Fragmented Wide QRS on a 12-Lead ECG
A Sign of Myocardial Scar and Poor Prognosis

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Background—Fragmented QRS (duration <120 ms) on a 12-lead ECG represents myocardial scar in patients with coronary artery disease. However, the significance of fragmented QRS has not been defined in the presence of a wide QRS (wQRS; duration ≥120 ms). We postulate that fragmented wQRS (f-wQRS) due to bundle branch block, premature ventricular complexes, or paced rhythms (f-pQRS) signify myocardial scar and higher mortality.

Methods and Results—Patients who underwent cardiac evaluation with nuclear stress imaging or cardiac catheterization and had wQRS (bundle branch block, premature ventricular complex, or pQRS) were studied. f-wQRS was defined by the presence of >2 notches on the R wave or the S wave and had to be present in ≥2 contiguous inferior (II, III, aVF), lateral (I, aVL, V6) or anterior (V1 to V5) leads. ECG analyses of 879 patients (age, 66.7±11.4 years; male, 67%; mean follow-up, 29±18 months) with bundle branch block (n=310), premature ventricular complex (n=301), and pQRS (n=268) revealed f-wQRS in 415 (47.2%) patients. Myocardial scar was present in 440 (50%) patients. The sensitivity, specificity, positive predictive value, and negative predictive value of f-wQRS for myocardial scar were 86.8%, 92.5%, 92.0%, and 87.5%, respectively. The sensitivity and specificity for diagnosing myocardial scar were 88.6% and 94.4%, 81.4% and 88.4%, and 89.8% and 95.7% for f-bundle branch block, f-premature ventricular complex, and f-pQRS, respectively. f-wQRS was associated with mortality after adjusting for age, ejection fraction, and diabetes (P=0.017).

Conclusions—f-wQRS on a standard 12-lead ECG is a moderately sensitive and highly specific sign for myocardial scar in patients with known or suspected coronary artery disease. f-wQRS is also an independent predictor of mortality. (Circ Arrhythmia Electrophysiol. 2008;1:258-268.)

Key Words: coronary disease ■ electrocardiography ■ scintigraphy ■ fragmented QRS ■ myocardial scar

Fragmentation of QRS complexes (fQRS) on a routine 12-lead ECG signifies myocardial scar detected by myocardial single-photon emission computed tomography (SPECT) imaging in patients with known or suspected coronary artery disease (CAD).1 fQRS includes various RSR’ pattern with different morphologies of the QRS complexes with or without the Q wave on a resting 12-lead ECG. Various RSR’ patterns include an additional R wave (R’) or notching in the nadir of the S wave, or the presence of >1 R’ (fragmentation) in 2 contiguous leads, corresponding to a major coronary artery territory.1 Notching and slurring of QRS complexes, which have similar morphologies to fQRS, is shown to represent myocardial infarction (MI) scar.2,3 Spectral analysis of high-frequency electrograms has revealed increased notches and/or “slurring” in the electrograms after myocardial injury.1 Similarly, RSR’ pattern (QRS ≥110 ms) not related to bundle branch block (BBB) also represents myocardial scar.5 We have earlier defined fQRS in the presence of a narrow QRS (QRS duration <120 ms) only, and therefore, fragmentation of QRS has not been defined in the presence of a wide QRS (wQRS, QRS duration ≥120 ms), such as BBB, premature ventricular complex (PVC), or paced QRS (pQRS).

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Typical BBB is associated with a RSR’ pattern due to partial transmyocardial depolarization of the ventricle due to relatively slow or absent conduction of the ipsilateral bundle branch. Typically, QRS complexes due to BBB have only 1 additional R’ (or 2 notches on the wave). We postulated that myocardial scar alters the QRS morphology similar to that encountered in narrow QRS complexes and results in an additional R’ or notch in the R wave or the S wave. These different fQRS morphologies probably represent intramyo-
cardiac conduction abnormalities and peri-infarction conduc-
tion block due to myocardial necrosis or scar.\textsuperscript{6} We, therefore,
defined fragmentation of QRS with BBB morphology (QRS ≥120 ms) as the presence of >2 notches (at least 1 notch more than the typical BBB) or multiple notches of the R wave or >2 notches in the nadir of the S wave. Myocardial
depolarization during a PVC or paced rhythm occurs due to intramyocardial conduction of impulses, which typically results in a wide QRS. Several smaller studies have shown that notching and qR pattern in the contour of BBB, PVC, and paced rhythm are associated with an old MI. The main
aim of the study was to identify the predictive value of fragmentation of wide QRS complexes (f-wQRS) for myocardial scar. f-wQRS on a standard 12-lead included fragmented BBB (f-BBB), fragmented PVC (f-PVC), and fragmented paced QRS (f-pQRS). We also postulated that f-wQRS is associated with a significantly increased all-
cause mortality when compared with wide QRS without fragmentation (wQRS).

