ECG Quantification of Myocardial Scar in Cardiomyopathy Patients With or Without Conduction Defects: Correlation With Cardiac Magnetic Resonance and Arrhythmogenesis

David G. Strauss, BA; Ronald H. Selvester, MD; João A.C. Lima, MD; Håkan Arheden, MD, PhD; Julie M. Miller, MD; Gary Gerstenblith, MD; Eduardo Marbán, MD, PhD; Robert G. Weiss, MD; Gordon F. Tomaselli, MD; Galen S. Wagner, MD; Katherine C. Wu, MD

Background—Myocardial scarring from infarction or nonischemic fibrosis forms an arrhythmogenic substrate. The Selvester QRS score has been extensively validated for estimating myocardial infarction scar size in the absence of ECG confounders, but has not been tested to quantify scar in patients with hypertrophy, bundle branch/fascicular blocks, or nonischemic cardiomyopathy. We assessed the hypotheses that (1) QRS scores (modified for each ECG confounder) correctly identify and quantify scar in ischemic and nonischemic patients when compared with the reference standard of cardiac magnetic resonance using late-gadolinium enhancement, and (2) QRS-estimated scar size predicts inducible sustained monomorphic ventricular tachycardia during electrophysiological testing.

Methods and Results—One hundred sixty-two patients with left ventricular ejection fraction ≤35% (95 ischemic, 67 nonischemic) received 12-lead ECG and cardiac magnetic resonance using late-gadolinium enhancement before implantable cardioverter defibrillator placement for primary prevention of sudden cardiac death. QRS scores correctly diagnosed cardiovascular magnetic resonance scar presence with receiver operating characteristics area under the curve of 0.91 and correlation for scar quantification of \( r=0.74 \) \((P<0.0001)\) for all patients. Performance within hypertrophy, conduction defect, and nonischemic subgroups ranged from area under the curve of 0.81 to 0.94 and \( r=0.60 \) to 0.80 \((P<0.001)\) for all. Among the 137 patients undergoing electrophysiological or device testing, each 3-point QRS-score increase (9% left ventricular scarring) was associated with an odds ratio for inducing monomorphic ventricular tachycardia of 2.2 (95% CI, 1.5 to 3.2; \( P<0.001 \)) for all patients, 1.7 (1.0 to 2.7, \( P=0.04 \)) for ischemics, and 2.2 (1.0 to 5.0, \( P=0.05 \)) for nonischemics.

Conclusions—QRS scores identify and quantify scar in ischemic and nonischemic cardiomyopathy patients despite ECG confounders. Higher QRS-estimated scar size is associated with increased arrhythmogenesis and warrants further study as a risk-stratifying tool. (Circ Arrhythmia Electrophysiol. 2008;1:327-336.)

Key Words: electrocardiography ■ imaging ■ infarction ■ arrhythmia

Several randomized trials have shown reduced mortality in patients with left ventricular (LV) systolic dysfunction who received an implantable cardioverter defibrillator (ICD) for the primary prevention of sudden cardiac death.\(^1\)\(^2\) However, fewer than 25% of such patients receive appropriate ICD firings, and not all appropriate shocks are life saving.\(^2\)

Improved risk-stratification algorithms in these patients may reduce the number of unnecessary device implantations. Multiple electrocardiographic-based risk-stratification tests have been investigated—including signal averaged ECG, heart rate variability, microvolt T-wave alternans, and QT variability—but none has shown sufficient predictive value for widespread clinical use.\(^3\)

Clinical Perspective see p 336

Myocardial scarring after myocardial infarction (MI) may create regions of slowed conduction and reentrant circuits supporting sustained monomorphic ventricular tachycardia (MVT).\(^4\) Cardiovascular magnetic resonance using late-gadolinium enhancement (CMR-LGE) can accurately identify and quantify myocardial necrosis at all stages of infarct healing.\(^5\)\(^6\) In addition, by characterizing and quantifying the

\( ^{1,2} \) For the primary prevention of sudden cardiac death. \(^{1,2} \) How-ever, fewer than 25% of such patients receive appropriate ICD firings, and not all appropriate shocks are life saving.2

\( ^3 \) Improved risk-stratification algorithms in these patients may reduce the number of unnecessary device implantations. Multiple electrocardiographic-based risk-stratification tests have been investigated—including signal averaged ECG, heart rate variability, microvolt T-wave alternans, and QT variability—but none has shown sufficient predictive value for widespread clinical use.\(^3\)

\( ^{4} \) Improved risk-stratification algorithms in these patients may reduce the number of unnecessary device implantations. Multiple electrocardiographic-based risk-stratification tests have been investigated—including signal averaged ECG, heart rate variability, microvolt T-wave alternans, and QT variability—but none has shown sufficient predictive value for widespread clinical use.\(^3\)

\( ^{5} \) Improved risk-stratification algorithms in these patients may reduce the number of unnecessary device implantations. Multiple electrocardiographic-based risk-stratification tests have been investigated—including signal averaged ECG, heart rate variability, microvolt T-wave alternans, and QT variability—but none has shown sufficient predictive value for widespread clinical use.\(^3\)

\( ^{6} \) Improved risk-stratification algorithms in these patients may reduce the number of unnecessary device implantations. Multiple electrocardiographic-based risk-stratification tests have been investigated—including signal averaged ECG, heart rate variability, microvolt T-wave alternans, and QT variability—but none has shown sufficient predictive value for widespread clinical use.\(^3\)
infarct region by CMR-LGE, it is possible to identify substrates for reentry as defined by inducibility of sustained MVT during electrophysiological testing²,⁸ and post-MI mortality.⁹ Recently, myocardial scarring/fibrosis has also been demonstrated by CMR-LGE in nonischemic LV dysfunction¹⁰,¹¹ and was associated with inducibility of ventricular arrhythmias by programmed stimulation¹² and increased mortality.¹³,¹⁴

