

# QRS fragmentation: Diagnostic and prognostic significance

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## Abstract

*Fragmentation of QRS (fQRS) complex is an easily evaluated non-invasive electrocardiographic parameter. Fragmentation of narrow QRS is defined as presence of an additional R wave (R') or notching in the nadir of the S wave, or the presence of > 1 R' in 2 contiguous leads, corresponding to a major coronary artery territory on the resting 12-lead ECG. Fragmentation of wide complex QRS consists of various RSR patterns, with more than 2 R waves (R'') or more than 2 notches in the R wave, or more than 2 notches in the downstroke or upstroke of the S wave. Presence of fQRS has been associated with alternation of myocardial activation due to myocardial scar and myocardial fibrosis. Initial studies reported higher sensitivity of fQRS than Q wave for detecting myocardial scar and postulated that the presence of fQRS could be a good predictor of cardiac events among the patients with coronary artery disease. The presence of fQRS has been investigated among the patients with ischemic and non-ischemic cardiomyopathy suggesting that this ECG parameter may affect prognosis and risk of sudden cardiac death, risk of implantable cardioverter-defibrillator therapy and response to cardiac resynchronization therapy. In addition, there is evidence that fQRS could play an important role as screening and prognostic tool among the patients with Brugada syndrome, long QT syndrome, arrhythmogenic right ventricular dysplasia and cardiac sarcoidosis. This paper reviews definition, diagnostic and prognostic value of fQRS in different patient populations. (Cardiol J 2012; 19, 2: 114–121)*

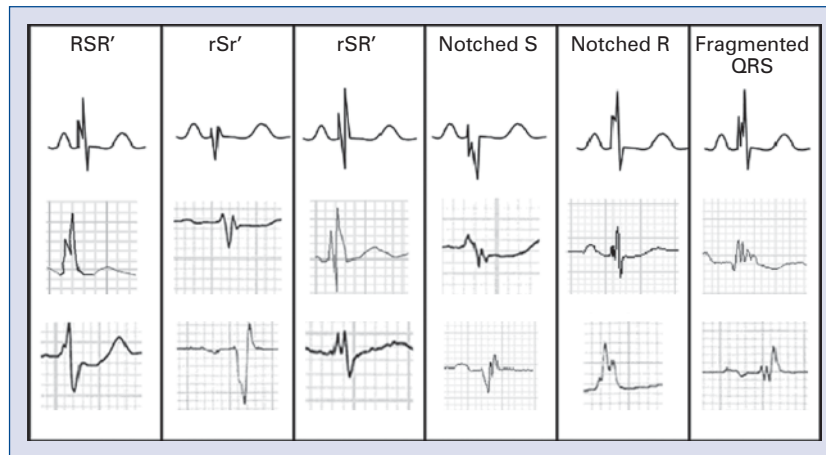
**Key words:** QRS fragmentation, risk, prognosis, coronary artery disease, Q wave, myocardial scar, diagnosis

## Introduction

Slurring and changes in the morphology of the QRS complex have been investigated since 1960's. Flowers et al. [1] demonstrated that the presence of fragmented QRS (fQRS) complexes (also called high-frequency components) are more common among patients with prior myocardial and among

patients with either right or left ventricular (LV) enlargement. Fragmentation of QRS but in particular late potentials, was investigated as a possible new tool to identify the high risk cardiac population. Friedman et al. [2], analyzing canine heart with induced myocardial infarction (MI) suggested that persistent changes in Purkinje fibers and myocardial fibrosis may cause slow and inhomogeneous

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**Figure 1.** Examples of QRS fragmentations as described by Das et al. [10]. Reproduced with permission [10].

myocardial activation. Gardner et al. [3] proposed that fQRS complex in infarcted canine heart is caused by slow and inhomogeneous activation related to healed myocardial scar rather than changes in transmembrane resting or action potentials [3].

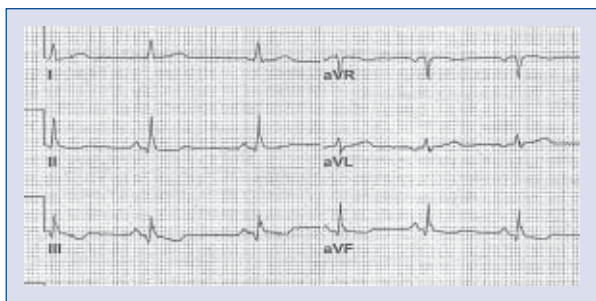
In the analysis of data from an epicardial and endocardial mapping from the patients undergoing LV aneurysm incision, Wiener et al. [4] demonstrated that the fragmented electrical activity was present in all patients with LV aneurysms. However, patients with ventricular tachycardia had fragmented electrical activity from a larger proportion of the endocardial border zone and had more prolonged electrograms in this zone than patients without ventricular tachycardia. The surgical excision of the area, which demonstrated fragmented activity during intraoperative epicardial and endocardial mapping among the patients with pharmacologically refractory ventricular arrhythmia, was associated with better survival and freedom from ventricular arrhythmia. It was proposed that endocardial electrical activity mapping and detection of fragmented activity was a useful tool for surgically guided therapy for ventricular aneurysm and ventricular tachycardia [5]. Varriale and Chryssos [6] suggested that RSR' complex associated with wide QRS complex (equal or greater than 110 ms) but unrelated to right bundle branch block (RBBB) or left bundle branch block (LBBB), could be associated with impaired depolarization within tissue surrounding the myocardial scar. Bayes de Luna [7] suggested that abnormalities of the second half of the QRS complex (terminal slurring, sometimes with R' in lead V<sub>1</sub>) during MI might represent necrosis in late depolarized basal zones. There is a large literature on late potentials assessed using signal-averaged ECG, but this review is focused on intra-QRS frag-

mentations that could be assessed in a standard 12-lead ECG.

