Continuous 12-Lead ST-Segment Recovery Analysis in the TAMI 7 Study

Performance of a Noninvasive Method for Real-Time Detection of Failed Myocardial Reperfusion

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Background. If a practical, reliable, noninvasive marker of failed reperfusion was available in real time, the benefits of further therapy in this patient subgroup could be tested. We developed a method of 12-lead ST-segment recovery analysis using continuously updated reference points to provide such a marker.

Methods and Results. In this study, our method was prospectively tested in 144 patients given thrombolytic therapy early in myocardial infarction. All patients had 12-lead continuous ST-segment monitoring and acute angiography, each analyzed in an independent, blinded core laboratory. ST-segment recovery and reevaluation were analyzed up to the moment of angiography, at which time patency was predicted. Predictions were correlated to angiographic infarct artery flow, with TIMI flow 0 to 1 as occluded and TIMI flow 2 to 3 as patent. Infarct artery occlusion was seen on first injection in 27% of patients. The positive predictive value of incomplete ST recovery or ST reevaluation by our method was 71%, negative predictive value 87%, with 90% specificity and 64% sensitivity for coronary occlusion. ST recovery analysis predicted patency in 94% of patients with TIMI 3 flow versus 81% of patients with TIMI 2 flow and predicted occlusion in 57% of patients with collateralized occlusion versus 72% of patients with noncollateralized occlusion. In a regression model including other noninvasive clinical descriptors, ST recovery alone contained the vast majority of predictive information about patency.

Conclusions. In a blinded, prospective, angiographically correlated study design, 12-lead continuous ST-segment recovery analysis shows promise as a practical noninvasive marker of failed reperfusion that may contribute substantially to currently available bedside assessment. Our data also suggest that patients with TIMI 2 flow or with collateralized occlusions may represent a physiological spectrum definable with ST-segment recovery analysis. (Circulation 1993;88:437-446)

KEY WORDS • ST-segment • myocardial infarction • ischemia • coronary artery disease

Reduction in mortality in patients given thrombolytic therapy during acute myocardial infarction1-5 presumably results from recanalization of the occluded infarct artery. Failed reperfusion occurs in about 25% of patients after thrombolytic therapy and is associated with higher mortality, more congestive heart failure and arrhythmias, and impaired systolic and diastolic left ventricular function.6-12 Patients with failed reperfusion might benefit from more aggressive treatment; however, to test such a hypothesis without subjecting all patients to acute catheterization, a reliable noninvasive technique for real-time determination of infarct artery patency would be necessary. Multiple noninvasive markers of reperfusion have been investigated, but problems with accuracy, timeliness, or other technical limitations have hampered the application of these approaches in real time.13-31

ECG-based measurements of ST-segment recovery have been correlated consistently with reperfusion.32-46 In studies using continuous ST-segment monitoring, 35% to 50% of patients have been found to have multiple periods of both ST recovery and reevaluation early in infarction, apparently reflecting cyclic variations of infarct artery flow.33,36,38,43-46 To be useful, a real-time noninvasive approach to patency assessment accommodates such dynamic behavior without loss of accuracy or practicality.
We have participated in the development of a microprocessor-assisted digital ECG that continuously updates 12-lead ST-segment measurements every 17 to 20 seconds in real time with hard-copy graphic trends and standard analog ECGs immediately accessible at the bedside. In conjunction with this recording capability, we have developed a continuously updated, patient-specific method of ST recovery analysis for real-time prediction of infarct artery patency. In a pilot experience this analytic method showed encouraging accuracy, including recordings from patients with angiographically documented cyclic changes in infarct artery patency. We now report the results of a prospective, blinded trial testing the predictive accuracy of our method in a larger cohort of patients characterized with simultaneous angiography.

Methods

Participating Centers
The TAMI 7 study was conducted at six regional medical centers in collaboration with 21 community hospitals. Institutional review board approval was obtained at all participating sites.