Although CMR-LGE before ICD placement has not been widely implemented in clinical practice, 12-lead ECGs are routinely performed, relatively inexpensive, and may be useful in the assessment and quantification of scar in patients with LV dysfunction. Beginning in the 1960s, Selvester et alⁱ⁵,¹⁶ developed a computer simulation of the electrical activation of the heart and studied the effect of scar, hypertrophy, and conduction defects on the body surface vectorcardiogram and ECG. They showed that myocardial scar in all parts of the LV produced characteristic and quantifiable changes in the vectorcardiogram and ECG and developed scores that considered Q- and R-wave durations, R/Q and R/S amplitude ratios, R- and S-wave amplitudes, and R-wave notches.¹⁷,¹⁸ Each QRS-point represented infarct involving the equivalent of 3% of the LV and hence higher scores indicated larger infarct sizes. In the absence of ECG “confounders” (ie, hypertrophy or conduction defects), the QRS scores correlated strongly with postmortem anatomic scar size,¹⁹ LV ejection fraction,²⁰ and cardiac mortality.²¹,²² The reader is referred to a recent review, which summarizes the complete development, validation, and clinical use of the QRS scoring of MIs.²³

Although modified QRS scores to quantify scar in the presence of ventricular hypertrophy, fascicular blocks, and bundle branch blocks were developed, they were never systematically validated.²³ In addition, QRS scoring has not been tested in patients with nonischemic cardiomyopathy. Thus, this study was performed to test the hypotheses that (1) QRS scores, adapted for each confounder, can identify and quantify scar in all patients with ischemic or nonischemic LV dysfunction referred for ICD implantation, and (2) higher QRS scores are associated with inducibility of ventricular arrhythmia during electrophysiological evaluation.

Methods

Patients

Patients referred for ICD placement for primary prevention of sudden cardiac death were prospectively enrolled between November 2003 and November 2007 as part of a single-center prospective cohort study.⁸,¹⁴ Patients were screened from the clinical ICD implantation schedule at our institution. All patients had to have (1) LV ejection fraction ≤ 35% measured by a clinically indicated non-CMR study (echocardiography or nuclear), (2) coronary angiography, (3) no other indications for ICD placement (eg, syncope, sustained ventricular arrhythmias, or cardiac arrest), and (4) no contraindications to CMR (eg, existing cardiac device). Patients were classified as “ischemic” if they had a known history of coronary artery disease and prior MI >1 month before enrollment.⁹ Patients were classified as “nonischemic” if they had no history of MI or revascularization and no evidence of coronary artery stenoses >50% of 2 or more epicardial vessels or left main or proximal left anterior descending coronary artery stenosis >50%.¹⁴ Exclusions were based on those of the Multicenter Automatic Defibrillator Implantation Trial II. Renal insufficiency with creatinine clearance <30 mL/min was added as an exclusion for CMR gadolinium contrast in July 2006. The study protocol was approved by the Johns Hopkins Hospital Institutional Review Board. All patients gave written informed consent.

ECG Acquisition and Analysis

Clinically indicated 12-lead ECGs before ICD implantation were acquired using a GE-Marquette system. ECG median beats were analyzed by 2 investigators using calipers and 2× magnification. At the time of analysis, investigators were blinded to all patient data (including cardiomyopathy etiology, CMR imaging results, and electrophysiological evaluation) except age, gender, and race. ECGs were first analyzed for the presence of conduction defects and hypertrophy, according to the following prespecified definitions:²³,²⁴

- Left bundle branch block (LBBB)—QRS duration ≥ 140 ms (men) or ≥ 130 ms (women), QS or rS in V1 and V2 with mid QRS slowing;
- Left superior (anterior) fascicular block (LAFB)—QRS duration ≥ 100 ms (with no upper limit for duration), left axis deviation ≥ 45° with separation of initial and terminal forces in the frontal plane (rS morphology in aVF and/or qR in aVL);
- Right bundle branch block (RBBB)—QRS duration ≥ 120 ms with rR in V1 (this may appear as “qR” in patients with large anterior infarcts due to a loss of the initial R-wave) and a wide S-wave in lead I;
- LAFB + RBBB—meeting both RBBB and LAFB criteria;
- Left ventricular hypertrophy (LVH)—increased voltage according to Sokolow-Lyon or Cornell criteria and not meeting other classifications; and
- No confounders—not meeting any previous criteria (note that this could include patients with prolonged QRS duration).

Left inferior (posterior) fascicular block does not affect the scoring system, and if signs of right ventricular hypertrophy are present then certain points in V1 and V2 cannot be counted (online-only Data Supplement).²³,²⁴ See the recent review for detailed explanations of the minor differences between these and the World Health Organization criteria.²³

QRS-score criteria were then applied for the specific underlying conduction type present (see the online-only Data Supplement for complete scores and instructions). There are 32 possible total points, and each point represents 3% of the LV mass. QRS scores for RBBB, LAFB, LAFB + RBBB, and LVH have relatively minor differences from the no confounder QRS score; however, the LBBB score is fundamentally different because the electrical activation wavefront has to proceed through the ventricular septum before activating the LV (Figure 1).

For localization of scar by QRS scoring, because the ECG is registered anatomically relative to the thorax, the LV walls, papillary muscles, and fascicles are labeled accordingly (online-only Data Supplement). We subdivided the ECG scar locations into anteroseptal or anterior-superior versus inferior or posterolateral for comparison with the CMR-LGE locations.

A trained observer, the QRS scores take <5 minutes to complete per patient.

