Usefulness of the presenting electrocardiogram in predicting myocardial salvage with thrombolytic therapy in patients with a first acute myocardial infarction

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Aims Patients with Q waves and T-wave inversion are generally at a later stage of the infarction process than patients without these changes. Our aim was to investigate whether a single assessment of electrocardiographic parameters at presentation would predict the proportion of myocardium salvageable by thrombolytic therapy.

Methods and Results Electrocardiographic algorithms to calculate the potential and final infarct size have been developed and allow the proportion of myocardium salvageable with therapy to be calculated. This was measured in 146 patients with acute myocardial infarction who had angiography at a median of 91 min after streptokinase. The relationship between myocardial salvage and the electrocardiographic parameters at presentation (Q waves, T-wave inversion, quantitative ST segment changes, and the initial QRS score), was examined together with the 90-min angiographic parameters (TIMI flow grade and collateral grade), clinical parameters (haemodynamics and age), and time to therapy. Parameters that correlated with myocardial salvage included the initial QRS score (r=0.56, P<0.001), maximum ST depression (r=0.27, P<0.01), T-inversion grade (r=−0.26, P<0.01), and TIMI flow grade at 90 min (r=0.21, P<0.02). The time from symptom onset to thrombolytic therapy did not correlate with salvage (r=−0.09). On multivariate analysis, only the initial QRS score and T-inversion grade on the initial electrocardiogram were independent predictors of salvage (multivariate r using both variables combined=0.57, P<0.001).

Conclusions The QRS score and T-wave inversion grade on the presenting electrocardiogram provide important information in predicting myocardial salvage. These parameters may help triage patients to appropriate therapies.

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Introduction

Eligibility criteria for thrombolytic treatment in acute myocardial infarction require a time duration from the onset of ischaemic symptoms of less than 12 h and also ST elevation or presumed new onset left bundle branch block on the presenting electrocardiogram[1–3]. Early and sustained reperfusion salvages ischaemic myocardium, and Thrombolysis in Myocardial Infarction (TIMI)-3 flow in the infarct-related artery at 90 min after therapy is associated with improved survival[4]. As patients' recognition of the duration of chest pain may be imprecise, a simple and objective assessment of the proportion of myocardium potentially salvageable by
reperfusion is useful. In those who have apparently presented after 12 h, this can alter the management strategy. The Selvester QRS score[5–7] measures infarct size with each of the 32 points in the score corresponding to ~3% of the left ventricular mass[7–11]. Using radionuclide techniques, a modified QRS score calculated from the admission electrocardiogram has been validated as a measurement of the potential infarct size, and the QRS score from the day 7 electrocardiogram as a measurement of the final infarct size[12]. This allows calculation of the proportion of myocardium salvageable with therapy.

During the evolution of acute myocardial infarction, pathological Q waves evolve and T-wave inversion develops. Measurement of these electrocardiographic parameters at presentation may reflect the progression of the infarction process and predict the extent of myocardial salvage to be gained from successful reperfusion. In this study, we investigated the relationship between myocardial salvage and the presenting electrocardiographic changes, together with other conventional parameters including the time to thrombolytic treatment and early infarct related artery flow[13].

**Methods**

**Study patients**

This study included patients with a first acute myocardial infarction recruited from the four highest enrolling centres in the HERO-I trial (a randomized, double-blind comparison of hirulog (bivalirudin) versus heparin in patients receiving streptokinase and aspirin for acute myocardial infarction)[13]. Each patient underwent angiography scheduled at 90 min for assessment of infarct-related artery flow and had serial electrocardiograms for infarct size quantitation. The electrocardiogram at enrollment to the trial (the initial electrocardiogram) and the electrocardiogram closest to hospital discharge (the final electrocardiogram) were chosen for analysis, which was performed by observers blinded to the angiographic findings. Recordings with bundle branch block or intraventricular conduction defects, multiple ventricular ectopic beats, concomitant anterior and inferior ST elevation, and technical problems were excluded. Patients with in-hospital reinfarction before the second electrocardiogram or in-hospital revascularization of the infarct-related artery within 48 h of the initial angiogram were also excluded.

**Calculation of myocardial salvage from the QRS scoring method**

The relevant leads defined for anterior infarction were leads V_{1-6}, I and AVL; and the relevant leads for non-anterior infarction were leads II, AVF and V_{5-6} together with leads V_{1-2} in the case of posterior infarction[12].

