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

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Abstract

Background: Fragmented QRS (fQRS, duration <120 ms) on a 12-lead ECG represents myocardial scar in patients with coronary artery disease (CAD). However, the significance of fQRS 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 (f-BBB); premature ventricular complexes (f-PVC) 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 (BBB, PVC 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-V3) leads. ECG analyses of 879 patients (age 66.7±11.4 years, male: 97%, mean follow-up 29±18 months) with BBB (n = 310), PVC (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-BBB, f-PVC 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 CAD. f-wQRS is also an independent predictor of mortality.

Key words: fragmented QRS, myocardial scar, mortality
Introduction

Fragmentation of QRS complexes (fQRS) on a routine 12-lead ECG signifies myocardial scar detected by myocardial SPECT imaging in patients with known or suspected coronary artery disease (CAD). 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 two contiguous leads, corresponding to a major coronary artery territory. Notching and slurring of QRS complexes, which have similar morphologies to fQRS is shown to represent myocardial infarction (MI) scar. Spectral analysis of high-frequency electrograms has revealed increased notches and/or "slurring" in the electrograms after myocardial injury. Similarly, RSR` pattern (QRS \( \geq 110 \) ms) not related to bundle branch block (BBB) also represents myocardial scar. 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 \( \geq 120 \) ms), such as bundle branch block (BBB), premature ventricular complex (PVC) or paced QRS (pQRS).

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 one additional R prime (or two 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 prime or notch in the R wave or the S wave. These different fQRS morphologies probably represent intramyocardial conduction abnormalities and peri-infarction conduction 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 one 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 as compared to wide QRS without fragmentation (wQRS).

Methods

ECGs of patients who visited Indiana University Hospitals including the Veterans Affairs Medical Center, for evaluation of coronary artery disease 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 stress test or cardiac catheterization was excluded. The 12-lead ECG analysis (GE, Marquette, Wisconsin, USA; model Mac 5000; filter range, 0.15 to 100 Hz; AC filter, 60 Hz, 25 mm/s, 10 mm/mV) was performed by two 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 catheterization results was determined. Mortality data were also compared between wQRS and f-wQRS groups.

**Inclusion Criteria:**

a. Patients with BBB or paced rhythm at baseline who underwent cardiac catheterization or a nuclear stress test for evaluation of CAD.

b. PVCs at baseline ECG or during stress test.

**Exclusion criteria**

a. Patients with cardiac catheterization without a left ventricular (LV) angiogram and no wall motion abnormality assessment by echocardiography
Uninterpretable or inadequate stress test to define myocardial scar.

**Wide QRS Complexes (wQRS) and Fragmented Wide QRS Complexes (f-wQRS):** 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 (V1 to V5) or in ≥ 2 lateral (I, aVL, and V6) or in ≥ 2 inferior leads (II, III and aVF).

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

**f-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 primes or > 2 notches in the S waves in two 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 two contiguous leads. 7

**f-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 primes or > 2 notches in the S waves in two contiguous leads.
**Gated SPECT Analysis:** Some of the patients underwent a rest/stress (low-dose/high-dose) Tc-99m sestamibi single-day stress protocol. 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=severely abnormal, and 4=absent tracer uptake). Individual epicardial coronary artery regional segments of the left anterior descending artery (7 segments) represented by leads V1 to V5 (anterior segments); the left circumflex artery (5 segments) represented by leads I, aVL, and V6 (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.

**Cardiac Catheterization:** Some of the patients underwent stress test as well as cardiac catheterization. During cardiac catheterization, the left ventriculography in RAO 30° projection was studied for akinesia or dyskinesia of at least one of the segments (basal anterior, anterolateral, apical, inferior, posterobasal) of the left ventricular wall, suggestive of myocardial scar in patients who underwent cardiac catheterization for evaluation or treatment of CAD.

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

*Myocardial scar:* Myocardial scar was defined by the presence of either of the following two 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 ($\geq 1$ segment) of respective left ventricular wall as demonstrated by the left ventriculography or echocardiography ($\geq 2$ segments).

*Mortality data:* Mortality data was obtained from the hospital medical records and social security death indices from the website available to the public.