CMR Acquisition and Analysis

The CMR protocol has been previously reported.⁸,¹⁴ In summary, patients underwent cine and CMR-LGE imaging using a 1.5-Tesla scanner (Signa CV/i, GE Healthcare Technologies or Siemens Avanto). Image analysis was performed with CINEtool (GE Healthcare Technologies) by 2 observers blinded to all other patient data. Cine images were used to measure LV ejection fraction and volumes and LGE images were used to measure total scar size for the entire LV. For the ischemic patients, after LGE endocardial and epicardial LV borders were outlined in short axis slices, the LGE area was outlined and pixels with signal intensity (SI) >50% of the maximal SI within the LGE area were labeled as scar “core.”¹⁸ A region of normal myocardium without artifacts was then selected, and the peak
was then quantified in the same manner as for the ischemic patients. In summary, patients were evaluated for the inducibility of sustained MVT or any ventricular tachycardia/fibrillation (VT/VF) that lasted >30 seconds or required cardioversion for hemodynamic compromise. Patients received 3 extrastimuli at 2 different drive cycle lengths delivered from the right ventricular apex (through the ICD at time of implantation) or the right ventricular apex and outflow tract during a full electrophysiology study.

**Statistical Analysis**

Continuous variables are expressed as mean±SD. Wilcoxon rank-sum and Fisher exact test were used to compare characteristics within the ischemic and nonischemic cohorts stratified by QRS scores. Ischemic patients were divided above and below the median QRS score (8 points=24% LV with scar), and nonischemic patients were divided by the presence or absence of QRS points. Spearman correlation, Bland-Altman plots, and Pitman test of difference in variance were used to assess the relation between the original simulation-developed QRS-estimated scar size and CMR-LGE scar measurements.25,26 Note that Bland-Altman plots graph the difference versus the average of the 2 estimates of scar size, and Pitman test assesses for a linear correlation between the difference and average. By the Pitman test, the lack of a correlation suggests that there is no significant difference in variance between patients with small versus large scar sizes. Nonparametric receiver operating characteristic (ROC) curves were used to assess the ability of the QRS score to diagnose the presence of CMR-LGE scar, and scatterplots were used to show the association between QRS score and CMR-LGE scar size. Logistic regression was used to calculate the odds ratios for inducing sustained MVT per incremental increase in QRS-estimated scar size. Fisher exact test was used to assess the difference in inducibility between high and low QRS-score groups. Kappa analysis (κ) was used to assess intra- and interobserver variability of QRS scoring in a subset of 30 randomly selected patients. P values <0.05 were considered statistically significant. Because there were multiple tests and multiple comparisons, a P<0.05 should be interpreted with caution.

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

### Results

**Study Patients**

We enrolled 162 consecutive patients—95 (85% men) in the ischemic (prior MI) cohort and 67 (66% men) in the nonischemic cohort. All 95 ischemic patients (100%) had CMR-LGE and 94 of 95 (99%) had at least 1 QRS point consistent with evidence of prior MI. Median QRS-estimated scar size was 24% LV (equivalent to 8 QRS points). Compared with patients with QRS-estimated scar ≥median, those <median had similar baseline characteristics except for a difference in the distribution of ECG conduction abnormalities (Table 1). In the nonischemic cohort, 30 of 67 patients (45%) had CMR-LGE and 46 of 67 (69%) had ≥1 QRS point. Compared with those with no QRS-estimated scar, nonischemic patients with ≥1 QRS point had similar baseline characteristics except for larger LV volumes (Table 1).

**Reproducibility of QRS Scoring**

The intra- and interobserver agreements for exactly matched QRS scores were 60% (κ=0.56) and 63% (κ=0.60), respectively. However, the absolute values of the intra- and interobserver differences were only 0.4 and 0.6 QRS points (equivalent to 1.2% and 1.8% of the total LV), respectively. When using a cutoff of within 1 QRS point for agreement, the intra- and interobserver agreement improved to κ=0.96 and κ=0.86, respectively; and with a cutoff of within 2 QRS...
points, the agreement was $\kappa = 1.00$ and $\kappa = 0.96$, respectively. These results are similar to those previously reported for QRS scoring.$^{17,23}$

**QRS Scores to Identify CMR**

**Late-Gadolinium Enhancement**

Figure 2 shows QRS scoring and CMR analysis for 2 patients with LBBB—patient A has a nonischemic cardiomyopathy with midwall septal scar and patient B has an ischemic cardiomyopathy with inferior and posterolateral scar. Table 2 shows the agreement between ECG and CMR-LGE identification of scar location in the ischemic group. In the presence of a single-territory infarct, the QRS scores identified anterosuperior or anteroseptal CMR-LGE in 53 of 54 patients (98%) and inferior or posterolateral CMR-LGE in 23 of 26 patients (88%). In the presence of 2 distinct CMR-LGE regions, QRS scores identified both locations in 9 of 15 patients (60%) and in the remainder, the larger of the 2 infarcts (generally anterior) was detected and the smaller one was not.

In the nonischemic patients, QRS scores correctly identified the absence of CMR-LGE in 19 of 37 patients (51%). Because regions of CMR-LGE often crossed multiple coronary territories, exact localization was difficult to assess. In those patients with predominantly anterosuperior or anteroseptal CMR-LGE, QRS scores correctly identified the CMR-LGE in 10 of 10 patients (100%). In predominantly inferior or posterolateral CMR-LGE, QRS score correctly identified 6 of 9 patients (67%). Eleven nonischemic patients had evidence of scar at the inferior or superior right ventricle (RV) insertion sites (5 superior+inferior, 1 superior only, and 5 inferior only). Of the 6 patients with superior RV insertion scar, all had QRS points in 2 of the 3 leads I, aVL or V4, which correlate with the anterosuperior wall where the RV inserts. Patients with inferior RV insertion scar had QRS-estimated septal or apical scar.

Figure 3 contains ROC curves showing the ability of QRS scores to diagnose the presence of CMR-LGE scar. For all patients grouped together, the area under the curve was 0.91 (95% CI, 0.86 to 0.95) with sensitivity, specificity, and accuracy of 98%, 51%, and 87%, respectively, at a cutoff of $\geq 1$ QRS point (3% LV), and of 75%, 95%, and 80% at a cutoff of $\geq 5$ points (15% LV). When considering only the nonischemic patients, the area under the curve was 0.81 (95% CI, 0.76 to 0.86) with sensitivity, specificity, and accuracy of 99%, 46%, and 82%, respectively, at a cutoff of $\geq 1$ QRS point (3% LV), and of 78%, 91%, and 84% at a cutoff of $\geq 5$ points (15% LV).

### Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Ischemic (Prior MI) (n=95)</th>
<th>Nonischemic (n=67)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>QRS Points &lt;8 (&quot;Low&quot;) (n=41)</td>
<td>QRS Points ≥8 (&quot;High&quot;) (n=54)</td>
</tr>
<tr>
<td>Age, y</td>
<td>64±11</td>
<td>60±11</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>33 (80)</td>
<td>48 (89)</td>
</tr>
<tr>
<td>Caucasian, n (%)</td>
<td>34 (83)</td>
<td>44 (81)</td>
</tr>
<tr>
<td>Heart failure class</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class I, n (%)</td>
<td>8 (18)</td>
<td>21 (39)</td>
</tr>
<tr>
<td>Class II, n (%)</td>
<td>16 (39)</td>
<td>16 (30)</td>
</tr>
<tr>
<td>Class III, n (%)</td>
<td>17 (41)</td>
<td>17 (31)</td>
</tr>
<tr>
<td>Entry LVEF, %</td>
<td>24±8</td>
<td>26±6</td>
</tr>
<tr>
<td>Received biventricular pacemaker, n (%)</td>
<td>6 (15)</td>
<td>12 (22)</td>
</tr>
<tr>
<td>ECG conduction, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No confounders</td>
<td>21 (51)</td>
<td>25 (46)</td>
</tr>
<tr>
<td>LVH</td>
<td>12 (29)</td>
<td>3 (6)</td>
</tr>
<tr>
<td>LBBB</td>
<td>4 (10)</td>
<td>7 (13)</td>
</tr>
<tr>
<td>LAFB</td>
<td>1 (2)</td>
<td>7 (13)</td>
</tr>
<tr>
<td>RBBB</td>
<td>2 (5)</td>
<td>4 (7)</td>
</tr>
<tr>
<td>LAFB+RBBB</td>
<td>1 (2)</td>
<td>8 (15)</td>
</tr>
<tr>
<td>QRS duration (ms)</td>
<td>115±24</td>
<td>124±29</td>
</tr>
<tr>
<td>Cardiovascular magnetic resonance analysis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEDV, mL</td>
<td>226±72</td>
<td>248±65</td>
</tr>
<tr>
<td>LVESV, mL</td>
<td>163±63</td>
<td>183±56</td>
</tr>
<tr>
<td>CMR LVEF (%)</td>
<td>28±8</td>
<td>27±8</td>
</tr>
<tr>
<td>LV mass, g</td>
<td>180±48</td>
<td>176±50</td>
</tr>
<tr>
<td>Scar analysis (% LV)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>QRS-estimated scar</td>
<td>14±6</td>
<td>29±5</td>
</tr>
<tr>
<td>CMR-LGE</td>
<td>17±8</td>
<td>26±11</td>
</tr>
</tbody>
</table>

Each QRS point corresponds to a scar size of 3% of the LV. MI indicates myocardial infarction; LVEF, left ventricular ejection fraction; LVH, left ventricular hypertrophy; LBBB, left bundle branch block; LAFB, left superior (anterior) fascicular block; RBBB, right bundle branch block; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; CMR, cardiovascular magnetic resonance; LV, left ventricle; LGE, late-gadolinium enhancement.
CI, 0.70 to 0.91). ROC curves are also shown for no confounders, confounders only, LVH, and LBBB, among which the diagnostic performance of the QRS score was similar and highest accuracy was achieved at 3 to 5 QRS points. Only 1 patient with LAFB, RBBB, or both had no CMR-LGE, and thus ROC curves could not be calculated for these subsets.

Comparison of QRS-Estimated Scar
With CMR-LGE
QRS-estimated scar was compared with 3 measures of CMR-LGE: core; core\(^{\frac{1}{2}}\) gray; and core\(^{\frac{1}{2}}\) gray, using Bland-Altman analysis and Pitman test of difference of variance. The QRS scores for quantifying scar in all patients had equivalent Spearman correlations with all 3 CMR-LGE scar quantification methods. However, Bland-Altman plots showed that QRS score overestimated CMR-LGE core by 7.3% and core\(^{\frac{1}{2}}\) gray by 3.3%, but underestimated core\(^{\frac{1}{2}}\) gray by 0.7%. The overall difference between QRS score and CMR-LGE was smallest for core\(^{\frac{1}{2}}\) gray, but there was systematic underestimation of larger CMR-LGE scar (Pittman test: \(r=-0.37, P<0.001\)). This was not seen with CMR-LGE core\(^{\frac{1}{2}}\) gray (Pittman test: \(r=-0.09, P=0.24\));

<table>
<thead>
<tr>
<th>ECG Findings</th>
<th>Anteroseptal-Anteroseptal Only</th>
<th>Inferior-Posterolateral Only</th>
<th>Both Locations</th>
</tr>
</thead>
<tbody>
<tr>
<td>No confounders</td>
<td>23/23 (100%)</td>
<td>14/15 (93%)</td>
<td>5/8 (63%)</td>
</tr>
<tr>
<td>LVH</td>
<td>8/8 (100%)</td>
<td>4/5 (80%)</td>
<td>1/2 (50%)</td>
</tr>
<tr>
<td>LBBB</td>
<td>4/5 (80%)</td>
<td>3/3 (100%)</td>
<td>2/3 (67%)</td>
</tr>
<tr>
<td>LAFB</td>
<td>7/7 (100%)</td>
<td>...</td>
<td>0/1 (0%)</td>
</tr>
<tr>
<td>RBBB</td>
<td>4/4 (100%)</td>
<td>1/1 (100%)</td>
<td>1/1 (100%)</td>
</tr>
<tr>
<td>LAFB + RBBB</td>
<td>7/7 (100%)</td>
<td>1/2 (50%)</td>
<td>...</td>
</tr>
<tr>
<td>Total</td>
<td>53/54 (98%)</td>
<td>23/26 (88%)</td>
<td>9/15 (60%)</td>
</tr>
</tbody>
</table>

cmr indicates cardiovascular magnetic resonance; LGE, late-gadolinium enhancement; LVH, left ventricular hypertrophy; LBBB, left bundle branch block; LAFB, left superior (anterior) fascicular block; RBBB, right bundle branch block.
thus it was selected as the optimal standard for comparison to QRS score for all subsequent analyses.

