Consideration of the Impact of Reperfusion Therapy on the Quantitative Relationship between the Selvester QRS Score and Infarct Size by Cardiac MRI

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Background: It has previously been shown that there is a good agreement between the Selvester QRS score and myocardial infarct (MI) size determined by postmortem histopathology in patients with nonreperfused MI. Currently, however, most patients with acute coronary thrombosis receive reperfusion therapy. Therefore, the aim of this study was to test the hypothesis that early reperfusion alters the quantitative relationship between Selvester QRS score and MI size.

Methods: Twenty-seven patients with acute first-time reperfused MI were studied. Infarct size was determined by delayed contrast-enhanced magnetic resonance imaging (DE-MRI) and estimated with the 50-criteria/31-point Selvester QRS scoring system 1 week after admission. The findings in the present study were compared with previous postmortem studies exploring the quantitative relationship between Selvester QRS score and MI size in nonreperfused patients.

Results: The quantitative relationship between QRS score and MI size by DE-MRI in the present study of early reperfused MI was significantly different from previous postmortem histopathology studies of nonreperfused MI ($P < 0.0001$). In the present study, each QRS point represented approximately 2% of the left ventricle, compared to approximately 3% in previous postmortem histopathology studies of nonreperfused MI. When only considering small to moderate MI sizes, there was no significant difference in the quantitative relationship between QRS score and infarct size ($P > 0.05$).

Conclusions: There is a different quantitative relationship between QRS score and MI size in early reperfused MI compared to nonreperfused MI, partly explained by differences in MI size. Thus, the Selvester QRS scoring system may not be linearly related to MI size.

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The size of an established myocardial infarct (MI) is an important prognostic factor for mortality and quality of life in a patient with ischemic heart disease.¹ The 12-lead electrocardiogram (ECG) has earlier been shown useful for quantifying MI size using the Selvester QRS scoring system, developed based on a computer simulation of the human depolarization sequence.² The original Selvester QRS criteria were validated and slightly modified by postmortem histopathology studies, so that each

of the 50 criteria attained optimal sensitivity while maintaining at least 95% specificity in normal subjects. Each QRS point was shown to represent approximately 3% MI of the left ventricle (LV).^{3–6} The Selvester method was developed before reperfusion therapy was established as a clinical treatment for patients presenting with symptoms suggestive of acute coronary thrombosis. Currently, most patients with acute ST segment Elevation MI (STEMI) receive reperfusion therapy

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with thrombolytic agents or percutaneous coronary intervention (PCI). Hence, the relationship between the Selvester method and early reperfused MI might be different than that for nonreperfused MI due to differences in infarct characteristics, such as subepicardial myocardial sparing and patchy infarct borders in the former.⁷⁻⁹

Thus, to further develop the Selvester QRS scoring system for current clinical application, an accurate noninvasive non-ECG method for MI quantification is required. During recent years, delayed contrast-enhanced magnetic resonance imaging (DE-MRI) has emerged as the reference method for MI visualization in vivo.¹⁰ This technique has previously been used to evaluate the performance of the Selvester QRS scoring.¹¹ In patients with early reperfused MI, it has been shown that the Selvester QRS scoring system overestimates MI size acutely¹² and over time,¹³ when each QRS point is considered to represent 3% MI of the LV.

The aim of this study was therefore to test the hypothesis that the quantitative relationship between Selvester QRS score and MI size after early reperfusion quantified by DE-MRI is different from the previously reported relationship between Selvester QRS score and MI size in nonreperfused MI quantified by postmortem histopathology.

METHODS

Patient Population

The present study was approved by the local ethics committee, and all patients gave their written informed consent to participate in the study. Inclusion criteria were negative admission biochemical markers, a completely occluded coronary artery by angiography, and successful primary PCI with stenting; defined as TIMI grade 3 flow. Exclusion criteria were historical or ECG evidence of prior MI, contraindications for magnetic resonance imaging (MRI) (factors such as pacemakers, defibrillators, or cerebral aneurysm clips, etc.) or ECG confounding factors (bundle branch or fascicular block, ventricular hypertrophy or preexcitation). Patients with isolated posterolateral ST deviation on the admission ECG were excluded. Twenty-seven patients, which met STEMI criteria on admission ECG,^{14,15} (26 males, age range 42–83 years) were prospectively enrolled, and underwent DE-MRI and had a standard 12-lead ECG recorded 1 week after the admission.

