Prognostic Impact of Early ST-Segment Resolution in Acute ST-Elevation Myocardial Infarction
Rolf Schröder, MD

Simple and rapid measures are needed for timely assessment of the quality of reperfusion therapy in acute ST-elevation myocardial infarction (STEMI). Although successful recanalization of the epicardial vessel is a necessary condition, it is the microvascular flow that most strongly correlates with outcome. ST-segment changes reflect myocardial rather than epicardial flow and hence yield prognostic information beyond that provided by coronary angiogram alone. Numerous studies have shown a remarkably consistent relationship between the degree of ST resolution and subsequent mortality. In a 2001 editorial in Circulation, Gibson wrote, “In a time of dizzying advances in diagnostic modalities, it is refreshing to see what a useful, simple, noninvasive, broadly accessible, easily repeatable/applied, and affordable tool the ECG is.”

Methods of Measuring ST-Segment Deviation Recovery
Because reperfusion is a dynamic process, it was suggested that continuous monitoring of ST-segment resolution might be advantageous. Although continuous monitoring could elucidate the dynamics of ST-segment recovery, the prognostic implications of early ST-segment fluctuations are unclear. No conclusive studies of sufficient sample size exist with regard to the utility of continuous ST-segment monitoring in predicting mortality risk. Fortunately, an early variability of ST-segment resolution at most plays only a minor role in the quality of outcome prediction by static ECG analysis. The domain for continuous ST monitoring may be a later time period between 6 and 24 hours after fibrinolysis, when the goal of ST monitoring shifts toward the detection of silent reocclusion.

Sum STR
In most studies, resolution of the sum of ST-segment elevation (sum STR) after reperfusion therapy either by fibrinolysis or primary percutaneous coronary intervention (PCI) is used to predict infarct size, left ventricular function, epicardial vessel patency, and mortality. Sum STR is expressed as the percentage from baseline. Measuring ST-segment elevations from all leads related to infarct location, however, is time consuming. In an ECG substudy of the Intravenous NPA for the Treatment of Infarcting Myocardium Early (InTIME II) Study in 2719 patients with ECG recordings made 90 minutes after fibrinolysis, we found, with regard to predictive accuracy combined with simplicity, 2 methods that are superior to the conventional model of sum STR: (1) the single lead showing maximum deviation (single-lead STR) and (2) the existing ST-segment deviation in the single ECG lead of maximum deviation present at a given time point after fibrinolysis (max STE).

Single-Lead STR
Single-lead STR is measured by comparing one ECG lead with the most prominent ST-segment deviation at baseline and at a given time point after fibrinolysis, irrespective of the ECG lead measure at baseline. This comparison provides percentages of ST-segment deviation recovery independent from any changes in the patient’s position or the position of the lead electrodes. In anterior STEMI, only ST-segment elevation resolution is considered. In inferior STEMI, the difference is measured between either the ST-segment elevation on one of the inferior leads (II, III, aVF, V5, or V6) or the ST-segment depression on one of the precordial leads (V1 to V4), whichever lead shows the largest deviation either at baseline or at the given time.
Max STE

Max STE represents the existing maximum ST-segment deviation that is present at a given time of assessment. Max STE is measured as per single-lead STR, but it is not compared with ST-segment deviation on the baseline ECG.

Cutoffs for Defining Risk Groups

The optimal cutoffs for defining mortality risk groups were assessed by appropriate statistical methods.\(^9,10,12,13\) Applying 2 cutoffs provides a clearer definition of high- and low-mortality risk groups.

Sum STR is conventionally categorized as complete (≥70%), partial (70% to 30%), and no (<30%) ST-segment elevation resolution.\(^9\) The corresponding cutoffs for single-lead complete STR are also ≥70%, both for anterior and inferior infarction. For the single-lead high-risk group of no STR, the cutoffs were <50% resolution in anterior STEMI and <20% in inferior STEMI, respectively.

The classification of max STE low- and high-risk groups is illustrated in Table 1. Patients at neither low nor high risk form the medium-risk group. Anterior STEMI needs to be stratified into potentially small or large infarcts according to a baseline single-lead ST elevation of ≤4.5 mm or >4.5 mm, respectively (10 mm = 1 mV). Because in many patients the percentage of ST-segment deviations will not be near the cutoff values, risk groups are easily recognized in most cases.