Methods
ECGs of patients who visited Indiana University Hospitals including the Veterans Affairs Medical Center, for evaluation of CAD were studied in this retrospective study. The institutional review board of Indiana University and Veterans Affairs Medical Center approved the study protocol. 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. The study group included patients
who underwent a nuclear stress test or cardiac catheterization for evaluation of CAD from January 1, 2002, onwards. Standard 12-lead
ECGs with wQRS (BBB and PVCs) were collected from the stress test and cardiac catheterization laboratory records. Paced QRS complexes (pQRS) were collected from the ECGs of patients with an
implantable cardioverter defibrillator (ICD) or pacemaker who had
paced rhythm on standard 12-lead ECG and had undergone stress test or cardiac catheterization within 6 months of the device implant. Any
patient who had a coronary event between the ECG recording and the cardiac catheterization findings was excluded from the analysis. The
12-lead ECG analysis (GE, Marquette, Wis; model Mac 5000; filter range, 0.15 to
100 Hz; AC filter, 60 Hz, 25 mm/s, 10 mm/mV) was performed by 2 independent readers blinded to nuclear stress results, cardiac catheterization findings, and follow-up data. Any disagreement was
resolved with mutual consent. An independent reader blinded to the
ECG findings evaluated the SPECT images, echocardiography, and
cardiac catheterization data. The predictive value of wQRS for
myocardial scar defined by nuclear imaging and/or cardiac catheter-
ization results was determined. Mortality data were also compared
between wQRS and f-wQRS groups.

The inclusion criteria are as follows:
1. Patients with BBB or paced rhythm at baseline who underwent
cardiac catheterization or a nuclear stress test for evaluation of
CAD.
2. PVCs at baseline ECG or during stress test.

The exclusion criteria are as follows:
1. Patients with cardiac catheterization without a left
ventricular (LV) angiogram and no wall motion abnor-
mality assessment by echocardiography.
2. Uninterpretable or inadequate stress test to define
myocardial scar.

Wide QRS Complexes and Fragmented Wide
QRS Complexes
wQRS (duration ≥120 ms) included QRS complexes due to BBB, PVC, and pQRS. f-wQRS (QRS duration ≥120 ms) was defined to
be present if fragmented wQRS (f-BBB, f-PVC, and f-pQRS) were
recorded in ≥2 contiguous anterior leads (V\textsubscript{1} to V\textsubscript{6}) or in ≥2 lateral
(I, aVL, and V\textsubscript{6}) or in ≥2 inferior leads (II, III, and aVF).

Fragmented BBB
Right BBB (RBBB) and left BBB (LBBB) were defined by the
standard ECG criteria (QRS duration ≥120 ms) (Figures 1 and 2).
Incomplete BBB (BBB duration of <120 ms) were not included in
f-BBB group. f-BBB was defined as various RSR\textsuperscript{+} patterns with or
without a Q wave, with ≥2 R waves (R\textsuperscript{+}) or ≥2 notches in the R
wave, or ≥2 notches in the downstroke or upstroke of the S wave, in
2 contiguous leads corresponding to a major coronary artery
territory.

Fragmented PVC
PVC for the study was defined as PVC without any evidence of
supraventricular fusion (Figure 3). f-PVC was defined by the
presence of ≥2 R\textsuperscript{+} or ≥2 notches in the S waves in 2 contiguous
leads. In addition, f-PVC also included PVCs with only 2 notches in
the R wave but were >40 ms apart and present in 2 contiguous
leads.\textsuperscript{7}

Fragmented pQRS
Paced QRS (pQRS) was defined as a wide QRS complex (duration
>120 ms and without any evidence of QRS fusion) initiated by a
paced spike in patients with a pacemaker or ICD (Figure 4).
Fragmented paced QRS (f-pQRS) was defined by the presence of >2
R\textsuperscript{+} or >2 notches in the S waves in 2 contiguous leads.