ECG Recordings and Analysis

All patients had a standard 12-lead ECG recorded using a MEGACART-R (Siemens-Elema AB, Solna, Sweden). The frequency response was set at the range of 0.05 to 150 Hz, and the sampling rate was 500 Hz. On the 1-week ECG, the 50 criteria/31 point Selvester QRS scoring system was applied in the Duke University ECG Core laboratory to estimate the size of infarction. Q-, R-, and S-wave amplitudes, Q- and R-wave durations, and R/Q and R/S ratio were manually measured in leads I, II, aVL, aVF and in the precordial leads. The QRS score designates points for Q-wave presence or duration, R/S ratio and R/Q ratio changes, and increased or decreased R-wave amplitude and duration. Each criterion is weighted from 1 to 3 points according to the estimated percentage of infarction of the LV that it represents. The summed QRS points constitute the global QRS score. The Selvester¹⁶⁻¹⁸ QRS scoring method for estimation of MI size was previously developed based on computer simulation of the body surface ECG in a model that included the propagated electromotive surfaces in the heart as documented by Durrer et al.² and the known torso volume conductor variables. Local myocardial cellular elements were systematically removed to simulate infarcts of varying sizes in the distributions of the three major coronary arteries. The QRS MI scoring system was constructed so that each point would represent loss of 3% of the LV myocardial volume. This procedure was repeated in step-wise manner to consider the range of infarct sizes from 3% to 48%.

The analysis of the QRS score was performed twice and compared with the QRS scores designated by a second observer. All QRS scoring was performed blinded to the results of the DE-MRI.

MRI Imaging and Analysis

Short-axis DE-MRI images covering the entire LV¹⁷ and 3 LV long-axis images were acquired using either of two 1.5 T systems: Magnetom Vision (Siemens, Erlangen, Germany) with a CP body array coil, or Philips Intera CV (Philips, Best, The Netherlands) with a cardiac synergy coil. All subjects were placed in supine position. The DE-MRI images were acquired using a segmented inversion-recovery gradient-recalled echo (IR-GRE) sequence. Image acquisition was performed during breath-hold in end-diastole and was triggered

by ECG. Twenty to 30 minutes prior to image acquisition, a Gd-based contrast agent was administered intravenously (0.2 mmol/kg body weight). DE-MRI using the IR GRE sequence uses an increase in regional fractional distribution of extracellular MRI contrast media within the injured area to achieve contrast between infarcted and noninfarcted myocardium.^{19–22} The inversion time was manually adjusted to null the signal from noninfarcted myocardium.

The MR images were analyzed using freely available in-house developed and validated software (Segment v1.8 R0795, <http://segment.heiberg.se>).²³ The infarct size was assessed from the short-axis images and quantified using a previously described semiautomatic method.⁷ In short, the endocardial and epicardial borders were manually traced in each DE-MRI short-axis images. Thereafter, the hyperenhanced myocardium was automatically quantified using a computer algorithm, taking partial volume effects in the periphery of the infarction into account. Regions where the computer algorithm was clearly wrong, manual adjustments were made. Infarct size was expressed as a percentage of the LV. The assessment of infarct size was performed by an observer blinded to all other data.

Statistical Analysis

All results were expressed as mean $\pm$ SD. The Pearson product moment correlation coefficient (r) was used to define the linear correlation between DE-MRI measurements of MI size and QRS score. Unpaired t -tests were used to compare the regression line equation from the pooled postmortem data published by Ideker et al.³ and Roark et al.⁴ with the regression line equation of the present DE-MRI study. The data from those previous studies were obtained from combining the published raw data from the anterior ($n = 21$)³ and inferior ($n = 31$)⁴ MI locations. All statistical analyses were performed using SAS enterprise guide 4.1. P -values < 0.05 were considered to indicate statistical significance.

RESULTS

Patient Characteristics

Patient baseline characteristics are described in Table 1 and Figure 1. There were 12 (44%) patients with an anterior location and 15 (56%) patients with an inferior location on admission ECG. Coronary angiograms confirmed this location by

Table 1. Patient Characteristics

Male	26 (96)
Age (y)	61 $\pm$ 9 (42–83)
Occluded artery	
LAD	12 (44)
RCA	14 (52)
LCX	1 (4)
Ischemia localization (ECG)	
Anterior	12 (44)
Inferior	15 (56)
Primary MI location (MRI)	
Anterior	11 (41)
Inferior	15 (56)
None	1 (4)
Primary MI location (QRS score)	
Anterior	11 (41)
Inferior	11 (41)
None	5 (19)
MI size in % of LV (MRI)	
Anterior	7 $\pm$ 7%
Inferior	8 $\pm$ 6%
MI size in % volume LV (QRS score)	
Anterior	12 $\pm$ 7%
Inferior	13 $\pm$ 10%