For assessing the correlation between QRS scores and CMR-LGE in quantifying scar, the ischemic and nonischemic patients were grouped together to achieve a more complete dynamic range of scar size. Figure 4 shows scatterplots and Bland-Altman plots comparing ECG-estimated to CMR-estimated scar size in subsets of no cofounders, LVH, LAFB or RBBB or both, and LBBB. The Spearman correlations for these subsets ranged from $r=0.66$ to $r=0.80$, $P<0.001$ for all. The Bland-Altman plots showed small mean differences between ECG- and CMR-estimated scar (0.9% to 2.6% LV scar) for no cofounders, LVH, and LAFB or RBBB (Figure 4A and 4C). The mean difference for LBBB was larger (7.6% LV scar), although this subgroup had the strongest Spearman correlation ($r=0.80$) (Figure 4D).

QRS Scar and Arrhythmogenesis
Electrophysiological or device testing was performed in 137 patients before ICD placement, and 37 of 82 (45%) of ischemics and 7 of 55 (13%) of nonischemics had inducible MVT. For each 3 QRS-point increase (9% LV scarring), the odds ratio for inducing MVT was 2.2 ($P=0.001$) for all patients, 1.7 ($P=0.04$) for ischemics, and 2.2 ($P=0.05$) for nonischemics (Table 3). In a multivariate logistic regression with all patients controlling for LV ejection fraction and ischemic versus nonischemic etiology, the QRS score ($P=0.006$) was the only statistically significant variable for predicting MVT.

Using the same low versus high QRS-score subdivisions as shown in Table 1, patients in the high QRS-score groups had increased rates of inducibility for MVT compared with the low QRS-score groups: in the ischemic group (55% [27 of
versus 30% [10/33], \( P = 0.04 \), and in the nonischemic group (18% [7 of 39] versus 0% [0/16], \( P = 0.09 \)). ROC analysis showed that the median QRS-score cutoff used for stratifying the ischemic group had the highest accuracy for predicting MVT. Although the relation between QRS score and inducible MVT was not statistically significant in the nonischemics, it is notable that no patients with a QRS score of 0 had MVT.

**Discussion**

The present study demonstrates that QRS scores accurately identify the presence and correlate well with the extent of myocardial scar in ischemic and nonischemic cardiomyopathy patients with all types of ventricular conduction. In addition, increasing QRS-estimated scar is associated with higher rates of inducible MVT during electrophysiological or device testing. QRS scoring is an inexpensive, readily available, and easily implemented method, validated previously in identifying MI in patients without ECG confounders. These results suggest that QRS scoring may be able to detect an arrhythmogenic substrate in patients with both ischemic and nonischemic LV dysfunction.

Overall, for all patients and conduction types, the sensitivity, specificity, and accuracy for detection of scar by QRS scoring were 98%, 51%, and 80% at a cutoff of 1 QRS point and 75%, 95%, and 80% at a cutoff of 5 points. Previous studies evaluated the diagnostic performance of the QRS

| Table 3. Odds Ratios for Inducing Sustained Monomorphic Ventricular Tachycardia at Electrophysiological or Device Testing per 3 QRS Point (9% LV Scar) Increase |
|---------------------------------|-----------------|-----------------|
| Odds Ratio | 95% Confidence Interval | \( P \) |
| All patients | 2.2 | 1.5–3.2 | <0.001 |
| Ischemics | 1.7 | 1.0–2.7 | 0.04 |
| Nonischemics | 2.2 | 1.0–5.0 | 0.05 |

LV indicates left ventricle.
QRS scoring in the absence of confounders for quantifying predominantly acute nonreperfused MI, in comparison with necropsy. A strong correlation was found for all MI locations in patients with single infarcts \( r = 0.72 \) to \( 0.80 \). Recent studies with small numbers of patients (<30 each) compared the no confounder QRS score with CMR-LGE scar and found a strong correlation in patients at 1 week after first-time reperfused MI \( r = 0.79, P < 0.001 \), but only a modest correlation in patients with chronic infarcts \( r = 0.40, P < 0.05 \). In our study of patients with LV dysfunction of ischemic or nonischemic etiology, we found high correlations between ECG and CMR that were similar in magnitude to those reported in the necropsy studies. In quantifying scar extent, the QRS score had the highest level of agreement with CMR-LGE core + gray (bias of \(-0.7\%\)). However, at higher scar sizes, the QRS score systematically underestimated CMR-LGE core + gray and thus, the best correlation between the 2 methods over the entire range of scar sizes occurred using core + \( \frac{1}{2} \) gray CMR-LGE. Notably, in the initial necropsy comparisons, total infarct size was in fact measured by including and multiplying the volume of heterogeneous peri-infarct tissue by a fraction, similar to our use of multiplying the “gray” (heterogeneous) zone by \( \frac{1}{2} \). Similar to prior studies comparing ECG with CMR scar quantification, the absolute quantification of scar was different between the 2 methods, as is also the case with CMR comparisons with nuclear techniques. Nonetheless, the high correlation between ECG and CMR in the current study supports potential diagnostic use.

