

# Fragmented QRS Complex: A Novel Marker of Cardiovascular Disease

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## ABSTRACT

QRS complex fragmentation, defined as changes in QRS morphology with different RSR' patterns: additional R waves, notched S wave, or  $> 1R'$  wave, has recently been linked with various cardiac conditions and even been postulated to be predictive of outcomes in certain pathologies. The current article aims to consolidate the available information about this morphological ECG abnormality and its predictive value.

### Introduction

Fragmented QRS complexes (fQRS) are defined as various RSR' patterns with or without Q waves on a 12-lead resting ECG. Based on their duration, they are subclassified into fQRS complexes (QRS duration  $< 120$  ms) and fragmented wide-QRS complexes (f-wQRS; QRS duration  $> 120$  ms). 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.<sup>1</sup>

### Significance in Ischemic Heart Disease

Slurring and notching of the QRS complexes similar to fQRS has long been associated with post myocardial infarction (MI) cardiac scars. However, fQRS has been proven to be a sign of a scar from a remote MI as detected by single photon emission computed tomography (SPECT); it shows greater sensitivity in detecting regional perfusion abnormalities than Q waves alone and of increasing the sensitivity in detecting MI scars when combined with Q waves.<sup>2</sup> Fragmented QRS complexes on an ECG are a marker of higher-stress myocardial perfusion imaging and functional abnormalities. Regional fQRS patterns denote the presence of a greater corresponding focal regional myocardial scar on stress myocardial perfusion imaging.<sup>3</sup> Das et al proved that the presence of fQRS predisposed susceptible patients to a higher propensity of adverse cardiac events like MI, the need for revascularization, or cardiac death, and even increased the all-cause mortality in patients with known ischemic heart disease and in those under evaluation for coronary artery disease (CAD). Hence it is safe to assume that the presence of fQRS in the resting 12-lead ECG of a patient with CAD or with suspected CAD portends an increased risk for adverse outcomes (Table 1).<sup>4</sup>

Presence of fQRS by itself was not found to be associated with an increased risk of recurrent cardiovascular

events (defined as cardiac death, nonfatal MI, or unstable angina) in the general population; in another study, however, among patients with resolved Q waves, fragmented QRS was associated with an increased risk of cardiac events, and is thought to warrant additional investigation.<sup>6</sup> The sensitivity of the Q wave for diagnosing myocardial scarring was very low (22.2%, 17.1%, and 50% for anterior, posterolateral, and inferior segments, respectively), whereas it was substantially higher for fQRS (72.7%, 62.9%, and 82.7% for anterior, posterolateral, and inferior segments, respectively). When the data for the Q wave and/or fQRS were analyzed for myocardial scarring, there was an additional increment in sensitivity (up to 76.4%, 68.6%, and 90.5% for anterior, posterolateral, and inferior segments, respectively). Furthermore, the overall sensitivity of fQRS (85.6%) was substantially higher than that of the Q wave (36.3%) when the data were analyzed for myocardial scarring, independent of the regional correlation with Single-Photon Electron Computed Tomography (SPECT) analysis. Of note, there was another increment in sensitivity (91.4%) when the Q wave and/or fQRS was used as a criterion for diagnosing myocardial scarring independent of regional correlation.<sup>1</sup> The specificity of ECG signs for a myocardial scar as tested with the Q wave, fQRS, and the Q wave and/or fQRS was high for anterior segments (99.7% vs 98% vs 98.4%, respectively) and lateral segments (99.7% vs 90.5% vs 97.5%, respectively). However, there was a compromise in specificity for ECG signs of inferior myocardial scar (98.9% vs 90.5% vs 91% for the Q wave, fQRS, and Q and/or fQRS, respectively). When the data were analyzed to compare the pathological Q wave with the fQRS for myocardial scarring, independent of regional correlation, the specificity of the Q wave was 99.2%, the specificity of the fQRS was 89%, and the specificity of the Q wave and/or fQRS was 89%. The posttest probability of the fQRS and/or the Q wave was 85.2%, the posttest probability of the fQRS alone was 77.6%, and the posttest probability of the Q wave alone was 82%. The negative predictive value