LAD = left anterior descending artery; LCX = left circumflex artery; MI = myocardial infarction; MRI = magnetic resonance imaging; RCA = right coronary artery. Values are given as n (%) or in mean $\pm$ SD.

documenting left anterior descending artery occlusion in all patients with anterior ST elevation and either right coronary artery (14/15) or left circumflex artery occlusion (1/15) in the patients with inferior ST elevation. Ninety-two percent (11/12) of the patients with anterior location on admission ECG had anterior MI on the DE-MRI. However, 1 patient had no evidence of MI, and therefore, the infarction process was considered to have been aborted by the reperfusion therapy. This patient had, however, angiographic evidence of coronary artery occlusion and elevated biochemical markers after the reperfusion therapy, indicative of acute myocardial necrosis. There were 9 patients with both anterior and lateral QRS criteria and 2 patients with lateral criteria only. All 15 patients with inferior ischemia on admission ECG had inferior MI location confirmed by DE-MRI and all had QRS criteria for inferior MI, with or without posterior MI criteria.

Relationship between MI Size by DE-MRI and QRS Scoring

Figure 2A shows the relationship between Selvester QRS score and DE-MRI measured MI size

Figure 1. Infarct characteristics. n = number of patients.

for all 27 patients in the present study. There was a strong correlation between the QRS score and the MI size assessed by DE-MRI ($r = 0.72$, $P < 0.001$). The equation of the linear regression for QRS score and MI size by DE-MRI was $y = 1.7x + 0.52$ with a standard error of 0.05. Thus, each QRS point represented approximately 2% MI of the LV as measured by DE-MRI in these patients undergoing early reperfusion therapy. In 19% (5/27) of the patients, a QRS score of 0 was found. Of those 5 patients, 1 had admission ST segment indication of anterior ischemia and 4 had inferior ischemia. On their DE-MRI studies, the patient with the anterior ischemia had no MI, as discussed above, and the 4 patients with inferior ischemia had MI size of <2% of the LV.

Figure 2B shows the combined data from patients with nonreperfused MI in the 1982–1983 studies by Ideker et al. and Roark et al.^{3,4} to present the

relationship between Selvester QRS score and post-mortem anatomic sizes of the 52 patients with non-reperfused anterior and inferior infarcts. There was a similar correlation between the QRS score and anatomically measured MI sizes as for the patients with early reperfused infarcts in the present population ($r = 0.78$ vs $r = 0.72$). However, the linear regression equation for the postmortem MI's was $y = 3.1x + 2.17$. Thus, each QRS point represented approximately 3% of the LV. However, when only those MI sizes from the nonreperfused postmortem study which were within the same range as for the present study, the quantitative relationship was $y = 2.3 + 3.54$ (Fig. 2C). Thus, when the larger MIs were excluded in the nonreperfused postmortem study, the quantitative relationship between QRS score and MI size was closer to that found in the present study showing approximately 2% MI of the LV for each QRS point met.

Figure 2. The relationship between QRS score and MI size as assessed by (A) DE-MRI in the present study and (B,C) postmortem histopathology from previous studies.^{3,4} In (B) all patients are shown and in (C) only patients with 30% or less MI of LV are shown. There was a difference in the slope of the regression line between (A) and (B). However, when only considering small to moderate MI sizes (C), the slope of the regression line was closer to (A) than to (B) indicating the weighting of Selvester QRS score might not be linearly related to MI size. LV = left ventricle; MI = myocardial infarction; MRI = magnetic resonance imaging.

In 5 patients there was a 1-point difference in QRS score between the 2 observers. These differences were adjudicated in conference for comparison with the DE-MRI findings.

DISCUSSION

The present study shows that the quantitative relationship between QRS score and MI size determined by DE-MRI in early reperfused patients with first time MI is different from the quantitative relationship between QRS score and MI size determined by postmortem histopathology in non-reperfused patients.

The differences observed between the findings in the present study compared to findings in previous postmortem studies in patients with nonreperfused MI can partly be explained by differences in the distribution of MI sizes in the different studies. Mean infarct size in the present study was 7% of the LV compared to 18% in the previous postmortem studies. When comparing the MIs from the present study with those of the same range of MI sizes in the postmortem studies the quantitative relationship were similar. Thus, it seems like the relationship between QRS score and infarct size may not be linear.