Gated SPECT Analysis
Some of the patients underwent a rest/stress (low dose/high dose)
Tc-99m sestamibi single-day stress protocol.\textsuperscript{1} A semiquantitative
sum stress score, sum rest score, and sum difference score were
calculated on a standard 17-segment, 5-point scale (0=normal,
1-equivocal or mildly abnormal, 2-moderately abnormal, 3=se-
verely abnormal, and 4-absent tracer uptake). Individual epicardial
coronary artery regional segments of the left anterior descending
terminal (7 segments) represented by leads V\textsubscript{1} to V\textsubscript{6} (anterior
segments); the left circumflex artery (5 segments) represented by leads
I, aVL, and V\textsubscript{6} (lateral or posterolateral segments); and the right
coronary artery (5 segments) represented by leads II, III, and aVF
(inferior segments) were scored according to standard
nomenclature.\textsuperscript{8,9}

Cardiac Catheterization
Some of the patients underwent stress test as well as cardiac
catheterization. During cardiac catheterization, the left ventriculog-
raphy in RAO 30° projection was studied for akinesis or dyskinesia
of at least one of the segments (basal anterior, anterolateral, apical,
inferior, posterobasal) of the LV wall, suggestive of myocardial scar in
patients who underwent cardiac catheterization for evaluation or
prevention of CAD.

Echocardiography
Myocardial scar was confirmed by echocardiography in patients who
did not have left ventriculography performed during cardiac cathe-
terization. Wall motion and thickening were assessed using a
standard 16-segment LV model from digitally stored images and a
previously validated 6-grade scoring system.\textsuperscript{10} Myocardial coronary
segments were assigned according to standard nomenclature. The
presence of regional akinesia was determined by ≥2 akinetic
segments corresponding to a major epicardial coronary artery.

Myocardial Scar
Myocardial scar was defined by the presence of either of the following 2 findings:
1. A fixed perfusion defects (>2 segments) on myocardial SPECT imaging.
2. Total occlusion or >70% occlusion of a major epicardial coronary artery with akinesia or dyskinesia (>1 segment) of respective LV wall as demonstrated by the left ventriculography or echocardiography (>2 segments).

Mortality Data
Mortality data were obtained from the hospital medical records and social security death indices from the Web site available to the public.

Statistical Analysis
Continuous variables were expressed as the mean±SD, and categorical variables were expressed as frequency and percentage. Comparison of continuous variables and dichotomous variables was performed with t test and Fisher exact test. Survival curves for fragmented and nonfragmented w-QRS groups were estimated by the Kaplan-Meier estimator and compared by log-rank test. Cox proportional hazard model was used to model the association between mortality and fragmented w-QRS by adjusting for potential confounders. The assumption of proportional hazard was tested by the method proposed by Lin et al. All analyses were performed by SAS 9.1 (SAS Inc., Cary, NC).

Results
The study population included 902 patients. Twenty-three patients with uninterpretable ECGs, suboptimal echocardiography, or inadequate stress test results were excluded. A final cohort of 879 patients (age, 66.7±11.4 years; male, 97%; mean follow-up, 29±18 months) was included in the study. This study population included 310 patients with BBB (BBB group), 301 patients with PVCs (PVC group), and 268 patients with a pacemaker or ICD (pQRS group). There was 99% concordance in ECG results of the 2 readers. f-wQRS was present in 415 (47.2%) patients. Myocardial scar was present in 440 (50%) patients. Cardiac catheterization was performed in 474 (54%) patients, and nuclear imaging was performed in 588 (67%) patients. One hundred eighty-three (21%) patients, who had a nuclear imaging study, also underwent cardiac catheterization. Both tests had 91% concordance of results for diagnosing a myocardial scar (Table 1).

f-wQRS as a Sign of Myocardial Scar
Sensitivity, specificity, positive predictive value, and negative predictive value of f-wQRS for detection of myocardial
scar were 86.8%, 92.5%, 92.0%, and 87.5%, respectively (Table 2). Sensitivity, specificity, and predictive values for subgroups are shown in Table 2.

**BBB Group (n=310)**
The BBB group included 129 patients with LBBB and 181 patients with RBBB. f-BBB (f-RBBB, 88[48.6%]; f-LBBB, 82[63.6%]) was present in 170 (54.8%) patients (Figures 1 and 2). Myocardial scar was present in 183 (59.4%) of the 310 patients. Sensitivity and specificity of f-BBB for diagnosing a myocardial scar were 88.6% and 94.4%, respectively.

**PVC group (n=310)**
f-PVC was present in 125 (41.5%) patients (Figure 3). Myocardial scar was present in 129 (42.9%) patients. Sensitivity and specificity of f-PVC for myocardial scar was 81.4% and 88.4%, respectively.

**pQRS group (n=268)**
The pQRS included 120 patients with an ICD and 148 patients with a pacemaker. Nuclear imaging in Figure 4 shows f-pQRS with myocardial scar (upper panels) and pQRS without fragmentation and no myocardial scar (lowest panel). f-pQRS was present in 120 (44.8%) patients and myocardial scar was present in 127 (47.4%) patients. Sensitivity and specificity of f-pQRS for myocardial scar was 89.8% and 95.7%, respectively.