Table 1. Predictive Value of ECG Signs for Myocardial Infarction<sup>5</sup>

ECG Signs	MI	Sensitivity (95% CI)	Specificity (95% CI)
	Any MI	51 (46, 55)	
fQRS	STEMI	55 (45, 64)	96 (94,98)
	NSTEMI	50 (44,54)	

Abbreviations: CI, confidence interval; fQRS, fragmented QRS; MI, myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction, ECG, electrocardiogram. Sensitivity and specificity (95% CI) of fQRS, STEMI, and NSTEMI.

of the fQRS and/or the Q wave was 94.2%, the negative predictive value of the fQRS was 87.6%, and the negative predictive value of the Q wave was 70.0%.<sup>1</sup>

#### Studies on significance of fQRS complexes in ischemic heart disease:

Das MK, Khan B, Jacob S, Kumar A, Mahenthiran J. Significance of a fragmented QRS complex vs a Q wave in patients with coronary artery disease.

Michael MA, El Masry H, Khan BR, Das MK. Electrocardiographic signs of remote myocardial infarction.

Mahenthiran J, Khan BR, Sawada SG, Das MK. Fragmented QRS complexes not typical of a bundle branch block: a marker of greater myocardial perfusion tomography abnormalities in coronary artery disease.

Das MK, Saha C, El Masry H, et al. Fragmented QRS on a 12-lead ECG: a predictor of mortality and cardiac events in patients with coronary artery disease.

Das MK, Michael MA, Hussam S, et al. Usefulness of fragmented QRS on a 12-lead electrocardiogram in acute coronary syndrome for predicting mortality.

Pietrasik G, Goldenberg I, Zdzienicka J, Moss AJ, Zareba W. Prognostic significance of fragmented QRS complex for predicting the risk of recurrent cardiac events in patients with Q-wave myocardial infarction.

Oeff M, Gödde P, Agrawal R, Endt P, Trahms L, Schultheiss HP. Magnetcardiographic detection of abnormal intraventricular activation in patients with ischemic heart disease with and without tachycardia [in German].

#### As a Marker for Prediction of Arrhythmias

Fragmentation of QRS complexes is thought to be associated with ventricular tachyarrhythmias. A study, where the fragmentation of the QRS complex was quantified using

a fragmentation index, found a direct correlation between fQRS complexes and sustained, monomorphic ventricular tachycardia (V-tach).<sup>7</sup> The fragmentation index in the study was correlated to the extent of regional wall-motion-irregularity and global ejection fraction. Another study using magnetic field maps and body surface potential maps found fragmentation, especially true of the ST-T trajectory plots but also for the QRS complex, made patients more vulnerable for ventricular arrhythmias.<sup>8</sup> There is further evidence in the literature for the subepicardial origin of fQRS complexes causing V-tach, which were resistant to medical management as well as endocardial ablation,<sup>9</sup> and were only terminated with epicardial ablation. A recent article pronounced fQRS complexes to be a marker of Brugada syndrome and a predictor of ventricular fibrillation during follow-up.<sup>10</sup> Another article proved that *SCN5A* mutations, closely associated with the Brugada syndrome, occurred more in patients having fQRS complexes than in patients without fQRS.<sup>11</sup> It also showed patients with fQRS complexes were more prone to get recurrent syncope due to ventricular fibrillation. It is also essential to differentiate between fQRS complexes and electrocardiographic early repolarizations (defined as “an elevation of the QRS ST-junction of at least 0.1 mV from baseline in the inferior or lateral lead, manifested as QRS slurring or notching”)<sup>12</sup>; especially in light of male patients with early repolarizations having a greater incidence of syncopal attacks and idiopathic ventricular fibrillation.<sup>13</sup> The conditions are easily distinguishable if their definitions, as noted above, are kept in mind.