Patient Population
All patients were identified prospectively. Inclusion and exclusion criteria have been detailed previously. In summary, patients between the ages of 18 and 76 years presenting with between 30 minutes and 6 hours of persistent chest pain and diagnostic ST-segment changes unresponsive to sublingual nitroglycerin were included if they were able to give informed consent and had no recent bleeding diathesis, surgery, stroke, trauma, severe hypertension, or other advanced comorbid diseases. For the primary ST-segment analysis, additional prospective ECG-based exclusion criteria included new bundle branch block or axis shift, use of a ventricular pacemaker, sustained ventricular rhythm, or artifact at the time of catheterization or for >2 hours before catheterization.

Thrombolytic Regimens and Initial Care
A total of five thrombolytic drug regimens were evaluated over the TAMI 7 study. Agent and dosing modality for each regimen have been detailed previously. In summary, all regimens included rapid or "front-loaded" drug delivery of recombinant tissue plasminogen activator. All patients received 325 mg aspirin, oxygen, lidocaine, and nitrates. Intravenous heparin infusion of 1000 U per hour was begun at the completion of thrombolytic infusion. Intravenous metoprolol (15 mg divided over three doses) was administered unless abnormalities of heart rate, blood pressure, or other contraindications were encountered.

Angiography
All patients underwent acute catheterization to evaluate infarct-related artery patency as close as possible to 90 minutes after initiation of thrombolytic therapy. Angiograms were analyzed by a cardiologist and technician at the Core Angiographic Laboratory at the University of Michigan, blinded to all ST data. For the correlation with ST recovery analysis, patency was evaluated at the first contrast injection of the infarct artery.

For the purposes of this study, TIMI flow 0 to 1 was taken as occluded, TIMI flow 2 to 3 was taken as patent. The presence or absence of collateral flow was noted qualitatively as present or absent but was not considered in the primary analysis.

ST-Segment Monitoring
All patient studies were recorded with the Mortara ST Monitoring System (Mortara Instrument, Milwaukee, Wis), a portable, programmable, digital 12-lead ST-segment monitor whose capabilities and signal processing characteristics have been described previously. This device acquires, digitizes, and immediately analyzes a 12-lead ECG every 17 to 20 seconds, using the patient's own previous baseline as a template for comparison of ST levels. All measurements are made on median beat ECG complexes to enhance signal/noise content. Impedance monitored skin prep and bony landmarks for stable lead positioning in our work have been described previously and were used routinely in this study in all participating centers. All patients were at bed rest throughout the study period. For the purposes of this study, real-time alarms and bedside access to ST trends were disabled, creating a "black box" recorder.

ST-Segment Analysis
All stored ECGs were downloaded as a digital data stream to floppy discs for analysis in the Ischemia Monitoring Core Laboratory at Duke University. All studies were read by an experienced cardiologist blinded to all angiographic and clinical data except for the time of onset of chest pain; the time of onset of thrombolytic therapy; and the hard copy ECG(s) taken before initiation of monitoring. Before distribution of each study to the blinded reader, an electronic "mark" was placed into the data stream at the moment of first contrast injection of the infarct artery. This mark interrupted the ECG data in the scanning program at the moment of catheterization, preventing the blinded reader from accessing any ECGs subsequent to the mark. Thus, the "end" of each study, where the blinded reader was required to predict infarct artery patency based on ST recovery, was simultaneous with the first angiographic injection of the infarct artery in all cases.

Our technique of ST-segment recovery analysis has been described in detail previously. In summary, PC-based playback software provides two primary tools: a three-dimensional graphic display of 12-lead ST levels over time (illustrated in Fig 1) and a 12-lead superimposition display for visual review of every analog ECG. These tools are used through three phases of study analysis: determination of the ST measurement matrix (single most abnormal lead or summed 12-lead deviation); determination of transition peaks and troughs within the trend of the matrix over time; and interpretation of the matrix measurements at the moment of the "marked" ECG (the "end" of each study) for noninvasive patency prediction.