QRS Scoring in the Presence of Conduction Abnormalities

As opposed to traditional ECG diagnostic assessment, our study shows that the ECG can be used to quantify scar even in the presence of fascicular blocks, bundle branch blocks, and hypertrophy. This is consistent with the systematic computer simulations of these pathologies by Selvester et al., which suggested that once the correct underlying activation sequence is taken into account, the ECG can in fact detect and quantify infarction. QRS scoring generally has good agreement with the extent of CMR-LGE scar \( r = 0.60, P < 0.0001 \) and in assessing the presence or absence of scar (ROC area under the curve = 0.81; 95% CI, 0.70 to 0.91), including the small scar seen at the RV and LV insertion points. However, there were some discrepancies between 2 techniques. This disagreement may be attributable to a combination of both false-positive QRS points and false-negative CMR detection of scar. Diffuse myocardial interstitial changes or other pathophysiological mechanisms (eg, electrical-mechanical dissociation) that are not detected by CMR may alter electrical depolarization and provide an arrhythmic substrate. This requires further study.

QRS-Estimated Scar Size and Arrhythmogenic Substrate

In this study, we have shown that QRS scoring to estimate LV scar size can be used to identify patients with arrhythmogenic substrate as defined by inducibility of sustained MVT (odds ratio for inducing MVT of 2.2 for every 3 QRS-point increase). This is consistent with prior studies that used CMR quantification of myocardial scar to predict inducibility of MVT in ischemic\(^7,8\) and nonischemic patients. Although QRS scoring cannot characterize myocardial scar as accurately as CMR-LGE, the ECG-based approach is advantageous in which it is inexpensive, universally available, and simple to perform. Further study will be required to determine whether QRS scoring not only identifies arrhythmogenic substrate, but also can predict the occurrence of ventricular arrhythmias and increased mortality in patients currently being referred for ICD therapy. Previous studies have shown that the “no confounder” QRS score does have strong prognostic value in coronary artery disease patients.\(^21,22\)

Limitations

There are inherent limitations with the relatively small number of patients, especially after subdivision by the different conduction types and ischemic versus nonischemic etiology. Of note, only 10 patients with LAFB, 7 patients with RBBB, and 10 patients with RBBB + LAFB were studied. Furthermore, there were significantly more patients with anterosuperior-anteroseptal scar than inferior-posterolateral scar. Larger numbers of patients will be required to assess the sensitivity and specificity of each of the QRS criteria in the presence of conduction abnormalities to localize and quantify LV scar. Although the semiautomated CMR-LGE technique is highly reproducible,\(^8,14\) it is unknown how well it detects and quantifies diffuse microscopic nonfocal scar that may affect the QRS complex. Furthermore, proarrhythmic electrophysiological changes may affect the QRS complex, but these conditions may not be detected by CMR-LGE. ECGs were also clinically acquired at the time of CMR/ICD implantation and because the tracings were not systematically obtained by the same individual, electrode lead misplacement may certainly affect the QRS configuration and QRS scoring.

The use of inducibility for MVT is a limitation because the value of such an end point in predicting clinical prognosis is controversial and unreliable, particularly in nonischemic cardiomyopathy. Future investigation is required to examine the ability of QRS scoring to predict outcomes such as mortality or ICD firings in a larger cohort of patients. Finally, QRS scoring is unlikely to be used in clinical practice unless automated versions become available for widespread use.
Conclusions
In conclusion, our study demonstrates that QRS scores can identify and quantify CMR-LGE scar in ischemic and nonischemic cardiomyopathy patients even in the presence of traditional ECG “confounders.” In addition to being inexpensive and readily available, the ECG is advantageous because completely automated scoring systems can also be implemented.32 This may facilitate wider application to the identification of patients with potentially arrhythmogenic myocardial substrate, including those with less severe LV dysfunction, regardless of etiology. Future research is needed to investigate the prognostic potential of QRS scoring in predicting adverse arrhythmic outcomes in patients with chronic LV dysfunction.

Acknowledgments
The authors thank Dr Myron L. Weisfeldt for his valuable input. The authors also thank research coordinators Larissa Bell, BSN, Angela Steinberg, BSN, and Barbara Butcher, CCRN, and CMR technologist, Terry Frank. Dr Tomasselli is the Michel Mirowski, MD, Professor of Cardiology.

Sources of Funding
This work was supported by the Donald W. Reynolds Cardiovascular Research Center at Johns Hopkins University, the National Heart, Lung, and Blood Institute, the National Institutes of Health (K23 HL044444 to K.C.W.), and the Sarnoff Cardiovascular Research Foundation (to D.G.S.).

Disclosures
Drs Wu and Lima received research grant support from GE Healthcare Technologies. Dr Wagner received research grant support from Medtronic, Physiocontrol, and Welch Allyn. Dr Tomasselli received research grant support from Boston-Scientific.

References


**CLINICAL PERSPECTIVE**

Implantable cardioverter-defibrillators reduce mortality in patients with left ventricular systolic dysfunction; however, fewer than 25% of such patients receive appropriate firings, and not all appropriate shocks are lifesaving. Recent cardiac magnetic resonance studies have shown that increased myocardial scar, which can provide a substrate for malignant reentrant arrhythmias, is associated with arrhythmogenesis and mortality in ischemic and nonischemic cardiomyopathy. In the present study, we show that the widely available and inexpensive 12-lead ECG Selvester QRS score can quantify myocardial scar in reference to cardiac magnetic resonance in ischemic and nonischemic cardiomyopathy. Although the QRS score has been extensively validated to quantify infarct size, this is the first study to apply QRS scoring to patients with nonischemic scar. In addition, we show that modified versions of the QRS score can quantify scar in patients with left ventricular hypertrophy, left and right bundle branch blocks, and fascicular blocks, which are traditionally thought to confound the ECG diagnosis of infarction. Finally, we show that higher QRS-estimated scar size is associated with an increased odds ratio of inducible sustained monomorphic ventricular tachycardia during electrophysiological testing. Additional studies should further validate the use of QRS scoring to estimate scar size in patients with conduction defects and nonischemic cardiomyopathy and to assess the ability of QRS scoring to risk-stratif patients for sudden cardiac death.
ECG Quantification of Myocardial Scar in Cardiomyopathy Patients With or Without Conduction Defects: Correlation With Cardiac Magnetic Resonance and Arrhythmogenesis


_Circ Arrhythm Electrophysiol._ 2008;1:327-336; originally published online December 2, 2008; doi: 10.1161/CIRCEP.108.798660

_Circulation: Arrhythmia and Electrophysiology_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Copyright © 2008 American Heart Association, Inc. All rights reserved.

