation heralded more advanced coronary artery disease, including 15% of patients with left main coronary stenosis. These patients also had nearly twice the rate of non–Q wave MI on hospital admission compared with patients without ECG changes (39% vs. 19%, four-way $p < 0.001$), as was observed in TIMI IIIB (4).

Current management was relatively aggressive for patients with ST segment deviation, with intravenous heparin, aspirin, beta-blockers and intravenous nitrates used in a higher percentage of these patients than those with other ECG findings. However, many gaps appear to exist between current recommendations (15–18) and actual practice, even in the teaching hospitals that participated in this registry. In this cross section

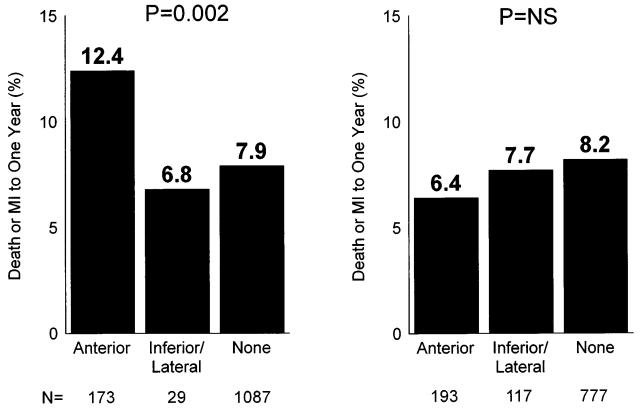
Table 3. Adjusted 42-Day and 1-Year Kaplan-Meier Event Rates

	All Pts (n = 1,416)	LBBB (n = 127)	ST Dev ≥1 mm (n = 202)	Isolated T Wave Changes (n = 310)	No ECG Changes (n = 777)	p Value	
						Four Way*	ST vs. No ST Dev
42-day event rates							
Death	2.4	5.2	2.5	2.8	1.8	0.198	0.091
MI	2.2	1.8	1.5	2.4	2.3	0.725	0.41
Death or MI	4.0	6.6	3.6	3.7	3.7	0.443	0.123
Rehosp for rest angina	5.3	6.7	7.3	5.6	4.5	0.13	0.032
Death, MI or rec isch	16.1	14.2	23.6	17.9	13.9	< 0.001	< 0.001
PTCA	20.7	3.4	24.9	23.9	20.4	0.024	0.538
CABG	13.4	10.5	25.8	16.3	10.7	< 0.001	< 0.001
PTCA or CABG	33.4	12.6	50.8	39.3	30.4	< 0.001	0.001
1-yr event rates							
Death	7.2	18.2	9.8	5.6	5.5	< 0.001	< 0.001
MI	4.0	6.3	6	3.7	3.5	0.446	0.13
Death or MI	9.5	22.9	11	6.8	8.2	< 0.001	0.001
Rehosp for rest angina	15.9	13.4	17.7	16.8	15.4	0.753	0.293
Death, MI or rec isch	28.3	34.0	36.1	30.4	25.5	0.003	0.001
PTCA	22.9	7.6	25.3	26.2	22.8	0.037	0.621
CABG	16.1	10.8	27.2	17.9	14.3	0.004	0.002
PTCA or CABG	36.4	16.6	51.1	42.3	33.9	< 0.001	0.001

*Mantel-Haenzel statistic comparing all four electrocardiographic (ECG) groups; p value obtained from Cox proportional hazards analysis with age, gender and race included. All comparisons between T wave inversion group and no ECG changes were p = NS. rec isch = recurrent ischemia with ECG changes or requiring admission to the hospital; other abbreviations as in Tables 1 and 2.

of clinical practice, nearly 20% of patients with ST segment deviation were *not* treated with aspirin, despite the overwhelming evidence supporting its benefit in this patient group (15,16,18–20). Although less firmly established, several studies have suggested that intravenous heparin is beneficial in unstable angina and non–Q wave MI (17,18,21), yet it was used in only 51% of patients, even if ST segment deviation was present on hospital admission. These data suggest that significant opportunities exist for improvement in the management (and thus outcome) of patients with unstable angina and non–Q wave MI, and that if currently available therapies such as aspirin, heparin and beta-blockers are used more consistently, a significant number of lives would be saved each year.

Figure 2. Relation between location of ECG changes and 1-year death or MI. Rates are adjusted Kaplan-Meier event rates. **Left,** ST segment deviation; **right,** T wave inversion (includes only those patients with isolated T wave inversion.)



Degree of ST segment deviation. Although ST segment deviation ≥1 mm is associated with an adverse prognosis (9–14), as recently confirmed in the TIMI IIIB trial (5), it has not been clear whether the presence of 0.5-mm ST segment deviation is a nonspecific finding (as it is in exercise testing) (22) or a reliable marker of adverse clinical outcome. We observed that patients with unstable angina and non–Q wave MI presenting with only 0.5-mm ST segment deviation have an adverse early and late outcome, similar or worse than that of patients with ST segment deviation ≥1 mm. On multivariate analysis, it was an independent predictor of 1-year outcome. Thus, on admission ECGs, the presence of 0.5-mm ST segment deviation appears to indicate a true ischemic ECG change that is associated with an adverse prognosis. For clinicians, the presence of this degree of ST segment deviation (and not T wave changes) should signal the need for vigilance and aggressive management. These data also support the use of ≥0.5-mm ST segment deviation as an entry criterion for clinical trials of unstable angina and non–Q wave MI.