Transition peaks and troughs within the ST matrix were used to identify periods of ≥50% ST recovery and periods of ST reelevation, as has been described previously, and as is illustrated in Fig 1. Each transition point as it occurs is used as a new, updated reference for subsequent comparative measurements over the course of the study.
Using this self-referenced system of measurement, the
“current” ECG is continuously characterized as occurring
during a period of persistent ST elevation, a period of ST
recovery, a period of “fingerprint-matched” ST reeleva-
tion, or an active transition period. If the first contrast
injection, indicated by the “marked” ECG at the “end” of
each study, occurred during a recovery interval, the infarct
artery was predicted to be patent. If the marked ECG
occurred during a period of persistent ST elevation or ST
reelevation, the artery was predicted to be occluded. If the
marked ECG occurred during a period of active tran-
sition, the artery patency was considered indeterminate.
The range of predictions was characterized over an 11-
point ST recovery analysis score, ranging from +5 to −5
where 0 to 5 indicated the blinded reader’s certainty level
(5 as certain, 0 as uncertain) and “+” and “−” indicated
“patent” or “occluded,” respectively. Thus, an ST score of
+5 indicated a high certainty that the artery was patent,
based on the blinded ST recovery analysis; a score of −5
indicated a high certainty that the artery was occluded; a
score of 0 indicated complete uncertainty as to the artery's patency at that moment. Recovery interval scores (predicting patency) included the range from +3 to +5; (re)elevation scores included the range from −3 to −5; indeterminate scores included the range from −2 to +2. Examples predicting a patent, an occluded, and an indeterminate infarct artery based on ST recovery are illustrated in Fig 1.

Clinical Descriptors

To assess the information content of the ST recovery assessment relative to other clinical variables, routine bedside descriptors were collected on all patients. These descriptors included patient age, sex, weight; race; infarct location; time from onset of chest pain to onset of therapy; time from onset of therapy to catheterization; any sudden decrease in chest pain; and subjective chest pain severity (0 to 10 scale) at the moment of catheterization.

Data Analysis and Presentation

Continuous patient characteristics are summarized using the median and interquartile range (25th and 75th percentiles); discrete variables are described with percentages. The patency assessment scores based on ST recovery across the groups having patent and occluded arteries at the first diagnostic injection are presented as actual numbers. The effectiveness of a cutoff in the patency assessment score between −3 and −2 in detecting patients with an occluded artery was described using the sensitivity, specificity, and positive predictive value. The sensitivity represents the proportion of occluded patients that would be classified as occluded by the ST recovery interpretation score. The specificity is the proportion of patients with patent vessels that would be classified as patent based on the ST recovery interpretation. The positive predictive value describes the proportion of patients classified as occluded that actually have occluded arteries.

Multiple logistic regression analysis was used to develop a model to predict infarct artery patency. Candidate variables included the patency assessment score in addition to routinely available noninvasive clinical descriptors. Potential interactions between selected variables were explored. The concordance probability index (C-index), which represents the area under a true receiver operating characteristic (ROC) curve, was used to assess the discriminatory ability of the regression model. In this situation, the C-index represents the probability that, of two patients chosen at random, one open and one closed, the patients with the highest prediction of being occluded would be the one actually occluded.

Results

Of the 232 patients enrolled in the TAMI 7 trial, 9 had no enzymatic evidence of myocardial infarction and 3 did not receive thrombolytic therapy. Of the 220 patients with CPK-confirmed infarction treated with thrombolytic therapy, all 144 with adequate ST-segment monitor and angiographic data were included in the primary analysis. The 76 patients eliminated included 8 with no acute catheterization; 4 in whom the ST monitor was not applied; 3 in whom the ST monitor data were destroyed in transfer; 9 with pacemaker or bundle branch block (“biological” artifact) preventing analysis; 15 with prototype device hardware or software failure (“device” artifact); and 37 with improper initiation or continuation of monitoring from the time of presentation to the moment of catheterization (“user” artifact).

The baseline clinical characteristics of the population included for and excluded from ST analysis are shown in Table 1. There were no significant differences suggesting a bias in the population analyzed. Of the 144 patients with complete ST monitor and angiographic data, 6 did not have complete chest pain information. Regression modeling was performed both excluding and including these six, as discussed below.

### Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Adequate ST monitor studies</th>
<th>Inadequate ST monitor studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patients (n)</td>
<td>144</td>
<td>76</td>
</tr>
<tr>
<td>Male sex</td>
<td>80%</td>
<td>72%</td>
</tr>
<tr>
<td>Caucasian</td>
<td>85%</td>
<td>79%</td>
</tr>
<tr>
<td>Median age (years)</td>
<td>57</td>
<td>60</td>
</tr>
<tr>
<td>Median weight (kg)</td>
<td>79.7</td>
<td>78.1</td>
</tr>
<tr>
<td>Risk factors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>61%</td>
<td>55%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>83%</td>
<td>80%</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>72%</td>
<td>76%</td>
</tr>
<tr>
<td>Tobacco abuse</td>
<td>32%</td>
<td>42%</td>
</tr>
<tr>
<td>Prior MI history</td>
<td>7%</td>
<td>12%</td>
</tr>
<tr>
<td>Multivessel CAD</td>
<td>47%</td>
<td>56%</td>
</tr>
<tr>
<td>Infarct artery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAD</td>
<td>42%</td>
<td>36%</td>
</tr>
<tr>
<td>Circumflex</td>
<td>10%</td>
<td>12%</td>
</tr>
<tr>
<td>Right</td>
<td>47%</td>
<td>47%</td>
</tr>
<tr>
<td>Unknown</td>
<td>0%</td>
<td>5%</td>
</tr>
<tr>
<td>Median time from symptoms to therapy (minutes)</td>
<td>156</td>
<td>185</td>
</tr>
<tr>
<td>Median time from therapy to catheterization (minutes)</td>
<td>145</td>
<td>135</td>
</tr>
<tr>
<td>Clinical Presentation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median heart rate (bpm)</td>
<td>78</td>
<td>73</td>
</tr>
<tr>
<td>Median blood pressure (mm Hg)</td>
<td>142/90</td>
<td>141/88</td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td>21%</td>
<td>25%</td>
</tr>
</tbody>
</table>

MI, myocardial infarction; CAD, coronary artery disease; LAD, left anterior descending; bpm, beats per minute.

### ST Recovery Score and Angiographic Correlation

An occluded infarct artery (TIMI 0 to 1 flow) was seen in 39 of 144, or 27% of patients. TIMI 2 flow was seen in 27 patients, and TIMI 3 flow in 78 patients. Collaterals to the infarct artery were seen in 54% of patients with TIMI 0 to 1 flow and in 27% of patients with TIMI 2 to 3 flow.

Table 2 shows ST analyses over the four grades of TIMI flow. Of the 144 ST analyses at the moment of first angiographic injection, 35 occurred during definite (re)elevation periods (predicting occluded), 91 occurred during definite recovery periods (predicting patent), and 18 occurred during active transition or indeterminate periods. Of the 35 patients with an ST analysis predicting occlusion, 25 (71%) were occluded angio-
Table 2. ST Analysis

<table>
<thead>
<tr>
<th>Angio flow</th>
<th>n</th>
<th>Occluded</th>
<th>Indeterminate</th>
<th>Patent</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIMI 0</td>
<td>34</td>
<td>23</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>TIMI 1</td>
<td>5</td>
<td>2</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>TIMI 2</td>
<td>27</td>
<td>5</td>
<td>4</td>
<td>18</td>
</tr>
<tr>
<td>TIMI 3</td>
<td>78</td>
<td>5</td>
<td>10</td>
<td>63</td>
</tr>
<tr>
<td>Total</td>
<td>144</td>
<td>35</td>
<td>18</td>
<td>91</td>
</tr>
</tbody>
</table>

graphically. Of the 91 patients an ST analysis predicting patency, 81 (89%) were patent angiographically. Of the 18 patients with indeterminate ST recovery analyses, 14 were patent and 4 were occluded. If studies with indeterminate ST analysis were combined with studies predicting patency, as a “probably not occluded” group, the infarct artery was patent in 95 of 109 (87%). Thus, noninvasive prediction of an occluded infarct artery by ST recovery analysis had a positive predictive value of 71%, negative predictive value of 87%, sensitivity of 64%, and a specificity of 90%, with 95% confidence intervals of 56% to 86%, 67% to 91%, 49% to 79%, and 84% to 96%, respectively.