**f-wQRS as a Predictor of Mortality**
Kaplan-Meier survival analysis revealed a significantly higher mortality in the f-wQRS group when compared with the wQRS group (P<0.001; Figure 5). The subgroup analysis also revealed that f-BBB, f-PVC, and f-pQRS were associated with a significantly reduced time to death compared with nonfragmented fBBB, PVC, and pQRS, respectively (P=0.05, 0.001 and 0.008, respectively; Figures 6 and 7). Further analysis of the fBBB group revealed that f-LBBB but not f-RBBB was associated with a significantly reduced time to death compared with nonfragmented LBBB (P=0.003) and RBBB (P=0.88), respectively. Cox proportional hazard regression model revealed that age, diabetes, ejection fraction (ejection factor), and f-wQRS were univariate predictors of mortality, whereas sex, history of coronary revascularization, aspirin therapy, β-blocker therapy, and angiotensin-converting enzyme inhibitor therapy were not predictors of mortality (Table 3). The multivariable regression model revealed that f-wQRS is associated with mortality after adjusting for age, ejection fraction, and diabetes.
Discussion
Until now, the ECG diagnosis of prior MI scar without the presence of Q wave in wQRS has not been described in a large cohort of patients. This study demonstrates that 12-lead ECG, an inexpensive and readily available diagnostic test, is a very valuable tool for diagnosing myocardial scar in patients with wQRS including BBB, PVC, and paced rhythm. The sensitivity and specificity of f-wQRS for diagnosing myocardial scar in patients with known or suspected CAD is 86.8% and 92.5%, respectively. This study is an extension of our prior studies. Our first study revealed that fragmented narrow QRS complexes ($<$120 ms) on a 12-lead ECG signify an old MI scar, and the second study revealed that fQRS is associated with a poor prognosis.1,12 Therefore, with the additional information from the present study, we have demonstrated that fragmented QRS complexes, whether narrow or wide, are markers for myocardial scar and poor prognosis in patients with known or suspected CAD.

Fragmentation of QRS
Normal ventricular depolarization occurs in 3 phases, involving the interventricular septum (phase 1), free wall of right ventricle (phase 2), and free wall of left ventricle (phase 3).13 Phases 2 and 3 normally occur simultaneously and are in almost opposite directions. As a result, only the net vector is registered on the surface ECG. In the presence of RBBB, phase 2 is delayed occurring after phase 3 resulting in prolongation of the QRS duration. Additionally, the right ventricular depolarization produces a higher voltage potential on the surface ECG, due to the absence of the opposing effect of simultaneous LV depolarization. This vectorially unopposed activation of right ventricle leads to a diminished S wave depth in V1, which may even disappear completely depending on the severity of the conduction abnormality. Therefore, ECG changes in RBBB are mainly a prolongation of QRS duration and a delayed terminal depolarization manifested as an R wave along with reduced S waves in V1 and V2 as well as a prominent slurred S wave in I, V5, and V6. A similar but vectorially opposite phenomenon occurs in LBBB and is manifested as RSR’ pattern in the left precordial leads. Similarly, the PVC morphology also depends on the site of origin and the physiology of intramyocardial conduction. PVCs in patients with structurally normal hearts have a wide QRS with a smooth contour of the R wave or a narrow notch $<$40 ms in the R wave.7 Likewise, right ventricular pacing is usually from the right ventricular apex and, therefore, it depolarizes the left ventricle similar to a PVC (LBBB, left superior axis) originating from that area.

Several studies have suggested that fragmentation of QRS occurs due to an alteration of the normal depolarization of the ventricles. Autopsies of patients with MI and LV aneurysm have confirmed significant myocardial necrosis, with “islands” of viable myocardial tissue interspersed in abundant fibrous tissue.14 The islands of chronically ischemic myocardium display slow activation as a result of partially depolarized and depressed action potential upstroke velocities. This
feature is responsible for inhomogeneous activation of the ventricles. This alters ventricular depolarization patterns, as shown by endocardial mapping and computer models, probably represent fragmentation in the QRS complex on the surface 12-lead ECG.\textsuperscript{15,16} We postulate that the fragmentations or fractionations in the presence of MI recorded in computer models, high-frequency ECG recordings, and magnetocardiography represents fQRS on a routine 12-lead ECG.\textsuperscript{17–19}