From the initial electrocardiogram, the initial QRS score was calculated using the standard 32 point QRS score criteria[10,11] to reflect the initial infarct size. Another QRS score, the potential QRS score, was calculated by summation of the maximum score allocated to each individual lead showing significant (≥1 mm) ST elevation (and ≥1 mm ST depression in leads V_{1-2} for posterior infarcts)[13]. This potential QRS score reflects the potential infarct size[12]. In a patient presenting with anterolateral ST elevation in leads V_{1-6}, I and AVL, for example, each of the chest leads from V_{1} to V_{6} and limb leads I and AVL were assigned the maximum score for that lead, and their summation value was the potential QRS score. In these leads, the presence of any Q waves, reduction of R wave amplitude and changes in the R/S wave ratio or R/Q wave ratio were scored according to the original QRS score description, and their summation value was the initial QRS score.

On the final electrocardiogram, the final QRS score was calculated using the standard 32 point QRS score criteria to determine the final infarct size. The ratio of the final QRS score over the potential QRS score equals the proportion of jeopardized myocardium that finally infarcted. The proportion of myocardial salvage equals one minus this ratio. When the final QRS score was larger than the potential QRS score, myocardial salvage was zero.

**Other measurements made on the initial electrocardiogram**

ST segment deviation was measured at 60 ms after the J point. Any deviation of ≥1 mm (0·1 mV) was considered significant. In the lead with the maximum ST elevation, three additional parameters were analysed and graded[14].

(A) Q waves: grade 1 = no pathological Q waves; grade 2 = shallow pathological Q waves with depth >25% of the R wave and width >40 ms; grade 3 = deep pathological Q waves with either a total loss of the R wave or depth >5 mm (0·5 mV) in the inferior or lateral limb leads and >10 mm (1 mV) in the chest leads. Isolated Q waves in lead III were not recorded as pathological Q waves[14].

(B) T-wave inversion: grade 1 = no T-wave inversion; grade 2 = shallow T-wave inversion including biphasic T-waves; grade 3 = deep T-wave inversion of >5 mm (0·5 mV) in the inferior or lateral limb leads and >10 mm (1 mV) in the chest leads[14].

(C) ST segment slope: grade 1 = upsloping ST-segment elevation of >30°; grade 2 = ST-segment elevation with a slope of 10–30°; grade 3 = planar ST-segment elevation with a slope of <10°[14].

**Angiographic analysis**

Infarct-related artery flow at 90 min was measured using the TIMI flow grade: 0 (no perfusion)=no flow beyond
the occlusion; 1 (penetration without perfusion)=slow and incomplete opacification of the vascular bed by contrast material; 2 (partial perfusion)=slow but complete opacification of the vascular bed by contrast material, with slower clearance; 3 (complete perfusion)=prompt and complete opacification of the vascular bed, with rapid clearance, as in an uninvolved artery\textsuperscript{15}]. Collaterals to the occluded coronary segments were graded: 0=no collateral vessels visualized; 1=filling of branches but not the main epicardial segment of the infarct related coronary artery; 2=filling of branches and a portion of the epicardial vessel; 3=filling of branches and the entire coronary vessel\textsuperscript{16}.

Statistics

The relationship between myocardial salvage and other parameters including the Q wave grade, T inversion grade, slope of ST-segment elevation, initial QRS score, TIMI flow grade, collateral grade, haemodynamic parameters on recruitment, age and time from symptom onset to the commencement of streptokinase were examined using linear regression. Repeat analysis in patients with TIMI 2 or 3 flow in the infarct-related arteries was pre-specified. Other variables including gender, smoking, history of hypertension, treatment assignment (heparin vs hirulog), and the presence of left main or three vessel disease were incorporated into a multivariate analysis of the predictors of myocardial salvage. Subgroup analysis was performed in patients with anterior infarction and non-anterior infarction. \(P\) values (2-tailed) of <0·05 were considered significant.

Results

Of 190 patients studied, 146 underwent angiography at a median of 91 min (interquartile range 78–108 min), and had electrocardiograms suitable for analysis.

Thirty-nine patients were excluded because their electrocardiograms were unsuitable for analysis and five patients were excluded due to early reinfarction or early revascularization before the second electrocardiogram. The second electrocardiogram was performed 3·7±1·9 days after enrolment. The time to streptokinase treatment was 3·7±2·5 h; six patients were treated within 1 h of the onset of chest pain. The patient characteristics are reported in Table 1, and the electrocardiographic and angiographic data in Table 2.