Of the 78 patients with TIMI 3 flow, 5 (6%) had ST (re)evaluation suggesting occlusion at the moment of angiography. Of the 27 patients with TIMI 2 flow, 5 (19%) had persistent ST elevation at the moment of angiography. Of the 18 patients with occluded arteries and no collaterals, 13 (72%) had persistent or recent ST elevation at the moment of angiography. Of the 21 patients with collateralized occlusions, 12 (57%) had persistent ST elevation at the moment of angiography.

Of the 20 patients in whom ST recovery analysis did not accurately predict angiographic patency, 13 (65%) had either TIMI 2 flow or a collateralized occlusion. In an additional five patients, an ST trend transition followed the moment of angiography within 5 minutes, suggesting a loss of precise synchrony between the angiographic log and the ST monitor clock. In the other two patients, a combination of low ST amplitudes and high noise content (poor signal/noise ratio) resulted in an inaccurate patency prediction.

Relative Role of Noninvasive Parameters

Tables 3 and 4 show the best models predicting infarct artery occlusion using clinical descriptors with and without ST-segment monitoring. In Table 3, in the absence of ST monitor data, more severe chest pain at the moment of catheterization was the strongest single predictor in the model. When ST recovery assessment is included in the model, younger age and greater body weight also added information as seen in Table 4, but no chest pain variable contributed. Since chest pain scores did not contribute to the model when ST recovery was included, the model was also developed using all 144 patients with otherwise complete data, as shown in Table 4. Clinical data including younger age, earlier time from onset of chest pain to onset of therapy, and earlier time to catheterization contributed 24% of the total combined information. ST-segment recovery analysis alone contributed 69%, a highly significant addition to the clinical descriptors (P<.00001). Including ST-segment analysis improved the model’s predictive power from a $\chi^2$ of 14.26 to 58.35.

In Fig 2, ROC curves and the related C-index values for detection of an occluded infarct artery are shown for the clinical model alone, for ST recovery alone, and for the optimal model using both in the 138 patients with complete chest pain scores. ST recovery assessment alone largely approximates the discriminative content of the optimal model and significantly outperforms clinical descriptors alone. Nonetheless, it can be noted that the highly specific profile of ST recovery alone appears to be complemented with enhanced sensitivity by the addition of clinical information into the optimal model.

Discussion

This study indicates that our method of ST-segment recovery analysis can significantly improve real-time noninvasive prediction of infarct artery patency. In our population overall, first angiographic injection showed a patent artery in 73%. In the context of this pretest probability, ST recovery analysis identified a patient group, 71% of whom had occluded arteries, with 65% sensitive and 90% specific detection of all coronary occlusions.

In our trial, angiography was used as the exclusive “gold standard” defining patency. TIMI 2 flow was defined as a patent vessel. TIMI 0 to 1 flow was defined as occlusion whether collaterals were present or absent. Of our 20 patients in whom patency prediction by ST recovery did not correlate with angiography, 13 had either TIMI 2 flow or a collateralized infarct artery. For this study, these predictions were taken as errors in every case. Debate continues over the functional sufficiency of TIMI 2 flow and the functional importance of collateralization to the infarct zone. The majority of our patients with TIMI 2 flow (81%) showed ST-segment recovery suggesting functional reperfusion but less consistently than patients with TIMI 3 flow (94%). The majority of our patients with collateralized occlusions (57%) had persistent ST elevation suggesting ongoing infarction but less consistently than patients with noncollateralized occlusion (72%). Our data suggest that the use of angiography alone probably leads to the incorporation of a physiological spectrum into each of these anatomically defined groups. Further evaluation of the prognostic significance of ST recovery in these subgroups is ongoing.

To emulate real time and avoid bias from ECG data acquired after the moment designated for analysis, the ST study reader was not given access to ECGs beyond the moment of initial angiography. In nine cases, this moment coincided with an active ST trend transition, yielding an indeterminate ST recovery analysis. As illustrated in Fig 3, in actual application such indeterminate periods are gen-

Table 3. Best Clinical Model for Noninvasive Patent Assessment: No ST Monitoring, All Other Variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient</th>
<th>$\chi^2$</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest pain score</td>
<td>0.170</td>
<td>3.40</td>
<td>.065</td>
</tr>
<tr>
<td>Age</td>
<td>-0.122</td>
<td>5.78</td>
<td>.016</td>
</tr>
<tr>
<td>Weight</td>
<td>0.022</td>
<td>2.19</td>
<td>.14</td>
</tr>
</tbody>
</table>