Fragmented BBB

Remote MIs in patients with a BBB are diagnosed by the presence of pathological Q waves. A Q-wave or T-wave inversion with LBBB in lead aVF signifies old inferior MI (sensitivity, 86% and specificity, 91%).\textsuperscript{20} However, other than the Q wave, there is no diagnostic sign of an old anterior or lateral wall MI in the presence of LBBB. Furthermore, with the recent improvements in the management of acute MI, including aggressive medical therapy, the use of thrombolytic agents, and early coronary revascularization, the incidence of Q-wave MI has decreased from 66.6% to 37.5%, and the incidence of non-Q-wave MI has increased reciprocally.\textsuperscript{21} This trend has made the recognition of an old MI in the presence of a BBB more difficult. Multiple Center Investigation of the Limit of Infarction Study demonstrated that late notching of the S wave in V\textsubscript{1} to V\textsubscript{4} as one of the specific ECG signs of MI in the presence of LBBB.\textsuperscript{22} The notching of the S wave in addition to the R waves in LBBB qualifies for the definition of f-BBB in our study because there are already 2 notches or an additional R’ wave. Our findings are also consistent with another smaller ECG study related to the MI scar. The RSR’ complex associated with a wide QRS (\textgtrless 110 ms), unrelated to RBBB or LBBB was identified in 26 patients with an old MI.\textsuperscript{5} In these patients, the RSR’ pattern was present in the precordial leads, inferior leads, or both. Severe segmental wall motion abnormalities (akinetin in 16 and dyskinetic in 10 patients) consistent with MI scar were detected using the equilibrium radionuclide study and the 2-dimensional echocardiogram in these patients. The major difference of our study with the above-mentioned study is that they did not include a typical BBB, paced rhythm, or PVC.

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figures.png}
\caption{Examples of fragmented paced QRS (f-pQRS) are shown in panels A to D. The corresponding myocardial SPECT imaging (upper panels show stress images and the lower panels show the corresponding rest images) of the patient in panel D demonstrates myocardial scar in the inferoseptal region. Asterisks denote f-pQRS complexes. Panel E shows an ECG with nonfragmented pQRS and the patient’s corresponding myocardial SPECT imaging, which reveals no myocardial scar.}
\end{figure}
pathological study confirmed that the Q wave and notches in the S wave upstroke or nadir represents MI scar. In our study, f-RBBB was not associated with significantly reduced time to death when compared with RBBB. It may be because RBBB may represent myocardial scar predominantly in the right ventricle or inferior wall, which is associated with a relatively better prognosis than LBBB. Furthermore, unlike LBBB, a RBBB does not significantly increase mortality on long-term follow-up. Therefore, RBBB represents a relatively low-risk group of patients.