Furthermore, the infarct characteristics were different in the present study compared to the previous studies in nonreperfused patients. Most of the infarcts in the present study were nontransmural, whereas 65% (34/52) of the infarcts were transmural at some point in the previous histopathology studies of nonreperfused patients.^{3,4} The transmural extent of infarction might also affect the quantitative relationship between QRS score and MI size. In fact, a recent study has shown that the QRS score is stronger related to the endocardial extent of MI than to the transmural extent of MI.²⁴ Thus, a subendocardial MI with a large endocardial extent may have a greater likelihood of generating Q waves than a transmural MI with smaller endocardial extent. Such an example is seen in Figure 3. Thus, subepicardial myocardial sparing in the ischemic injured region might change the relation between the QRS score and MI size relative to the LV.

There are also methodological differences for MI quantification between the current MRI study and the postmortem studies with respect to the endocardial delineation of the infarcted region. In the postmortem studies, the endocardial surface was

reconstructed in regions with myocardial thinning due to endocardial loss of necrotic tissue, to represent the amount of myocardium initially infarcted. In the present study, no endocardial reconstruction was performed, which may partly explain why each QRS point represented a smaller part of the LV. In the pathology studies,^{3,4,6} the amount of infarcted tissue in patchy infarcts could be estimated to the nearest 25% of tissue. Using DE-MRI, patchy MI borders appear as a gray periinfarction zone due to partial volume effects. Heiberg et al.⁷ have recently shown that this can be compensated for by weighting the signal intensity within the periinfarction gray zone to compensate for the partial volume effects that arise in this region. This method was therefore used for infarct quantification in the present study.

The timing of the examination (8 days after the acute event) was chosen for several reasons. First, to ensure that the initial injury currents, seen acutely as ST deviation, had resolved and the infarct-related QRS changes were established. Second, to avoid the early dynamic postinfarction period where both the amount of hyperenhanced myocardium and QRS score have been shown to decrease significantly.¹³

For further development of the QRS scoring system, to adhere to the current clinical situation where most patients with clinical signs of acute MI receive early reperfusion therapy, larger studies are required to obtain a study population with a good distribution of MI sizes and locations. This is best accomplished by multicenter studies. In order for DE-MRI to serve as the gold standard for MI quantification in multicenter studies, there is a need for a consensus for how infarcted myocardium should be quantified using the DE-MRI technique.²⁵

Limitations

The findings in the present study should be considered in the light of some limitations. First, the differences in methodology for MI quantification between the present study and the previous postmortem studies may explain some of the differences observed between early reperfused and non-reperfused patients. Second, the present study was undertaken in a highly selected population, all presenting with first-time MI, undergoing early primary PCI. On the other hand, this makes the study population homogenous with regard to therapy and lack of prior ischemic events, possibly confounding

Figure 3. Two cases illustrating the importance of the endocardial extent of infarction for the QRS score, irrespective of transmural extent of infarction. (A), A small transmural, non-Q-wave MI in the inferior LV wall with a QRS score of 0 and MI size of 2% of the LV by DE-MRI. (B), A nontransmural, Q-wave MI in the inferior LV wall with a QRS score of 8 with the following criteria met: Q duration > 30 ms in lead II; Q duration > 40 ms, R/Q ratio < 1 in lead aVF; R duration > 40 ms in lead V₁; R > 50 ms in lead V₂; Q duration > 30 ms in lead V₆. MI size by DE-MRI was only 7% of the LV. The endocardial extent, however, measured 24% of the LV endocardial extent, closely resembling the QRS score of 8 (24% of the LV). Arrows indicate either MI by DE-MRI or QRS changes generating QRS points. 2ch = 2-chamber long-axis view; LV = left ventricle; MI = myocardial infarction; DE-MRI = delayed contrast-enhanced magnetic resonance imaging. Adapted from Engblom et al.¹² with permission.

the outcome variables. Third, there was only one woman included. Thus, the findings can not be generalized to both genders. And finally, because of the small study group, the findings in the present study have to be confirmed in larger study population with MI in all locations in LV with a wider range of infarct sizes.

Conclusions

The quantitative relationship between Selvester QRS score and early reperfused MI size quantified by DE-MRI is different from the previously reported relationship between Selvester QRS score and nonreperfused MI size quantified by post-mortem histopathology, which could partly be explained by differences in MI sizes. Thus, the Selvester QRS score might not be linearly related to MI size, which has to be considered for future development of the scoring system.

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