Total model $\chi^2$ 14.26

n=138. C-index, 0.694.
TABLE 4. Best Clinical Models for Noninvasive Patency Assessment

<table>
<thead>
<tr>
<th>Variable</th>
<th>All clinical variables and ST monitoring (n=138)</th>
<th>All significant variables and ST monitoring (n=144)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Coefficient</td>
<td>$\chi^2$</td>
</tr>
<tr>
<td>ST recovery</td>
<td>-0.367</td>
<td>39.91</td>
</tr>
<tr>
<td>Time to treatment</td>
<td>-0.011</td>
<td>5.62</td>
</tr>
<tr>
<td>Age</td>
<td>-0.172</td>
<td>6.95</td>
</tr>
<tr>
<td>Time to catheterization</td>
<td>-0.0040</td>
<td>3.41</td>
</tr>
<tr>
<td>Total model $\chi^2$</td>
<td>58.35</td>
<td>0.888</td>
</tr>
</tbody>
</table>

...erally clarified by simply continuing to monitor the patient over an additional 5 to 15 minutes.

Despite the idiosyncrasies of our study design, ST-segment recovery analysis alone was far more predictive of patency than were clinical bedside descriptors, particularly chest pain, in a statistical model. The poor reliability of chest pain response and other descriptors seen in our model are consistent with previously reported findings in an independent patient population. It does appear from our data that optimally selected clinical information might be combined with ST-segment recovery analysis to further improve overall discriminative power and particularly sensitivity detecting coronary occlusion.

ST-segment recovery has been reported as an objective marker of reperfusion with remarkable consistency. Further application of previous studies has been hampered by the uncertainties of their retrospective analyses in small populations using static methods. A detailed comparison of our methodological differences relative to previous publications is beyond the scope of this report. Two broad areas of departure from previously published methods bear comment, however. Specifically, these two areas include the importance of continuous monitoring and the importance of multiple-lead monitoring.

The process of measuring ST-segment recovery is invariably defined in part by a two-point comparison. One of these two points is consistently the ST level at the moment of patient assessment—the "current" ECG. Determination of the reference ECG to which any current ECG may be compared is, in our methodology, a departure from previously published static and retrospective approaches. Rather than selecting a single "pretreatment" ECG or a fixed comparison interval, which may not accommodate patients with cyclic flow variation, our method uses continuous monitoring to update and redefine the reference ECGs every 17 to 20 seconds in an ongoing fashion. With continuous monitoring, fluctuations in ST-segment level are uniquely defined for each patient, including the true extremes of deviation "peaks" and recovery "troughs." Figs 4 and 5 show an example of how differently reperfusion might be profiled in the same patient. In Fig 4, fixed interval serial sampling suggests reperfusion at 90 minutes. In Fig 5, peaks and troughs identified with continuous monitoring in the same patient show first evidence of reperfusion at 27 minutes, with first evidence of stable reperfusion at 60 minutes.

Just as undersampling over time may yield misleading conclusions, so may undersampling over the precordial. Quantification of maximal deviation presumes that the locus of measurement reflects the epicenter of ST activity. Measurements from lead V1 in the patient...
illuminated in Fig 5 (at the edge of the infarct zone) would yield different quantitative results than measurements in lead V₂. Even the use of an initial 12-lead ECG to guide optimal placement of a single lead for monitoring is vulnerable to any subsequent shift of the epicenter of infarction. We use 12-lead surveillance of the precordium to continuously redefine the zone of peak ST activity and the most active single lead within that zone for all quantitative measurements.

Multiple-lead monitoring also enhances definition of each patient's infarct pattern of ST deviation, or precordial "fingerprint."53 As has been demonstrated previously, this patient-specific, coronary site–specific pattern evolves within seconds of coronary occlusion.53-55 After ST recovery, subsequent ST deviation is commonly detectable.56-64 Discrimination between "evolutionary" ST-T wave changes, transient ischemia from noninfarct artery disease, and reelevation from reocclusion of the infarct vessel is enhanced by the incorporation of qualitative multilead fingerprint matching.