### Table 1. Demographics of Patients With and Without f-wQRS

<table>
<thead>
<tr>
<th></th>
<th>Total (n=879)*</th>
<th>wQRS (n=464)</th>
<th>f-wQRS (n=415)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>66.7±11.4</td>
<td>65.9±12.5</td>
<td>67.6±10.0</td>
<td>0.03</td>
</tr>
<tr>
<td>Male, %</td>
<td>853 (97.0)</td>
<td>446 (96.1)</td>
<td>407 (98.1)</td>
<td>0.11</td>
</tr>
<tr>
<td>VA population, %</td>
<td>849 (96%)</td>
<td>451 (97%)</td>
<td>398 (96%)</td>
<td>0.19</td>
</tr>
<tr>
<td>Myocardial scar, %</td>
<td>440 (50.1)</td>
<td>58 (12.5)</td>
<td>382 (92.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BBB, %</td>
<td>310 (35.3)</td>
<td>140 (30.2)</td>
<td>170 (41.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LBBB</td>
<td>129 (14.7)</td>
<td>47 (10.1)</td>
<td>82 (19.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RBBB</td>
<td>181 (20.6)</td>
<td>93 (20.1)</td>
<td>88 (21.2)</td>
<td>0.67</td>
</tr>
<tr>
<td>PVC, %</td>
<td>301 (34.2)</td>
<td>176 (37.9)</td>
<td>125 (30.1)</td>
<td>0.02</td>
</tr>
<tr>
<td>Paced rhythm, %</td>
<td>268 (30.5)</td>
<td>148 (31.9)</td>
<td>120 (28.9)</td>
<td>0.34</td>
</tr>
<tr>
<td>History of myocardial infarction, %</td>
<td>383 (45.1)</td>
<td>74 (16.3)</td>
<td>309 (78.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Coronary artery disease risk factors, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>328 (37.5)</td>
<td>157 (33.8)</td>
<td>171 (41.6)</td>
<td>0.02</td>
</tr>
<tr>
<td>Hypertension</td>
<td>726 (82.9)</td>
<td>366 (78.9)</td>
<td>360 (87.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>532 (60.9)</td>
<td>254 (54.9)</td>
<td>278 (67.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Smoking</td>
<td>466 (53.0)</td>
<td>237 (51.1)</td>
<td>229 (55.2)</td>
<td>0.25</td>
</tr>
<tr>
<td>Family history of coronary artery disease</td>
<td>346 (39.4)</td>
<td>177 (38.2)</td>
<td>169 (40.7)</td>
<td>0.44</td>
</tr>
<tr>
<td>History of coronary revascularization, %</td>
<td>379 (43.3)</td>
<td>139 (30.1)</td>
<td>240 (58.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>44±16</td>
<td>49±14</td>
<td>38±15</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Drug therapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin therapy</td>
<td>539 (61.3)</td>
<td>252 (54.3)</td>
<td>287 (69.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>β-blocker therapy</td>
<td>577 (65.6)</td>
<td>275 (59.3)</td>
<td>302 (72.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ACE inhibitor therapy</td>
<td>513 (58.5)</td>
<td>237 (51.1)</td>
<td>276 (66.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cardiac catheterization, %</td>
<td>474 (53.9)</td>
<td>244 (52.6)</td>
<td>230 (55.4)</td>
<td>0.42</td>
</tr>
<tr>
<td>LAD &gt;70% obstruction</td>
<td>102 (13.8)</td>
<td>46 (11.2)</td>
<td>56 (17.1)</td>
<td>0.11</td>
</tr>
<tr>
<td>LAD total occlusion</td>
<td>65 (8.8)</td>
<td>13 (3.2)</td>
<td>52 (15.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RCA &gt;70% obstruction</td>
<td>77 (8.8)</td>
<td>33 (7.1)</td>
<td>44 (10.6)</td>
<td>0.07</td>
</tr>
<tr>
<td>RCA total occlusion</td>
<td>91 (10.4)</td>
<td>18 (3.9)</td>
<td>73 (17.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LCX &gt;70% obstruction</td>
<td>83 (11.3)</td>
<td>30 (7.3)</td>
<td>53 (16.2)</td>
<td>0.002</td>
</tr>
<tr>
<td>LCX total occlusion</td>
<td>54 (7.3)</td>
<td>11 (2.7)</td>
<td>43 (13.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nuclear scan, %</td>
<td>588 (66.9)</td>
<td>290 (62.5)</td>
<td>298 (71.8)</td>
<td>0.004</td>
</tr>
<tr>
<td>Inferior scar</td>
<td>164 (18.7)</td>
<td>27 (5.8)</td>
<td>137 (33.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lateral scar</td>
<td>43 (4.9)</td>
<td>4 (0.9)</td>
<td>39 (9.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anterior scar</td>
<td>62 (7.1)</td>
<td>6 (1.3)</td>
<td>56 (13.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Apical scar</td>
<td>154 (17.5)</td>
<td>25 (5.4)</td>
<td>129 (31.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Septal scar</td>
<td>42 (4.8)</td>
<td>6 (1.3)</td>
<td>36 (8.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Posterior scar</td>
<td>18 (2.1)</td>
<td>6 (1.3)</td>
<td>12 (2.9)</td>
<td>0.10</td>
</tr>
<tr>
<td>Length of follow-up, month</td>
<td>29.5 (18.0)</td>
<td>29.4 (17.2)</td>
<td>29.6 (18.8)</td>
<td>0.85</td>
</tr>
<tr>
<td>Death, %</td>
<td>233 (16.5)</td>
<td>84 (18.1)</td>
<td>149 (35.9)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

VA population indicates patients enrolled from Veterans Affairs Medical Center; ACE, angiotensin-converting enzyme; LAD, left anterior descending artery; RCA, right coronary artery; LCX, left circumflex artery.

*P values for binary and continuous variables are based on Fisher exact test and t test, respectively.
and f-RBBB does not represent a significantly higher risk for mortality when compared with RBBB, whereas f-LBBB is a significant predictor of myocardial scar and mortality.

Fragmented PVC
Notching of the PVC represents myocardial scar and Moulton et al. have shown that PVC with a normal contour or notching of QRS with a separation of <40 ms is associated with no myocardial disease, whereas notching (or selves) of the QRS with a separation of >40 ms was associated with significant myocardial disease. In another study, 12-lead ECGs and 2-minute multiple-lead rhythm strips revealed PVCs in 58 of 515 patients who underwent cardiac catheterization. Twenty-one patients with PVCs had prior MI diagnosed by regional akinesia or dyskinesia on left ventriculography. Standard criteria were used to diagnose prior MI from the sinus beats of the ECG. MI was diagnosed when a PVC had a QR or QRS pattern with Q wave >0.04 seconds. Morphological analysis of PVCs had a low sensitivity (29%) but high specificity (97%) and high predictive value (86%) for the diagnosis of MI, whereas a Q wave in sinus rhythm had a sensitivity of 52% and specificity of 97%. Our study has shown that f-PVC has a much higher predictive value for diagnosing MI scar.

