High QRS Score on Admission Strongly Predicts Impaired Myocardial Reperfusion in Patients With a First Anterior Acute Myocardial Infarction

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Background: In patients with acute myocardial infarction (AMI), QRS score at presentation electrocardiogram (ECG) may reflect the evolutionary stage of the infarction and allow one to predict the degree of myocardial reperfusion potentially achievable by reperfusion therapy.

Methods and Results: The relationship between QRS score on admission ECG and myocardial blush grade, an angiographic marker of myocardial reperfusion, was examined in 416 patients with a first anterior AMI who received reperfusion therapy within 6 h after symptom onset. Patients were classified into 3 groups according to QRS score: 0 or 1 (n=102), 2–4 (n=228), and ≥5 (n=86). Higher QRS scores were associated with a longer time to admission, a greater ST-segment elevation, a higher frequency of impaired initial and final culprit coronary vessel flow, a higher peak creatine kinase level, and a higher frequency of impaired myocardial reperfusion as defined by myocardial blush grade 0/1 on the final angiogram. Multivariate analysis showed that a high QRS score ≥5 was the strongest predictor of impaired myocardial reperfusion (odds ratio 20.3, P<0.001). These findings were similar when the data were stratified according to time to admission (≤2 h, >2 h).

Conclusions: In patients with a first anterior AMI treated by reperfusion therapy, admission high QRS score ≥5 strongly predicts impaired myocardial reperfusion, even when presentation is early (≤2 h). (Circ J 2011; 75: 626–632)

Key Words: Acute myocardial infarction; Electrocardiogram; Reperfusion

Optimal reperfusion for acute myocardial infarction (AMI) is being redefined to include intact microvascular flow and restored myocardial perfusion, as well as sustained epicardial patency.1 Recanalization of the infarct-related artery with resumption of blood flow to the infarct region triggers complex process, including varying degrees of small-vessel vasospasm, thrombus embolization, neutrophil plugging of capillaries, adhesion molecular generation and complement activation, oxygen free-radical production, microvascular compression from myocytes, interstitial edema, and hemorrhage.2–5 These events often increase vascular resistance and reduce microvascular flow.2–4 Various markers derived from electrocardiography (ECG), coronary angiography, contrast echocardiography, and magnetic resonance imaging have been used to evaluate myocardial reperfusion.6–12 Previous studies have shown that patients with impaired myocardial reperfusion have poor outcomes, even when infarct-related arteries are patent.7–10,12 Among currently available markers, myocardial blush grade is widely used to angiographically assess myocardial reperfusion. A lower myocardial blush grade is associated with a larger infarct size and impaired left ventricular function, as well as poor outcomes.6–8

During the evolution of AMI, pathologic Q waves evolve and R wave regression occurs. Selvester et al developed a quantitative QRS scoring system to estimate infarct size on the basis of these electrocardiographic variables and standard 12-lead ECGs.13,14 QRS score at presentation may reflect the evolutionary stage of the infarction and allow one to predict the degree of myocardial reperfusion potentially achievable by reperfusion therapy, but the association between baseline QRS score and myocardial reperfusion remains unclear.

In the present study, we assessed the relationship between QRS score at presentation and myocardial blush grade in patients with a first anterior AMI treated with reperfusion therapy. We also examined whether this relationship is influenced by time to presentation.
Methods

Study Group
Between July 1990 and January 2007, 561 consecutive patients with a first anterior AMI underwent emergency coronary angiography within 6 h from symptom onset and achieved Thrombolysis In Myocardial Infarction (TIMI) grade 2 or 3 flow of the left anterior descending coronary artery with reperfusion therapy. The diagnosis of anterior AMI was based on typical chest pain lasting ≥30 min, ≥2.0-mm ST-segment elevation in at least 2 contiguous precordial leads, and a typical increase in serum creatine kinase to more than twice the upper limit of normal. A total of 145 patients were excluded for one or more of the following reasons: poor quality ECG recordings on admission (n=24), conditions precluding the evaluation of ST-segment changes on ECG (left or right bundle branch block, left ventricular hypertrophy, or ventricular pacing; n=88), or inadequate assessment of myocardial blush grade after recanalization (n=60). Therefore, the final study group consisted of 416 patients (mean age, 61±11 years; range, 29–89 years; 341 men and 75 women). The study protocol was approved by the Ethics Committee of Yokohama
City University Medical Center. Oral and/or written informed consent was obtained from all patients.