Print ISSN: 1941-3149. Online ISSN: 1941-3084

The online version of this article, along with updated information and services, is located on the World Wide Web at:

http://circep.ahajournals.org/content/1/5/327

Data Supplement (unedited) at:

http://circep.ahajournals.org/content/suppl/2008/12/22/CIRCEP.108.798660.DC1

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation: Arrhythmia and Electrophysiology_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:

http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation: Arrhythmia and Electrophysiology_ is online at:

http://circep.ahajournals.org/subscriptions/
### QRS Score Instructions

1. Select column with appropriate conduction (tan highlights show differences in criteria between conduction types).
2. Age normalize all amplitude criteria to age 55 by increasing them 1% per year for 20-54 and decreasing them 1% per year for >55 yrs.
3. For females further decrease by 10% all QRSdur and QRSamp criteria.
4. Circle each QRS criteria met; if >1 criterion in a box met, select one with most points.

#### Waveform Definitions

- **Init R**: Initial R
- **.04R notch**: notch in initial 40 ms

#### Additional Rules

- **For LVH**: If ≥4 anterior/apical QRS points present (other than QS), then count QS in V1-V3.
- **For posterolateral criteria**: Exclude if right atrial overload present (suggesting RVH) if P positive amplitude in V1 or V2 ≥0.1 mV or aVF ≥0.175 mV.

#### 12 LV Segments

For each 1% scar place an X in corresponding LV segment to right of line. Total QRS points ______ *3 = _______ % LV scar

---

### Suppemental Data APPENDIX A: QRS-Score Criteria

<table>
<thead>
<tr>
<th>Lead</th>
<th>RBBB Criteria</th>
<th>LAFB Criteria</th>
<th>LAFB + RBBB Criteria</th>
<th>LVH Criteria</th>
<th>No Confounders Criteria</th>
<th>Max Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>R ≤ 0.2 mV 1</td>
<td>Q ≤ 0.2 mV 1</td>
<td>Q ≤ 0.2 mV 1</td>
<td>R ≤ 0.2 mV 1</td>
<td>Q ≤ 0.2 mV 1</td>
<td>1</td>
</tr>
<tr>
<td>II</td>
<td>Q ≤ 0.2 mV 2</td>
<td>Q ≤ 0.2 mV 2</td>
<td>Q ≤ 0.2 mV 2</td>
<td>R ≤ 0.2 mV 1</td>
<td>Q ≤ 0.2 mV 1</td>
<td>2</td>
</tr>
<tr>
<td>aVL</td>
<td>Q ≤ 0.2 mV 1</td>
<td>Q ≤ 0.2 mV 1</td>
<td>Q ≤ 0.2 mV 1</td>
<td>R ≤ 0.2 mV 1</td>
<td>Q ≤ 0.2 mV 1</td>
<td>1</td>
</tr>
<tr>
<td>aVF</td>
<td>Q ≤ 0.2 mV 1</td>
<td>Q ≤ 0.2 mV 1</td>
<td>Q ≤ 0.2 mV 1</td>
<td>R ≤ 0.2 mV 1</td>
<td>Q ≤ 0.2 mV 1</td>
<td>1</td>
</tr>
<tr>
<td>V1</td>
<td>R ≤ 0.1 mV 2</td>
<td>R ≤ 0.1 mV 2</td>
<td>R ≤ 0.1 mV 2</td>
<td>Q ≤ 0.1 mV 1</td>
<td>R ≤ 0.1 mV 1</td>
<td>2</td>
</tr>
<tr>
<td>V2</td>
<td>R ≤ 0.1 mV 2</td>
<td>R ≤ 0.1 mV 2</td>
<td>R ≤ 0.1 mV 2</td>
<td>Q ≤ 0.1 mV 1</td>
<td>R ≤ 0.1 mV 1</td>
<td>2</td>
</tr>
<tr>
<td>V3</td>
<td>R ≤ 0.1 mV 2</td>
<td>R ≤ 0.1 mV 2</td>
<td>R ≤ 0.1 mV 2</td>
<td>Q ≤ 0.1 mV 1</td>
<td>R ≤ 0.1 mV 1</td>
<td>2</td>
</tr>
<tr>
<td>V4</td>
<td>R ≤ 0.1 mV 2</td>
<td>R ≤ 0.1 mV 2</td>
<td>R ≤ 0.1 mV 2</td>
<td>Q ≤ 0.1 mV 1</td>
<td>R ≤ 0.1 mV 1</td>
<td>2</td>
</tr>
<tr>
<td>V5</td>
<td>R ≤ 0.1 mV 2</td>
<td>R ≤ 0.1 mV 2</td>
<td>R ≤ 0.1 mV 2</td>
<td>Q ≤ 0.1 mV 1</td>
<td>R ≤ 0.1 mV 1</td>
<td>2</td>
</tr>
<tr>
<td>V6</td>
<td>R ≤ 0.1 mV 2</td>
<td>R ≤ 0.1 mV 2</td>
<td>R ≤ 0.1 mV 2</td>
<td>Q ≤ 0.1 mV 1</td>
<td>R ≤ 0.1 mV 1</td>
<td>2</td>
</tr>
<tr>
<td>V7</td>
<td>R ≤ 0.1 mV 2</td>
<td>R ≤ 0.1 mV 2</td>
<td>R ≤ 0.1 mV 2</td>
<td>Q ≤ 0.1 mV 1</td>
<td>R ≤ 0.1 mV 1</td>
<td>2</td>
</tr>
<tr>
<td>V8</td>
<td>R ≤ 0.1 mV 2</td>
<td>R ≤ 0.1 mV 2</td>
<td>R ≤ 0.1 mV 2</td>
<td>Q ≤ 0.1 mV 1</td>
<td>R ≤ 0.1 mV 1</td>
<td>2</td>
</tr>
<tr>
<td>V9</td>
<td>R ≤ 0.1 mV 2</td>
<td>R ≤ 0.1 mV 2</td>
<td>R ≤ 0.1 mV 2</td>
<td>Q ≤ 0.1 mV 1</td>
<td>R ≤ 0.1 mV 1</td>
<td>2</td>
</tr>
<tr>
<td>V10</td>
<td>R ≤ 0.1 mV 2</td>
<td>R ≤ 0.1 mV 2</td>
<td>R ≤ 0.1 mV 2</td>
<td>Q ≤ 0.1 mV 1</td>
<td>R ≤ 0.1 mV 1</td>
<td>2</td>
</tr>
<tr>
<td>V11</td>
<td>R ≤ 0.1 mV 2</td>
<td>R ≤ 0.1 mV 2</td>
<td>R ≤ 0.1 mV 2</td>
<td>Q ≤ 0.1 mV 1</td>
<td>R ≤ 0.1 mV 1</td>
<td>2</td>
</tr>
<tr>
<td>V12</td>
<td>R ≤ 0.1 mV 2</td>
<td>R ≤ 0.1 mV 2</td>
<td>R ≤ 0.1 mV 2</td>
<td>Q ≤ 0.1 mV 1</td>
<td>R ≤ 0.1 mV 1</td>
<td>2</td>
</tr>
</tbody>
</table>