### Statistical analysis

Continuous variables were expressed as the mean $\pm$ standard deviation and categorical variables were expressed as frequency and percentage. Comparison of continuous variables and dichotomous variables was performed with T test and Fisher’s exact test. Survival curves for fragmented and non-fragmented 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. $^{11}$ All analyses were performed by SAS 9.1 (SAS Inc., Cary, NC, USA).
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 two 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 and 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 (Figure 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 as compared to 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 to nonfragmented fBBB, PVC and pQRS, respectively (p =0.05, 0.001 and 0.008, respectively, Figure 6-7). Further analysis of the fBBB group revealed that f-LBBB but not f-RBBB was associated with a significantly reduced time to death compared to nonfragmented LBBB (p =0.003) and RBBB (p =0.88), respectively. Cox proportional hazard regression model revealed that age, diabetes, ejection fraction (EF) and f-wQRS were univariate predictors of mortality, whereas sex, history of coronary revascularization, aspirin therapy, beta blocker therapy and ACE inhibitor therapy were not predictors of mortality. (Table 3) The multi-variable
regression model revealed that f-wQRS is associated with mortality after adjusting for age, EF 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 three 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 left ventricular depolarization. This vectorially unopposed activation of right ventricle leads to a diminished S wave depth in V₁, which may even disappear completely depending upon 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, V₆. A similar but vectorally opposite phenomenon occurs in LBBB and is manifested as RSR′ pattern in the left precordial leads. Similarly, the PVC morphology also depends upon 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. 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 left ventricular aneurysm have confirmed significant myocardial necrosis, with "islands" of viable myocardial tissue interspersed in abundant fibrous tissue. 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. 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}

\textbf{f-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 (MILIS) 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 two 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 (≥ 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 (akinet ic in 16 and dyskinetic in 10 patients) consistent with MI scar were detected using the equilibrium radionuclide study and the two-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. A
pathological study confirmed that the Q wave and notches in the S wave upstroke or nadir represents MI scar.\textsuperscript{23} In our study, f-RBBB was not associated with significantly reduced time to death as compared to 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 increased mortality on long-term follow-up.\textsuperscript{24} Therefore, RBBB represents a relatively low risk group of patients, and f-RBBB does not represent a significantly higher risk for mortality as compared to RBBB, whereas f-LBBB is a significant predictor of myocardial scar and mortality.

\textbf{f-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.\textsuperscript{7} 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.\textsuperscript{25} 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 $\geq 0.04$ sec. Morphologic 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.
f-pQRS: The usefulness of the 12-lead resting ECG is limited for diagnosing an old MI in paced ventricular 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 five 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). All criteria had a low specificity (range 42.3-69.2%). 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 (n=107) 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-pPVC (> 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 as compared to 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 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 magnetic resonance imaging (CMR) is considered to be the gold standard for defining myocardial scar, whereas our data for myocardial scar was collected from two 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 can not 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.

Disclosure: None (all authors)
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**Figure Legends:**

**Table 1:** Demographics of patients with and without fragmented wide QRS (f-wQRS). LAD: left anterior descending artery, LcX: left circumflex artery, RCA: right coronary artery, VA population: patients enrolled from Veterans Affairs Medical Center.

**Table 2:** Sensitivity, specificity, positive predictive value and negative predictive value (95% CI) for f-wQRS as a test for myocardial scar. f-BBB: fragmented bundle branch block, f-LBBB: fragmented left BBB, f-RBBB: fragmented right BBB, f-PVC: fragmented premature ventricular complex, f-pQRS: fragmented paced QRS, NPV: negative predictive value, PPV: positive predictive value.

**Table 3:** Proportional hazard model for predictors of mortality. *proportional hazard assumption is tested by method proposed by Lin et al. No violation was detected except revascularization.

**Figure 1:** Examples of fragmented LBBB (f-LBBB) of three different patients are shown in panels A, B and C. The corresponding myocardial SPECT imaging (upper panels show stress images and the lower panels show the corresponding rest images) of the patient in panel C demonstrates myocardial scar in the LAD territory. Asterisks denote fragmented QRS complexes. Examples of nonfragmented LBBB is shown in panel D.

**Figure 2:** Examples of fragmented RBBB (f-RBBB) 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 infero-lateral myocardial scar. Asterisks denote f-RBBB complexes. The ECG in panel E shows examples of nonfragmented RBBB.

**Figure 3:** Examples of fragmented ventricular premature complexes (f-PVCs) are shown in panels A, B and C. Asterisks denote fragmented QRS complexes. The corresponding myocardial SPECT imaging (upper panels show stress images and the lower panels show the corresponding rest images) of the patient in panel C demonstrates myocardial scar in the infero-apical territory. ECG in panel D shows examples of nonfragmented PVCs.