**Patient Data**
A physician obtained clinical histories for each patient in the study. Preinfarction angina was defined as the presence of typical chest pain within 24 h before the onset of AMI.16,17

**ECG**
A 12-lead ECG was recorded on admission at a paper speed of 25 mm/s and an amplification of 10 mm/mV. ST-segment elevation was measured 0.02 s after the J point by a single cardiologist blinded to all clinical and angiographic findings. The sum of ST-segment elevation in leads I, aVL, and V1-6 was calculated. In addition, each ECG was manually scored according to the Selvester QRS scoring system as previously described.13,14 Patients were classified into quartiles according to the QRS score on admission ECG: 102 patients belonging to the first quartile (low QRS score of 0 or 1), 228 the second and third quartiles (moderate QRS score of 2–4), and 86 the fourth quartile (high QRS score of ≥5). This classification was considered the most suitable on the basis of the relation between QRS score and myocardial blush grade (Figure 1A). Representative ECGs are shown in Figure 2.

**Coronary Angiography**
Coronary angiography was performed immediately after admission. The grade of collateral filling in the left anterior descending coronary artery was evaluated as described by Rentrop et al,18 and a good collateral channel was defined as grade 2 or 3. The allocation of recanalization therapy was left to the physician’s discretion. In the right coronary artery and the left circumflex coronary artery, stenosis was considered clinically significant if the lumen diameter was narrowed by ≥75% in any projection. Myocardial blush8 on the final angiogram was graded as follows by a single cardiologist who was blinded to all data apart from the coronary angiogram: 0, no myocardial blush or contrast density; 1, minimal myocardial blush or contrast density, but less than that obtained during angiography of a contralateral or ipsilateral non-infarct-related coronary artery; and 3, normal myocardial blush or contrast density, comparable to that obtained during angiography of a contralateral or ipsilateral non-infarct-related coronary artery. If myocardial blush persisted, this finding was graded as 0. Impaired myocardial reperfusion was defined as myocardial blush grade of 0 or 1.

**Cardiac Enzymes**
Blood samples were obtained on admission and at 3-h intervals during the first 24 h, at 6-h intervals for the next 2 days, and then daily until discharge.

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**Figure 2.** Representative electrocardiograms in patients with QRS scores of (A) 0 or 1, (B) 2–4, and (C) ≥5 on admission. (A) QRS score, 0; time from symptom onset to admission, 1.4 h; culprit lesion, segment 6; peak creatine kinase, 971 IU/L; blush grade, 3. (B) QRS score, 3; time from symptom onset to admission, 1.6 h; culprit lesion, segment 6; peak creatine kinase, 3,180 IU/L; blush grade, 2. (C) QRS score, 7; time from symptom onset to admission, 1.6 h; culprit lesion, segment 6; peak creatine kinase, 7,469 IU/L; blush grade, 0.
Table 1. Baseline Characteristics vs. Admission QRS Score and Time to Admission

<table>
<thead>
<tr>
<th></th>
<th>All patients</th>
<th>Early presentation (≤2h)</th>
<th>Delayed presentation (&gt;2 h)</th>
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<tr>
<td></td>
<td>QRS score</td>
<td>P value</td>
<td>QRS score</td>
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<tr>
<td></td>
<td>0, 1 (n=102)</td>
<td></td>
<td>0, 1 (n=65)</td>
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<td>2–4 (n=228)</td>
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<td>2–4 (n=119)</td>
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<tr>
<td></td>
<td>≥5 (n=86)</td>
<td></td>
<td>≥5 (n=48)</td>
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<tr>
<td>Age (years)</td>
<td>62±12</td>
<td>61±11</td>
<td>61±11</td>
</tr>
<tr>
<td>Men (%)</td>
<td>76</td>
<td>82</td>
<td>90</td>
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<td>Medications before AMI (%)</td>
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<td>Statins</td>
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<tr>
<td>Time to admission (h)</td>
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<td>HR on admission (beats/min)</td>
<td>79±18</td>
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<td>SBP on admission (mmHg)</td>
<td>149±28</td>
<td>145±27</td>
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<td>Killip class on admission ≥2</td>
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<td>24%</td>
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<td>ECG findings on admission</td>
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<tr>
<td>Summed ST elevation (mm)</td>
<td>14±8</td>
<td>19±10</td>
<td>26±11</td>
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<td>QRS score</td>
<td>0.5±0.5</td>
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<td>PCI (%)</td>
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<td>Stent implantation (%)</td>
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<td>Time to recanalization (h)</td>
<td>2.6±1.2</td>
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<td>Peak creatine kinase (IU/L)</td>
<td>1.48±1,131</td>
<td>3.609±2,089</td>
<td>7.114±2,548</td>
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</table>

Data are presented as means ± SD or percentages of patients. AMI, acute myocardial infarction; ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; HR, heart rate; SBP, systolic blood pressure; ECG, electrocardiogram; PCI, percutaneous coronary intervention.
Statistical Analysis