Relationships between electrocardiographic parameters and myocardial salvage

Parameters that correlated significantly with myocardial salvage included the initial QRS score (\(r=-0\cdot56, \ P<0\cdot001\)), Q wave grade (\(r=-0\cdot36, \ P<0\cdot001\)), number of leads with ST-segment depression (\(r=0\cdot28, \ P<0\cdot01\)), maximum ST-segment depression (\(r=0\cdot27, \ P<0\cdot01\)), T-wave inversion grade (\(r=-0\cdot26, \ P<0\cdot01\)), and TIMI flow grade at 90 min (\(r=0\cdot21, \ P<0\cdot02\)). The time to streptokinase treatment did not correlate with salvage (\(r=-0\cdot09, \ P=\text{ns}\), Table 3). In patients with patent infarct-related arteries (TIMI 3 flow or TIMI 2 or 3 flow), the correlations between the electrocardiographic parameters and myocardial salvage were similar (Table 4). The time to streptokinase treatment also did not correlate with salvage (\(r=0\) for patients with TIMI 3 flow and \(r=-0\cdot04\) for patients with TIMI 2 or 3 flow).

Predictors of myocardial salvage

On multivariate analysis, the initial QRS score and T-wave inversion grade were the only independent predictors of salvage (multivariate \(r\) using both variables combined as predictors=0·57, \(P<0\cdot001\)). Subgroup analysis in patients with anterior infarction (\(n=45\)) and patients with non-anterior infarction (\(n=101\)) showed similar results (multivariate \(r=0\cdot57, \ P<0\cdot01\), and \(r=0\cdot52, \ P<0\cdot001\), respectively).

Discussion

The major finding of the current study is that myocardial salvage does inversely correlate with the initial QRS score and T-wave inversion grade on the presenting electrocardiogram, but does not correlate with the time from pain onset to the beginning of streptokinase.

In animal studies, myocardial necrosis progresses with time following coronary occlusion\textsuperscript{17}. Other influences on the progression of infarction include the level of myocardial oxygen demand and residual collateral flow\textsuperscript{18}. Unlike experimental models, the exact duration of arterial occlusion based on subjective pain perception in humans is often imprecise. Spontaneous or intermittent reperfusion sometimes occurs\textsuperscript{19}, and in some patients, such as diabetics\textsuperscript{20}, myocardial ischaemia can be silent. Prodromal angina occurring before acute myocardial infarction\textsuperscript{21–23} may either mask or increase the

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Patient characteristics</th>
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<tbody>
<tr>
<td>Number of patients</td>
<td>146</td>
</tr>
<tr>
<td>Age (years)</td>
<td>62±11</td>
</tr>
<tr>
<td>Male</td>
<td>104 (71%)</td>
</tr>
<tr>
<td>Smoker</td>
<td>83 (57%)</td>
</tr>
<tr>
<td>Heparin therapy</td>
<td>49 (34%)</td>
</tr>
<tr>
<td>Hirulog therapy</td>
<td>97 (66%)</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>46 (32%)</td>
</tr>
<tr>
<td>History of bypass surgery</td>
<td>4 (3%)</td>
</tr>
<tr>
<td>History of angioplasty</td>
<td>4 (3%)</td>
</tr>
<tr>
<td>Anterior infarct</td>
<td>45 (31%)</td>
</tr>
<tr>
<td>Heart rate at enrolment (beats·min(^{-1}))</td>
<td>73±17</td>
</tr>
<tr>
<td>Systolic blood pressure at enrolment (mmHg)</td>
<td>131±23</td>
</tr>
<tr>
<td>Diastolic blood pressure at enrolment (mmHg)</td>
<td>79±12</td>
</tr>
<tr>
<td>Time to streptokinase treatment (h)</td>
<td>3·7±2·5</td>
</tr>
</tbody>
</table>

ECG predicting myocardial salvage in AMI 401

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The duration of chest pain does not necessarily correlate with the progression of myocardial necrosis nor, as in the current study, with myocardial salvage after therapy. The use of radionuclide techniques to measure myocardial salvage is more direct but technically demanding when early angiography is also performed. Christian et al. [24] studied 89 patients with a first episode acute myocardial infarction who were successfully reperfused. The time from onset of chest pain to reperfusion therapy did not correlate with final infarct size measured by technetium sestamibi scintigraphy (r = 0.18, P = 0.10) on univariate analysis, although on multivariate analysis it was a significant predictor of the final infarct size [24]. In the Collaborative Organization for RheothRx Evaluation (CORE) trial of 2770 patients with acute myocardial infarction who received thrombolysis within 12 h, patients treated within the first 2 h had smaller infarct size measured by technetium sestamibi scintigraphy and better left ventricular ejection fraction. However, no discernible differences could be found among those treated at subsequent time intervals (i.e.
2–4 h, 4–6 h, 6–12 h)\[25\]. In previous thrombolytic trials, the benefit of therapy was related to the time to treatment, with the greatest reduction of mortality seen in patients treated within the first hour\[2,26\]. In the current study, only six patients were treated within the first ‘golden’ hour.