Fragmented pQRS
The usefulness of the 12-lead resting ECG is limited for diagnosing an old MI in paced ventricular rhythms. Our results are concordant with the findings of several smaller studies of patients with paced rhythms. In a study of 45 patients with MI (anterior 23, inferior 22) and 26 healthy controls, pacing was applied from the right ventricular apex after coronary angiography. The sensitivity, specificity, and average diagnostic accuracy of the 5 known criteria for MI scar in the presence of paced ECG were assessed. These include: (1) notching (0.04 second in duration) in the ascending limb of the S wave of leads V3, V4, or V5 (Cabrera’s sign); (2) notching of the upstroke of the R wave in lateral leads (I, aVL, or V6, Chapman’s sign); (3) Q waves >0.03 second in duration in lateral leads; (4) notching of the first 0.04 second of the QRS complex in inferior leads (II, III, and aVF); (5) Q wave >0.03 second in duration in inferior leads. The most sensitive criteria, for anterior and inferior MI were Cabrera’s and Chapman’s (91.1% and 86.6%, respectively).

Table 2. Sensitivity, Specificity, Positive Predictive Value, and Negative Predictive Value (95% CI) for f-wQRS as a Test for Myocardial Scar

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>PPV (95% CI)</th>
<th>NPV (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>f-wQRS</td>
<td>86.8 (83.6, 90.0)</td>
<td>92.5 (90.0, 95.0)</td>
<td>92.0 (89.4, 94.7)</td>
<td>87.5 (84.5, 90.5)</td>
</tr>
<tr>
<td>f-BBB</td>
<td>88.6 (83.9, 93.2)</td>
<td>94.4 (90.4, 98.5)</td>
<td>95.9 (92.9, 98.9)</td>
<td>85.0 (79.0, 91.0)</td>
</tr>
<tr>
<td>f-LBBB</td>
<td>88.6 (81.9, 95.4)</td>
<td>90.2 (80.8, 99.7)</td>
<td>95.1 (90.4, 99.9)</td>
<td>78.7 (66.6, 90.9)</td>
</tr>
<tr>
<td>f-RBBB</td>
<td>88.5 (82.1, 95.0)</td>
<td>96.5 (92.5, 100)</td>
<td>96.6 (92.7, 100)</td>
<td>88.2 (81.5, 94.9)</td>
</tr>
<tr>
<td>f-PVC</td>
<td>81.4 (74.6, 88.2)</td>
<td>88.4 (83.5, 93.2)</td>
<td>84.0 (77.5, 90.5)</td>
<td>86.4 (81.2, 91.5)</td>
</tr>
<tr>
<td>f-pQRS</td>
<td>89.8 (84.4, 95.1)</td>
<td>95.7 (92.4, 99.1)</td>
<td>95.0 (91.0, 99.0)</td>
<td>91.2 (86.6, 95.8)</td>
</tr>
</tbody>
</table>

PPV indicates positive predictive value; NPV, negative predictive value.

Figure 5. Kaplan-Meier analysis shows the all-cause mortality in patients with fragmented wide QRS (f-wQRS) group and nonfragmented f-wQRS group. Number of patients at risk during follow-up is shown below the abscissa.

Figure 6. Kaplan-Meier analysis shows the all-cause mortality in patients with fragmented BBB (f-BBB) group and nonfragmented BBB (BBB group). Number of patients at risk during follow-up is shown below the abscissa.
All criteria had a low specificity (range, 42.3% to 69.2%). The combination of Cabrera’s and Chapman’s sign decreased the sensitivity to 77.7%, but increased the specificity to 82.2%. A recent study revealed that Cabrera’s sign (63.6%) was a moderately sensitive sign for MI scar but other known ECG signs had a poor sensitivity (9.1% to 40.9%). However, the specificity (81.6% to 100%) was relatively high for all ECG. In our study, both the above-mentioned signs were included in the definition of f-PVC (>2 QRS notches), with a sensitivity of 89.7% and a specificity of 95.7%. Additionally, our study involved a larger population with documented myocardial scar and unlike other studies did not include patients with nonischemic cardiomyopathy. Our definition of the f-PQRS (as well as f-BBB and f-PVC) is simple, easily interpretable, and more importantly has a higher predictive value than all the above-mentioned criteria combined.

f-wQRS as a Predictor of Mortality

Our study showed that wQRS is associated with a significantly higher mortality when compared with its absence (P=0.017) during a mean follow-up of 29 months. The study results are in concordance with the mortality rates reported in patients with a narrow fQRS (<120 ms). A large-scale study involving 46,933 veterans revealed that BBB and paced QRS were predictors of cardiovascular mortality. Similarly, many other studies have shown that wQRS itself is a predictor of mortality in patients with CAD, but our study further identifies f-wQRS as a marker of the higher risk population (f-BBB, f-PVC, and f-QRS) in the wQRS group. Our study does not provide the mechanism of death in patients with f-wQRS. One of the possible mechanisms of death may be myocardial scar–related heart failure or a coronary events in this high-risk population. fQRS is also associated with significantly higher arrhythmic events in

Figure 7. Kaplan-Meier analysis (left) shows all-cause mortality in patients with fragmented PVC (f-PVC) group and nonfragmented PVC group. Kaplan-Meier analysis (right) shows all-cause mortality in patients with fragmented paced QRS (f-pQRS) group and nonfragmented paced QRS (pQRS) group. Number of patients at risk during follow-up is shown below the abscissa.