- R ≤ 0.05 mV
- R/S ≥ 0.5 mV

**For LVH**: If ≥4 anterior/apical QRS points present (other than QS), then count QS in V1-V3.

**For posterolateral criteria**: Exclude if right atrial overload present (suggesting RVH) if P positive amplitude in V1 or V2 ≥0.1 mV or aVF ≥0.175 mV.

---

### Total QRS points ______ *3 = _______ % LV scar

---

### 12 LV Segments

For each QRS-score point scored to the left, circle the numbers to the right in the same row which shows the %LV scar in each of the 12 LV segments.
APPENDIX B: Left Bundle Branch Block QRS-Score Criteria

### APPENDIX B: Left Bundle Branch Block QRS-Score Criteria

#### LBBB QRS-Score Criteria

<table>
<thead>
<tr>
<th>Lead</th>
<th>Criteria</th>
<th>Pts</th>
<th>Max pts</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>R/Q ≤ 1.5</td>
<td>1</td>
<td>1*</td>
</tr>
<tr>
<td>aVL</td>
<td>R/S ≤ 1.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Q ≥ 50 ms</td>
<td>2</td>
<td>4**</td>
</tr>
<tr>
<td></td>
<td>Q ≥ 40 ms</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>R/S ≤ 0.5</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>R/Q ≤ 0.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>R/S ≤ 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>R/Q ≤ 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>Q ≥ 40 ms</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Q ≥ 30 ms</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>R/S ≤ 0.5</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>R/Q ≤ 0.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>aVF</td>
<td>Q ≥ 50 ms</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Q ≥ 40 ms</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>R/S ≤ 0.5</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>R/Q ≤ 0.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>R/S ≤ 0.5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Anteroseptal wall

- **V1**: NCHINIT40 = Notch in initial 40 ms
- R ≥ 0.3 mV
- R ≥ 0.2 mV
- R ≥ 20 ms

- **V2**: NCHINIT40 = Notch in initial 40 ms
- R ≥ 0.4 mV
- R ≥ 0.3 mV
- R ≥ 20 ms

#### Posterior lateral wall

- **V1**: S'/S ≥ 2.5
- S'/S ≥ 1.5
- S'/S ≥ 1.25

- **V2**: S'/S ≥ 2.5
- S'/S ≥ 2.0
- S'/S ≥ 1.5

#### Apical 4 segments

- **I**: any Q
- R/Q ≥ 1
- R/S ≥ 1

- **V5**: any Q
- R/R' ≥ 2
- R/R' ≥ 1
- R/S ≥ 2
- R ≤ 0.5 mV

- **V6**: Q ≥ 20 ms
- R/R' ≥ 2
- R/R' ≥ 1
- R/S ≥ 2
- R ≤ 0.5 mV

### Total Points

Total QRS points ______ *3 = ______ % LV scar

---

### Normal Coronary Artery Distribution into the 12 LV Segments

#### Criteria Definitions

1. **Exclude anteroseptal points** if right atrial overload (suggesting RVH) is present (P positive amplitude in V1 or V2 P ≥ 0.1 mV or aVF P ≥ 0.175 mV).
2. **Exclude anteroseptal points** if right axis deviation is present (mean QRS axis ≥ 90°).
3. **Exclude anteroseptal points** if right atrial overload (suggesting RVH) is present (P positive amplitude in V1 or V2 P ≥ 0.1 mV or aVF P ≥ 0.175 mV).

---

### LBBB QRS Score Instructions

1. Age normalize all amplitude criteria to age 55 by increasing them 1%/yr age 20-54 and decreasing them 1%/yr for >55 yrs.
2. For females further decrease by 10% all QRSdur and QRSamp criteria.
3. Circle each QRS criteria.
4. If >1 criterion in bracket (box) met, select one with most points.

---

### Additional Rules

- NCHINIT40 = Notch in initial 40 ms
- The definitions of S, S’, R and R’ are shown below.