**Figure 4:** 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 infero-septal 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.

**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.

**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 1

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<th>f-wQRS (n=415)</th>
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<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 MI (%)</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 CAD</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></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>379 (43.3)</td>
<td>139 (30.1)</td>
<td>240 (58.0)</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>Beta-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>Left main disease</td>
<td>37 (4.2)</td>
<td>11 (2.4)</td>
<td>26 (6.3)</td>
<td>0.006</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>

* p-values for binary and continuous variables are based on Fisher’s exact test and t test, respectively
Table 2: Sensitivity, specificity, positive predicted value and negative predicted value (95% CI) for f-wQRS as a test for myocardial scar.

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</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>
Table 3

Proportional Hazard Model for Predictors of Mortality*

<table>
<thead>
<tr>
<th>Variables</th>
<th>Univariate analysis</th>
<th>Multi-variable analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Factors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>f-wQRS</td>
<td>1.916</td>
<td>1.466</td>
</tr>
<tr>
<td>Age</td>
<td>1.060</td>
<td>1.046</td>
</tr>
<tr>
<td>Ejection fraction (EF) ≤ 35%</td>
<td>2.719</td>
<td>2.097</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.363</td>
<td>1.049</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.203</td>
<td>0.840</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>0.848</td>
<td>0.653</td>
</tr>
<tr>
<td>Revascularization</td>
<td>1.212</td>
<td>0.937</td>
</tr>
<tr>
<td>Aspirin</td>
<td>1.168</td>
<td>0.890</td>
</tr>
<tr>
<td>Beta blockers</td>
<td>0.932</td>
<td>0.712</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>1.224</td>
<td>0.938</td>
</tr>
</tbody>
</table>

* proportional hazard assumption is tested by method proposed by Lin et al. No violation was detected except revascularization.
Figure 1

Fragmented LBBB (f-LBBB)

D. Non-fragmented LBBB
Figure 2

Fragmented RBBB (f-RBBB)

A

B

C

D

E. Nonfragmented RBBB
Figure 3

Fragmented PVCs (f-PVCs)

A. Nonfragmented PVCs

B. Circulation Journal of the American Heart Association

C. Stress

D. Nonfragmented PVCs
Figure 4

A. Nonfragmented Paced Rhythm

B. Fragmented Paced Rhythm

C. Nonfragmented Paced Rhythm

D. Fragmented Paced Rhythm

E. Nonfragmented Paced Rhythm
Survival in fragmented wide QRS (f-wQRS) group vs. nonfragmented wQRS (wQRS) group

Log rank $p < 0.001$

Circulation Journal of the American Heart Association Arrhythmia and Electrophysiology
Figure 6

Survival in fragmented bundle branch block (f-BBB) group vs. nonfragmented bundle branch block (BBB) group

Survival vs. time (months)

Log rank p=0.05

<table>
<thead>
<tr>
<th>Group</th>
<th>0</th>
<th>20</th>
<th>40</th>
<th>60</th>
</tr>
</thead>
<tbody>
<tr>
<td>BBB</td>
<td>140</td>
<td>79</td>
<td>46</td>
<td>9</td>
</tr>
<tr>
<td>f-BBB</td>
<td>170</td>
<td>105</td>
<td>65</td>
<td>14</td>
</tr>
</tbody>
</table>
Figure 7

Survival in fragmented PVC (f-PVC) group vs. nonfragmented PVC (PVC) group

Survival in fragmented paced QRS (f-pQRS) group vs. nonfragmented paced QRS (pQRS) group

<table>
<thead>
<tr>
<th></th>
<th>PVC</th>
<th>f-PVC</th>
<th>Follow-up (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>176</td>
<td>125</td>
<td>155</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>7</td>
<td>88</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>7</td>
<td>57</td>
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<tr>
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<td></td>
<td></td>
<td></td>
<td>3</td>
</tr>
</tbody>
</table>

Log rank p = 0.008

Log rank p = 0.001
Fragmented Wide QRS on a 12-Lead ECG: A Sign of Myocardial Scar and Poor Prognosis
Mithilesh K. Das, Hussam Suradi, Waddah Maskoun, Jonathan Peng, Mark A. Michael, Changyu Shen, Gopi Dandamudi and Jo Mahenthiran

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