In contrast to the time to treatment, we found that the QRS score and T-wave inversion grade on the initial electrocardiogram were the only independent predictors of myocardial salvage. The initial QRS score consisted mainly of a quantitative measurement of Q wave evolution. By itself, the Q wave grade also correlated with salvage on univariate analysis. In our previous study on the HERO-1 patients\[14\], the incidence of TIMI 3 flow at 90 min was higher when pathological Q waves or T-wave inversion were absent, and this may explain why the TIMI flow grade was not an independent predictor. Many patients did not have angiographic collaterals, but collateral flow via small undetectable vessels might have modulated the evolution of the infarction process and reduced the ultimate infarct size. Other factors including spontaneous intermittent reperfusion\[19\] and ischaemic pre-conditioning\[20\] can also slow down myocardial necrosis, and have not been analysed in the current study. In patients with these protective factors, the evolution of changes in the QRS complex and T wave would be slower, which may reflect the higher proportion of potentially salvageable myocardium.

In the current study, we pre-specified analyses in the subgroups with TIMI 3 flow or TIMI 2 or 3 flow at 90 min, and confirmed a similar inverse relationship between the initial QRS score or T-wave inversion grade and myocardial salvage. Patients with higher initial QRS scores had less salvage even when infarct-related artery flow was fully restored. In the Late Assessment of Thrombolytic Efficacy (LATE) trial, where the benefit of thrombolytic therapy was seen to extend to 12 h, many patients did not have Q waves on their initial electrocardiogram and 27·5% of patients had a non-Q-wave myocardial infarction\[27\].

In another study of 481 patients with a first acute myocardial infarction treated with streptokinase, we reported an association between initial Q waves and a higher cardiac mortality at 30 days (7% vs 2%, *P*=0·01) and at 5 years (17% vs 7%, *P*<0·01)\[28\]. In that study, the presence of Q waves at presentation was an independent predictor of cardiac mortality, but time to streptokinase therapy was not\[28\]. Further studies will be needed to determine whether the presenting electrocardiographic parameters can help triage patients more appropriately. Reperfusion therapy may be beneficial in patients with ST elevation who present after 12 h of chest pain without significant Q wave evolution.

### Limitations

The final electrocardiogram in this study was taken at 3·7 ± 1·9 days after enrolment. A previous study showed that the development of Q waves, loss of R waves and changes in the QRS score were completed within the first 9 h after the onset of acute myocardial infarction\[29\]. In another study, the QRS score was similar at day 3 and at day 7 after acute myocardial infarction\[12\]. Thus the final electrocardiogram used in the current study should have contained most of the changes from infarct evolution. The r value of 0·57 in predicting myocardial salvage was relatively modest. In patients with a prior myocardial infarction, it can be difficult to ascertain whether the QRS and T wave changes at presentation are new or old.

### Conclusions

The QRS score and the T-wave inversion grade on the presenting electrocardiogram may be more important than the time to treatment in predicting myocardial salvage with thrombolytic therapy in patients with a first myocardial infarction, and could be useful for triaging patients to different therapies.

### References


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**Table 4** Correlation (r value) between electrocardiographic parameters and salvage in patients with patent infarct-related artery

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Whole group (n=146)</th>
<th>TIMI 3 flow (n=73)</th>
<th>TIMI 2–3 flow (n=113)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of leads with ST elevation</td>
<td>−0·09</td>
<td>−0·15</td>
<td>−0·06</td>
</tr>
<tr>
<td>Number of leads with ST depression</td>
<td>0·28**</td>
<td>0·28*</td>
<td>0·28*</td>
</tr>
<tr>
<td>Maximum ST elevation</td>
<td>0·03</td>
<td>0·04</td>
<td>0·05</td>
</tr>
<tr>
<td>Maximum ST depression</td>
<td>0·27**</td>
<td>0·24*</td>
<td>0·27*</td>
</tr>
<tr>
<td>Q wave grade</td>
<td>−0·36**</td>
<td>−0·26*</td>
<td>−0·36**</td>
</tr>
<tr>
<td>T-wave inversion grade</td>
<td>−0·26**</td>
<td>−0·26*</td>
<td>−0·29**</td>
</tr>
<tr>
<td>ST segment slope grade</td>
<td>−0·06</td>
<td>0·07</td>
<td>0·00</td>
</tr>
<tr>
<td>Initial QRS score</td>
<td>−0·56**</td>
<td>−0·51**</td>
<td>−0·53**</td>
</tr>
</tbody>
</table>

*P*<0·05; **P*<0·01.
infarction: collaborative overview of early mortality and ma-
major morbidity results from all randomised trials of more than
ation of eligibility for thrombolytic therapy in acute myocar-
plasminogen activator, streptokinase or both on coronary
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