Assessment of Epicardial Reperfusion

As a tool to identify epicardial reperfusion, all methods of ST resolution assessed by either continuous monitoring or static ECG recordings have the principal limitation that ST-segment changes integrate both epicardial and myocardial reperfusion. Patients with complete sum or complete single-lead STR\(^13,16,17\) or low-risk max STE\(^14\) at 90 minutes have a >90% probability of a patent infarct-related artery associated with successful reperfusion at the microvascular level. Approximately 50% of patients with no ST resolution or with high-risk max STE, however, still have a patent epicardial infarct artery. Lack of ST resolution is caused by the failure of reperfusion at the tissue level. Thus, ST resolution is an accurate predictor of infarct artery patency, but it is less accurate for predicting epicardial vessel occlusion.

Prediction of Mortality

Death from noncardiac causes such as cerebral hemorrhage cannot be predicted by ST-segment deviation recovery. Because noncardiac mortality rates were similar in the low-, medium-, and high-risk groups of all 3 ST resolution models, the proportion of noncardiac deaths is different. In the low-risk groups, more than one third of patients with no ST resolution or with high-risk max STE, however, still have a patent epicardial infarct artery. Lack of ST resolution is caused by the failure of reperfusion at the tissue level. Thus, ST resolution is an accurate predictor of infarct artery patency, but it is less accurate for predicting epicardial vessel occlusion.

### Table 1. Definition of Risk Groups by Max STE

<table>
<thead>
<tr>
<th>Anterior STEMI</th>
<th>Interior STEMI</th>
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<tbody>
<tr>
<td>Defined by baseline single ECG lead of maximum deviation as ST ↑ ≤4.5 mm</td>
<td>Defined by baseline single ECG lead of maximum deviation as ST ↑ &gt;4.5 mm</td>
</tr>
<tr>
<td>Existing ST deviation after fibrinolysis, low risk, no bundle-branch block</td>
<td>Any ST ↑ or ST ↓</td>
</tr>
<tr>
<td>ST ↑ ≤1 mm</td>
<td>ST ↑ and ST ↓ ≤1 mm*</td>
</tr>
<tr>
<td>Existing ST deviation after fibrinolysis, high risk, or any bundle-branch block†</td>
<td></td>
</tr>
<tr>
<td>ST ↑ &gt;5 mm</td>
<td>ST ↑ or ST ↓ &gt;2 mm*</td>
</tr>
</tbody>
</table>

*ST ↑ in leads II, III, aVF, V₅, or V₆ or ST ↓ in leads V₁–V₄, whichever is larger.
†ST ↑ ≤2 mm with an inferior infarction indicates medium risk.
all deaths resulted from noncardiac causes. Therefore, to judge the predictive power of ST-segment recovery, cardiac mortality analysis appears to be more informative than all-cause mortality analysis.

In multivariate analyses, sum STR, single-lead STR, and max STE were significant independent predictors of short-, medium-, and long-term mortality. High C index statistical values (area under the receiver-operating characteristic curve) reflected good discriminatory and predictive power for all 3. The predictive accuracy value was best for max STE, followed by single-lead STR and sum STR. The differences were statistically significant.

Figure 1 compares 30-day cardiac mortality rates for the low-, medium-, and high-risk groups of the 3 ST resolution models, and Figure 2 compares the subgroups of anterior and inferior STEMI for single-lead STR and max STE. As in all studies with various methods evaluating ST-segment recovery, anterior infarction is associated with less ST resolution than is inferior infarction, and the low-risk groups of complete STR are composed of more than twice as many patients with inferior than with anterior infarction. In all studies, the high-risk groups of patients were older and more often had diabetes, a history of heart failure, or hypertension.

Table 2, which uses data from the electrocardiographic substudy of the International Joint Efficacy Comparison of Thrombolitics (INJECT) trial data bank, 4-year mortality rates were compared for sum STR and max STE in 1398 patients. Long-term mortality is clearly predicted by the extent of initial ST-segment resolution. Again, the predictive power was significantly better for max STE as compared with the conventional method of sum STR.

### Impact of Time to Treatment on the Relationship Between STR Resolution and Mortality

Table 3 shows cardiac mortality rates with max STE groups for patients known to be at higher mortality risk in general. Mortality was exceptionally high in medium- and high-risk group patients who suffered a reinfarction within the first 30 days. That may be the reason why in some studies the nonfatal reinfarction rates were higher in low-risk groups. The total incidence of nonfatal and fatal recurrent infarction in most studies, however, is similar within the 3 ST resolution risk groups.