#### Studies on fQRS complexes as predictors of arrhythmia:

Stroink G, Meeder RJ, Elliott P, Lant J, Gardner MJ. Arrhythmia vulnerability assessment using magnetic field maps and body surface potential maps.

Ouyang F, Bänsch D, Schaumann A, et al. Catheter ablation of subepicardial ventricular tachycardia using electroanatomic mapping.

Das MK, Zipes DP. Fragmented QRS: a predictor of mortality and sudden cardiac death.

Morita H, Kusano KF, Miura D, et al. Fragmented QRS as a marker of conduction abnormality and a predictor of prognosis of Brugada syndrome.

#### Role in the Diagnosis and Predicting Prognosis of Structural Heart Disease

Fragmented QRS complexes have been noticed in various structural heart disorders too. In arrhythmogenic right ventricular dysplasia/cardiomyopathy, fQRS complexes have been noted to have similar diagnostic efficacy as the recording of traditionally diagnostic  $\epsilon$  potential in the right precordial leads with a highly amplified and modified ECG recording technique, so as to increase the detection

rate of the  $\epsilon$  potentials.<sup>14</sup> There have been Case Reports suggestive of the fact that it was very important to isolate the critical site at the origin of a V-tach for successful ablation, and fQRS complexes can provide a clue about the origin site.<sup>15</sup>

There have also been studies which have shown fQRS complexes to have a high specificity, high negative predictive value, and moderate positive predictive value in detecting left ventricular aneurysms, especially in patients without a left bundle branch block.<sup>16</sup> Fragmentation of the QRS complexes have helped detect sites of ablation in cases of ventricular arrhythmias in left ventricular aneurysms.<sup>17</sup> Even for patients with idiopathic dilated cardiomyopathy, fQRS complexes were found to be more abundant and associated with late potentials, repetitive ventricular premature beats, or cardiac death and both the number of maxima observed in a complex and the duration of the fQRS complex seemed to have an inverse relationship with ventricular ejection fraction.<sup>18</sup>

A recent article has also linked fQRS complexes with suspected cardiac involvement of sarcoidosis. Presence of the fQRS complexes have been shown to indicate the presence of greater infiltrative myocardial disease as corroborated by gadolinium delayed enhancement cardiac magnetic resonance imaging.<sup>19</sup>

#### **Studies on the association of fQRS complexes with structural heart disease:**

Peters S, Trümmel M, Koehler B. QRS fragmentation in standard ECG as a diagnostic marker of arrhythmogenic right ventricular dysplasia-cardiomyopathy.

Kusano KF, Emori T, Morita H, Ohe T. Ablation of ventricular tachycardia by isolating the critical site in a patient with arrhythmogenic right ventricular cardiomyopathy.

Reddy CV, Cheriparambill K, Saul B, et al. Fragmented left sided QRS in absence of bundle branch block: sign of left ventricular aneurysm.

Ogawa M, Miyoshi K, Morita N, et al. Successful catheter ablation of ventricular tachycardia originating from the idiopathic saccular apical left ventricular aneurysm.

Maehara K, Kokubun T, Awano N, et al. Detection of abnormal high-frequency components in the QRS complex by the wavelet transform in patients with idiopathic dilated cardiomyopathy.

Homsy M, Alsayed L, Vaz D, Das MK, Mahenthiran J. 2064 Fragmented QRS complexes on 12-lead ECG as a marker of greater myocardial infiltration by cardiac magnetic resonance gadolinium-delayed enhancement images in patients with sarcoidosis.

#### **Stratification of Implantable Cardioverter Defibrillator Use: Future Direction**

There has been a retrospective study done which shows that in patients who have an implantable cardioverter defibrillator (ICD), the device is more likely to discharge if the patient has a preexisting fQRS complex on the ECG. Hence in the future, it may become a tool in the selection of appropriate candidates for ICD implantation.<sup>20</sup>

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