Table 3. Proportional Hazard Model for Predictors of Mortality

<table>
<thead>
<tr>
<th>Variables</th>
<th>Univariate Analysis</th>
<th>Multivariable Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factors</td>
<td>RR</td>
<td>95% CI</td>
</tr>
<tr>
<td>f-wQRS</td>
<td>1.916</td>
<td>1.466 2.505</td>
</tr>
<tr>
<td>Age</td>
<td>1.060</td>
<td>1.046 1.075</td>
</tr>
<tr>
<td>Ejection fraction ≤35%</td>
<td>2.719</td>
<td>2.097 3.525</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.363</td>
<td>1.049 1.770</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.203</td>
<td>0.840 1.724</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>0.848</td>
<td>0.653 1.100</td>
</tr>
<tr>
<td>Revascularization</td>
<td>1.212</td>
<td>0.937 1.568</td>
</tr>
<tr>
<td>Aspirin</td>
<td>1.168</td>
<td>0.890 1.534</td>
</tr>
<tr>
<td>β-blockers</td>
<td>0.932</td>
<td>0.712 1.221</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>1.224</td>
<td>0.938 1.597</td>
</tr>
</tbody>
</table>

Proportional hazard assumption was tested by method proposed by Lin et al. No violation was detected except revascularization. ACE indicates angiotensin-converting enzyme.
patients with an ICD. Therefore, it is possible that f-wQRS, which represents abnormalities of impulse conduction, may create a milieu for malignant reentrant ventricular arrhythmias and death.

Limitations

Our study population comprised of patients with at least a low-to-moderate risk for CAD, and therefore, the data cannot be applied to the general population as well as to patients with various non-CAD diseases and cardiomyopathy such as dilated cardiomyopathy or infiltrative heart diseases. The other limitation of our study population is predominantly male veterans. Cardiac MRI (CMR) is considered to be the gold standard for defining myocardial scar, whereas our data for myocardial scar was collected from 2 different diagnostic modalities (cardiac catheterization and stress nuclear imaging). However, these modalities are used more commonly in practice than CMR. Furthermore, CMR is expensive and cannot be used in patients with a pacemaker or an ICD.

Conclusions

f-wQRS on a standard 12-lead ECG, which includes f-BBB, f-PVC, and f-pQRS, is a moderately sensitive and highly specific sign for myocardial scar in patients with known or suspected CAD. f-wQRS is also an independent predictor of mortality after adjusting for age, ejection fraction, and diabetes.

Disclosures

None.

References

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29. Pietrasik G, Goldenberg I, Zdziezienka J, Moss AJ, Zareba W. Prognostic significance of fragmented QRS complex for predicting the risk of...
We previously found that fragmented QRS complexes are a marker for myocardial scar and a greater risk for cardiac events in patients with known or suspected coronary artery disease who have a QRS duration of <120 ms. Traditional measures of ECG detection of scar, such as prior infarct, are more difficult when the QRS duration is prolonged by bundle branch block, pacing, or ectopic ventricular activation. This study evaluated the relation of fragmentation of wide QRS complexes (f-wQRS) to myocardial scar. Nearly half of the patients with wide QRS complexes in this study had f-wQRS as defined as ≥2 notches on R wave or S wave in ≥2 contiguous inferior (II, III, aVF), lateral (I, aVL, V6), or anterior (V1 to V5) leads. f-wQRS had a sensitivity of 87% and a specificity of 93% for myocardial scar. Patients with f-wQRS had greater mortality when compared with patients without fragmentation of QRS (36% vs. 18%) during a 29-month follow-up, and f-wQRS was an independent predictor of mortality. Fragmentation of wide QRS complexes is a simple ECG sign that identifies a high-risk group of patients with myocardial scar.
Fragmented Wide QRS on a 12-Lead ECG: A Sign of Myocardial Scar and Poor Prognosis
Mithilesh K. Das, Hussam Suradi, Waddah Maskoun, Mark A. Michael, Changyu Shen, Jonathan Peng, Gopi Dandamudi and Jo Mahenthiran

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