Continuous data are expressed as mean±SD, and categorical data as percentages. Analysis of variance was used to calculate P-values for continuous variables. Chi-squared analysis was used to compare categorical variables. Differences were considered statistically significant at P<0.05. A multivariate analysis was used to identify predictors of impaired myocardial reperfusion among the variables associated with impaired reperfusion on univariate analysis, including heart rate, Killip class, and a greater summed ST-segment elevation. A striking gradient in peak creatine kinase levels was associated with an increasing QRS score: patients with a QRS score of 0 or 1 or of ≥5 had impaired myocardial reperfusion as indicated by blush grades of 0 or 1. In sharp contrast, myocardial reperfusion was complete in only 1% of patients with a QRS score of ≥5 and killed in 87%. As compared with patients who had a QRS score of 0 or 1 or of ≥5, a higher proportion of patients with a QRS score of 2–4 had intermediate myocardial reperfusion, as reflected by a blush grade of 2. When patients were subdivided according to the 2-h time window from symptom onset, similar relations between admission QRS score and blush grade were evident (Figure 1B).

Results

Patients’ Characteristics

The baseline characteristics of the 3 groups are shown in Table 1. Patients with higher QRS scores were more likely to have the following characteristics: male sex, a lower frequency of preinfarction angina, a longer time to admission, a more rapid heart rate, a lower systolic blood pressure, a higher Killip class, and a greater summed ST-segment elevation. A striking gradient in peak creatine kinase levels was associated with an increasing QRS score: patients with a QRS score of ≥5 had an approximately fivefold higher peak creatine kinase level than those with a QRS score of 0 or 1. Other baseline characteristics were similar among the 3 groups. When patients were further stratified according to the time from symptom onset to admission (≤2h, >2h; Table 1), times to admission and recanalization did not differ among the 3 groups, but the differences in the other aforementioned characteristics were similar to those in the study group as a whole.

Angiography

Patients with higher QRS scores had higher frequencies of occlusion of the proximal left anterior descending coronary artery, initial TIMI flow grade 0 or 1, poor collateral circulation, and a lower frequency of complete recanalization as indicated by TIMI flow grade 3 (Table 2). There was no difference in multivessel disease among the 3 groups. These distinguishing features were similar irrespective of the time window from symptom onset. Figure 1A shows that the distribution of blush grade clearly differed according to QRS score on admission. Among patients with a QRS score of 0 or 1, a high proportion (75%) had complete myocardial reperfusion as indicated by blush grade of 3, whereas only 2% had impaired myocardial reperfusion as indicated by blush grade of 0 or 1. In sharp contrast, myocardial reperfusion was complete in only 1% of patients with a QRS score of ≥5 and impaired in 87%. As compared with patients who had a QRS score of 0 or 1 or of ≥5, a higher proportion of patients with a QRS score of 2–4 had intermediate myocardial reperfusion, as reflected by a blush grade of 2. When patients were subdivided according to the 2-h time window from symptom onset, similar relations between admission QRS score and blush grade were evident (Figure 1B).

Prediction of Impaired Myocardial Reperfusion

In the multivariate models, a high QRS score of ≥5 was the strongest predictor of impaired myocardial reperfusion (Table 3). The other variables associated with impaired myocardial reperfusion on univariate analysis, including heart rate, Killip class, and final TIMI flow grade were not significant predictors on multivariate analysis. When patients were subdivided according to the 2-h time window from symptom onset, similar relations between admission QRS score and blush grade were evident (Figure 1B).
onset, a high QRS score of ≥5 was found to strongly contribute to impaired myocardial reperfusion in both subgroups (≤2h: OR, 30.3; 95%CI, 14.5–65.3; P<0.001; >2h: OR, 15.0; 95%CI, 8.30–24.3, P<0.001).

Discussion

In patients with a first anterior AMI who underwent reperfusion therapy within 6 h after symptom onset, a high QRS score ≥5 on admission was an independent, strong predictor of impaired myocardial reperfusion, even among those with early (≤2h) presentation. This simple, inexpensive marker can be available before angiography and may be useful for the design of personalized therapeutic strategies.