Left bundle branch block. Although patients with LBBB have recently been identified to be at high risk after acute MI in thrombolytic trials (23,24), their outcome has not been well characterized when presenting with a self-limited episode of ischemic pain. We observed that LBBB comprised 7% of the overall group of patients (and 15% of patients >75 years old). Patients with LBBB had more evidence of left ventricular failure, with 34% taking angiotensin-converting enzyme inhibitors at baseline, and over 20% having congestive heart failure

Table 4. Relation of Degree of ST Segment Deviation and Outcome*

	Degree of ST Segment Deviation				
	≥2 mm (n = 63)	1 mm (n = 139)	0.5 mm (n = 187)	None (n = 900)	p Value†
Death by 42 d	0.8	3.0	7.1	1.1	0.002
Death or MI by 42 d	2.8	3.4	10.7	2.4	0.001
Death, MI, RI by 42 d	19.5	22.7	25.8	13.0	< 0.001
Death or MI by 1 yr	14.9	9.7	16.3	6.1	< 0.001

*Adjusted Kaplan-Meier event rates. †Cox proportional hazards model. d = days; RI = recurrent ischemia with electrocardiographic changes in hospital or requiring admission to hospital; other abbreviations as in Table 1.

at presentation. Although fewer patients underwent cardiac catheterization, of those who did, >34% had no significant coronary stenoses, indicating possible misdiagnosis or the concomitant presence of cardiomyopathy. They were managed more conservatively in the hospital, with a lower rate of revascularization. However, during follow-up their mortality rate was 18% by 1 year, nearly double that of patients presenting with ST segment deviation. As such, this group of patients deserves careful attention and potentially more aggressive medical management.

Implications for clinical trials. The major implication of this analysis for clinical trials, which usually focus on high risk patients, is that a much more accurate assessment of risk can be made using different ECG criteria than those in current practice. Although isolated T wave inversion clearly represents an ECG change, it appears *not* to be a marker of adverse prognosis (Table 3). Thus, the use of isolated T wave inversion as an entry criterion would select relatively low risk patients. Using the standard criterion of ST segment deviation ≥1 mm or T wave inversion to select a "high risk" patient group, the 1-year rate of death or MI in this cohort was 8.5%. If one restricted this to only ST segment deviation ≥1 mm, the event rate would be higher (11%), but it would comprise only 12% of the total group. With the new criteria identified in this analysis—ST segment deviation ≥0.5 mm or LBBB—the pool of patients who fall into a *truly* high risk group is greatly expanded to nearly one-third the entire group of patients with unstable angina and non–Q wave MI, and their 1-year event rate was 15.8%.

Table 5. Multivariate Predictors of Death or Myocardial Infarction at One Year for 1,411 Patients

Characteristic	RR (95% CI)	p Value*
Age (decade)	1.43 (1.26–1.61)	< 0.001
Thrombolysis in prior wk	9.40 (2.94–30.01)	< 0.001
LBBB	2.80 (1.81–4.32)	< 0.001
ST Dev ≥0.5 mm	2.45 (1.74–3.45)	< 0.001
Other major illness	1.94 (1.33–2.84)	< 0.001
TIMI IIIB exclusion: unable to comply with follow-up	5.61 (1.74–18.06)	0.004
Nitrates in prior wk	1.60 (1.16–2.20)	0.004

*Cox proportional hazards analysis. CI = confidence interval; RR = risk ratio; TIMI = Thrombolysis in Myocardial Ischemia; other abbreviations as in Table 1.

Study limitations. The ECG interpretations in this study were not carried out using the Minnesota code, which has been used extensively (25,26). However, the Minnesota code is complex and not used clinically, whereas the coding used in this study is similar to that used in clinical cardiology, making the findings in this study all the more useful clinically. Interpretation of the ECGs was done by visual inspection, and not by tracing the ECGs, and computerized enhancement was done as in TIMI IIIB (5). However, the ECG interpretation was carried out by a single electrophysiologist who had no knowledge of the clinical characteristics and outcome, thereby adding standardization to the ECG findings. Finally, this study is an observational study, and as such, the treatment strategies employed by physicians were not standardized. However, this is a multicenter study with careful screening and follow-up of all consecutive patients to avoid any selection or reporting bias, thus giving an accurate picture of clinical outcomes in current practice.

Conclusions. The ECG remains one of the most useful and cost-effective tools in the evaluation of patients with unstable angina and non–Q wave MI. A group of patients with unstable angina and non–Q wave MI at high risk for adverse outcome (15.8% death or MI by 1 year) can be identified not only by the presence of ST segment deviation ≥1 mm, but also by ST segment deviation ≥0.5 mm or LBBB at the time of presentation (together comprising over one-third of all patients). In contrast, isolated T wave inversion did not influence outcome, suggesting that clinicians should focus less on T waves and more on subtle degrees of ST segment deviation. Our data highlight the chronic and recurrent nature of unstable angina and the need for improved application of currently available medical treatments and a search for more effective therapies for these high risk patients.

Appendix

TIMI III Registry ECG Ancillary Study Group

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TIMI III Registry ECG Ancillary Study Clinical Centers

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