In all subsets, low risk was associated with a cardiac mortality rate ≤2%. The only exception was patients with fibrinolysis initiated later than 4 hours after symptom onset. Time to treatment reflects the extent of necrosis before therapy. Treatment later than 4 hours after symptom onset in high max STE is associated with a 30-day cardiac mortality of ≤20%, and at 4-year follow-up, the mortality rate approaches 50% (Table 2). These findings reemphasize the critical role of treatment delay.

### TABLE 2. Four-Year Mortality Rates by ST Resolution Risk Groups in 1398 INJECT Trial Patients

<table>
<thead>
<tr>
<th></th>
<th>Sum STR Risk Groups</th>
<th>Max STE Risk Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Patients (%)</td>
<td>Complete</td>
</tr>
<tr>
<td>Total mortality</td>
<td>262 (18.7)</td>
<td>87 (12.8)</td>
</tr>
<tr>
<td>Cardiac mortality*</td>
<td>237 (17.0)</td>
<td>71 (10.4)</td>
</tr>
<tr>
<td>Onset to treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤4 h</td>
<td>175 (15.8)</td>
<td>59 (10.4)</td>
</tr>
<tr>
<td>&gt;4–6 h</td>
<td>62 (21.6)</td>
<td>12 (10.4)</td>
</tr>
</tbody>
</table>

Values represent number of deaths (%).

*Includes cause unknown.
TABLE 3. Thirty-Day Cardiac Mortality Rates by Max STE Risk Groups in Selected Subsets of Patients in InTIME II Study

<table>
<thead>
<tr>
<th>Max STE Risk Groups, %</th>
<th>No. of Patients</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Low</td>
</tr>
<tr>
<td>Female</td>
<td>667</td>
</tr>
<tr>
<td>Age &gt;70 y</td>
<td>641</td>
</tr>
<tr>
<td>Angina pectoris</td>
<td>639</td>
</tr>
<tr>
<td>Previous MI</td>
<td>414</td>
</tr>
<tr>
<td>Diabetes</td>
<td>398</td>
</tr>
<tr>
<td>In hospital</td>
<td></td>
</tr>
<tr>
<td>Killip class &gt;1*</td>
<td>283</td>
</tr>
<tr>
<td>Recurrent MI</td>
<td>138</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
</tr>
<tr>
<td>≤4 h</td>
<td>2162</td>
</tr>
<tr>
<td>&gt;4–6 h</td>
<td>547</td>
</tr>
</tbody>
</table>

*Present at enrollment.

Time Points for Measuring ST-Segment Deviation Resolution

To facilitate making a more rapid decision about the use of rescue PCI, an (earlier) evaluation of ST resolution at 60 minutes was proposed. An increasing number of patients over time, however, develop ST-segment deviation recovery that fulfills the low-risk criteria. Whenever a patient reaches a low-risk category, the outcome is excellent. At 60, 90, and 180 minutes, low-risk groups make up ~30%, 40%, and 50% of all patients, respectively. An early strategy of rescue PCI may unnecessarily expose patients to the risk inherent in the invasive procedure.

A stepwise risk evaluation with a first 12-lead ECG recorded at 60 minutes may be useful. For those patients who do not already fulfill the low-risk group criteria it may be time to prepare for an invasive strategy. With a second ECG taken at 90 minutes, decisions could be reconsidered or consolidated. When streptokinase is being used, slightly more time may be allowed (up to ~120 minutes).

Conclusion

Assessment of the degree of ST-segment deviation resolution on a 12-lead ECG early after reperfusion therapy either by fibrinolysis or primary PCI provides strong, remarkably robust, and unambiguous information in patients presenting within 6 hours of the onset of STEMI. Evaluation of the percentage of ST-segment resolution on the single worst ECG lead (single-lead STR) or even only an estimation of the existing ST-segment deviation on the single worst ECG lead present at a given time point of assessment after fibrinolysis (max STE) is sufficient. Physicians who look after patients with STEMI know that the extent of the remaining ST-segment deviation strongly indicates outcome. Categorization into max STE risk groups classifies the patients as being at high or low mortality risk. When a patient is identified to be at low risk, the prognosis is sufficiently good that an immediate adjunctive coronary intervention can safely be avoided. Patients and their families may promptly be assured, and early discharge after appropriate screening for residual ischemia can be scheduled. Patients at high risk may be promptly referred for an invasive evaluation.

References

18. Purcell IF, Newall N, Farrer M. Change in ST segment elevation 60 minutes after thrombolytic initiation predicts clinical outcome as accurately as later electrocardiographic changes. *Heart*. 1997;78:465–471.
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