As infarction evolves towards irreversible necrosis at area at risk, Q waves develop in the infarct leads with ST-segment elevation. Initial Q waves at presentation reflect a more advanced stage of infarction. Baseline Q wave presence has been shown to be associated with larger infarct size and an increased risk of death and to surpass time from symptom onset as a prognostic marker of mortality in patients with AMI treated with primary percutaneous coronary intervention as well as fibrinolysis.18–21 Time from symptom onset is widely used as a useful predictor of the potential benefits of reperfusion therapy. This practice is mainly supported by the results of animal studies, showing that myocardial necrosis progresses with time after coronary occlusion.22 Other factors affecting the progression of infarction include residual collateral flow and the level of oxygen demand.23 In contrast to experimental models, however, the duration of coronary occlusion evaluated on the basis of subjective symptom perception in humans is often imprecise.24 The timing of symptom onset is unclear in some patients. The evaluation of symptom onset is often challenging in patients whose symptoms wax and wane or who have preinfarction angina. Moreover, intermittent reperfusion or the presence of preinfarction angina, which sometimes occur, can slow the development of myocardial necrosis.16,23 It is thus not always easy to estimate the progression status of myocardial necrosis solely on the basis of time from symptom onset in humans. Q waves at presentation might be a better and a more objective indicator of the evolution of infarction, as compared with time from symptom onset.24 In previous studies assessing the clinical significance of baseline Q wave presence in patients with AMI,20,21 however, more than half of patients had Q waves at presentation. QRS score is a weighted, quantitative index of myocardial damage that incorporates not only the number of Q waves, but also increased Q wave width and decreased R wave amplitude and width, both of which are markers of severe myocardial injury.13,14 It may thus be a more accurate indicator of the stage of infarction than merely the presence or absence of Q waves.

The present results show that a high QRS score on admission ECG, indicating a more advanced stage of infarction (ie, the presence of broader irreversible transmural myocardium damage at admission) was strongly related to impaired myocardial reperfusion as indicated by myocardial blush grade of 0 or 1. Iwakura et al have also reported that severer myocardial damage before recanalization, as indicated by a greater number of Q waves on the admission ECG, is closely related to the no-reflow phenomenon in patients with successful coronary recanalization after angioplasty.26 In animal models, the no-reflow zone is located within areas of necrosis and it has been suggested that some kind of no-reflow phenomenon is already established before reperfusion.27,28 In the present study, the stage of the infarction process as indicated by QRS score was clearly related to myocardial reperfusion. Patients with a QRS score of 0 or 1, speculated to be in the very early stage of infarction, were likely to achieve complete myocardial reperfusion as indicated by myocardial blush grade of 3. In contrast, patients with a QRS score of ≥5, speculated to be in a very advanced stage of infarction, were likely to have impaired myocardial reperfusion as indicated by a myocardial blush grade of 0 or 1. In these patients, myocardial reperfusion may have been largely established before reperfusion therapy. Moreover, the degree of myocardial reperfusion may vary widely among patients with a QRS score of 2–4, speculated to be in the middle of the infarction process. More severe and extensive pre-existing myocardial damage is thus likely to be a strong determinant of impaired myocardial reperfusion. Patients with high QRS scores would be expected to have less salvageable myocardium, as supported by an extremely high peak creatine kinase level.

The reasons for greater likelihood of impaired myocardial reperfusion among patients with a QRS score of ≥5 are unclear, but they might be related to the distinctly higher clinical risk profile in this subgroup of patients. They had a lower prevalence of preinfarction angina, delayed presentation, a more advanced Killip class, and greater baseline ST-segment elevation. Angiographically, they also had higher frequencies of occlusion of the proximal left anterior descending coronary artery, poor collateral circulation, and impaired initial and final culprit coronary vessel flow. Importantly, however, a high QRS score was a strong significant predictor of impaired myocardial reperfusion independent of these higher risk baseline characteristics.

Study Limitations

The present study had several limitations. This was a small retrospective study in a single center; patient accrual required nearly 16 years. In addition, 145 patients were excluded largely because of confounding ECG factors. We believe, however, that the strict entry criteria enabled us to demonstrate that the QRS score on admission ECG is a clinically useful predictor of myocardial reperfusion. Furthermore, because we examined only patients with a first anterior AMI, considered a high-risk group, the present findings cannot be extrapolated to all patients presenting with AMI. Further prospective studies in larger numbers of patients are needed to verify the present results.

Clinical Implications

In the present study a high QRS score on admission ECG was strongly associated with impaired myocardial reperfusion, irrespective of the time to admission. This may in part explain the previous finding that baseline Q wave presence is associated with mortality irrespective of time to admission.20,21 The standard 12-lead ECG is an inexpensive, non-invasive, and readily available clinical tool. The measurement of QRS score might facilitate the triage of patients with AMI by clinicians. A more aggressive approach to promote myocardial reperfusion might be warranted in patients with a high QRS score, even in those with early presentation. The converse is also true, that is, patients with a low QRS score are likely to benefit from reperfusion therapy, even when admission is delayed. Moreover, it might be useful to incorporate baseline QRS score into the design and evaluation of future clinical trials aimed at myocardial reperfusion.
References