Some important limitations to our study and the final data analysis deserve emphasis. First, it must be appreciated that entry criteria for the TAMI 7 trial included ≥200 µV ST elevation on ECG. In addition to this selective criteria, 8 of the 220 TAMI 7 patients (4%) evolved persistent bundle branch block or required ventricular pacemakers and so were excluded from the analysis. In another 60 patients, combined device and human errors resulted in incomplete monitoring records. Losing another 8 patients with incomplete angiographic data, our study subjected only 65% of the 220 TAMI 7 patients to our primary analysis. This denominator is suboptimal. However, the data as acquired had no apparent bias (Table 1) and resulted from a consider-able effort over multiple community and university hospitals. These efforts ultimately produced the largest angiographically correlated acute infarction 12-lead ECG data base ever reported. In current trials, using a commercial-grade instrument interactively in real time and with a more consistent approach to training staff, technical performance has improved.

Even with the compilation of the largest experience yet published, our final population size is still too small to address several important questions. Confidence limits on the predictive performance we observed are fairly wide. The precise effects of collaterals, the classification of TIMI 2 flow, and the potential for varying the method in anterior versus inferior infarctions all must await the results of larger investigations already in progress.

Despite these limitations, the experience we report has several important ramifications. As a noninvasive, ECG-based technique, ST-segment monitoring can be initiated in small community hospitals from the onset of treatment with thrombolytic therapy, as was repeatedly demonstrated by the many such hospitals who participated in the TAMI 7 study. ST-segment recovery analysis provides an updated assessment as frequently as every 17 seconds, with the potential for real-time use in the busy environment of acute patient care whether ST levels are stable or unstable. Our data show that the incorporation of these practical elements may contribute substantially to current methods of bedside assessment in this patient population. A larger clinical experience and further technical enhancements might further enhance this contribution. In addition, combination of this approach with clinical descriptors and possibly with other noninvasive markers of reperfusion such as cardiac enzymes might lead to a regression-based probabilistic "instrument" that could improve sensitivity without detriment to specificity, ie, that could improve overall accuracy identifying patients with occluded infarct arteries. Our regression model suggests, however, that continuous 12-lead ST-segment recovery

![Fig 4. Serial 12-lead ECGs from a patient presenting with anterior myocardial infarction, illustrating patency prediction using static method measuring ST recovery by comparing ST levels at fixed 30-minute intervals to the ST levels seen on the pretreatment (P) ECG. Reperfusion is defined by ≥50% ST recovery. Peak ST level in lead V₁ of pretreatment ECG is 5.8 mm. At 30 minutes and 60 minutes, ST levels are 7.7 and 6.6 mm, respectively, interpreted as persistent infarct artery occlusion. At 90 minutes, ST level is 2.6 mm, a 65% recovery, suggesting reperfusion.](http://circ.ahajournals.org/lookup/suppl/doi:10.1161/01.CIR.85.11.449.137226/-/DC1/fig4.jpg)
Fig 5. Continuously updated ST-segment recovery analysis in same patient shown in Figs 1 and 4. Trend of summed deviation over time, at right, with markers showing timing of selected ECGs at left as well as previous updated reference peak or trough. ST elevation of 5.8 mm in peak lead V3 worsens to a first transition peak (T1 in Fig 1) of 7.5 mm by 6 minutes after onset of therapy. From this reference peak, ST recovery to 3.7 mm (or 50% recovery) 27 minutes after onset of therapy suggests reperfusion. From this reference trough (T2 in Fig 1), reelevation to 7.7 mm in the same fingerprint pattern over the next 3 minutes suggests rapid reocclusion of the artery, with progressive ST elevation to the true ST maximum of 18-mm elevation at the transition peak 50 minutes after onset of therapy (T3 in Fig 1). Subsequent ST recovery referenced to this peak shows >50% recovery to the 6.6-mm level over the next 10 minutes, suggesting reperfusion at 60 minutes, different from the static interpretation of this same ECG in Fig 4.

analysis alone provides a basis for real-time noninvasive triage that opens the door to future investigation into therapeutic strategies in patients with failed thrombolysis.

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