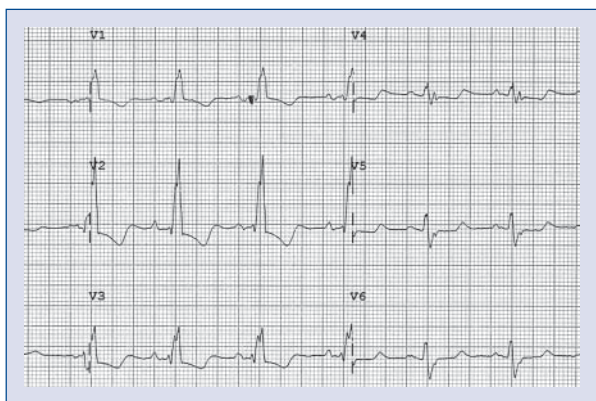
Contemporary definition of the fQRS was defined by Das et al. [8], as presence of an additional R wave (R') or notching in the nadir of the S wave, or the presence of > 1 R' in 2 contiguous leads, corresponding to a major coronary artery territory on the resting 12-lead ECG with filter range 0.16–100 Hz, AC filter 60 Hz, paper speed 25 mm/s and 10 mm/mV. Fragmentation of wide complex QRS (BBB and paced rhythms) was defined by Das et al. [8], as various RSR patterns with or without a Q wave, with more than 2 R waves (R') or more than 2 notches in the R wave, or more than 2 notches in the downstroke or upstroke of the S wave, in 2 contiguous leads corresponding to a major coronary artery territory. Figure 1 shows examples of fQRS as described by Das et al. [8]. In Figure 2, there is an example of QRr' pattern in the patient with prior inferior MI. Definition of fragmented premature ventricular complexes (PVC) was similar to fragmentation of BBB and paced rhythm but also included PVC with 2 notches in the R wave which were more than 40 ms apart and present in 2 contiguous leads [9]. Examples of fragmentation of RBBB and LBBB are shown in Figures 3 and 4, respectively.

### Fragmented QRS and myocardial scar

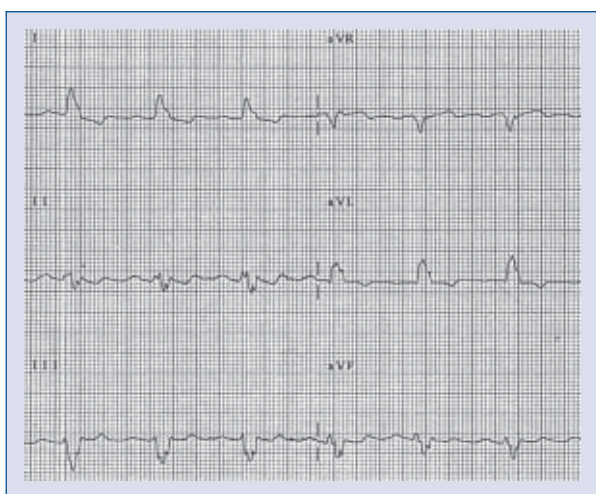
Based on this definition of fragmented QRS, Das et al. [8] compared sensitivity and specificity of Q wave and fQRS for detecting myocardial scar in a cohort of 479 consecutive patients with and without prior history of coronary disease who were referred for nuclear stress test. In this analysis, fQRS complexes have higher sensitivity than Q waves for detecting regional myocardial scar as well



**Figure 2.** QRr' pattern in the patient with prior inferior myocardial infarction.

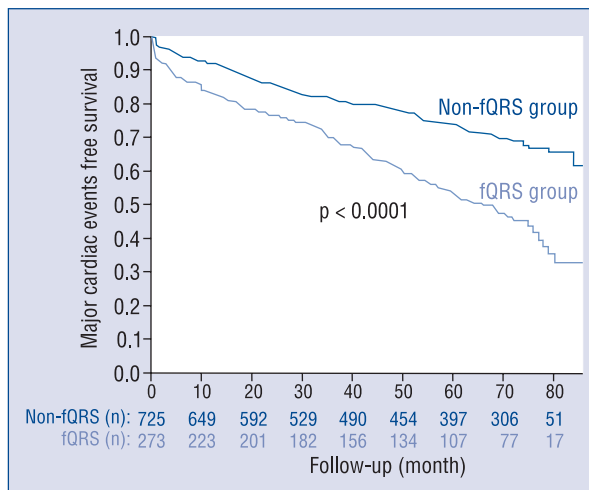


**Figure 3.** QRS fragmentation in the anterior leads in the patient with right bundle branch block and dilated cardiomyopathy.



**Figure 4.** QRS fragmentation in the inferior leads in the patient with left bundle branch block and ischemic cardiomyopathy.

as detecting myocardial scar independently of the regional correlation (fQRS vs Q wave: 85.6% vs 36.3%). However, when comparing specificities,



**Figure 5.** Kaplan-Meier analysis showing cardiac events in patients with fragmented QRS (fQRS group) and without fragmented QRS (non-fQRS group). Reproduced with permission [10].

fQRS was less specific than Q wave for myocardial scar (85.6% vs 99.2%). Using similar cohort of patients, Das et al. [10] demonstrated that the presence of fQRS was associated with higher all-cause mortality (34% vs 26% in patients without fQRS) and cardiac event rate (Fig. 5) defined as MI, cardiac death and need for revascularization (50% vs 28% in patients without fQRS). In the multivariate Cox regression analysis, fQRS was independent predictor of cardiac events (HR 1.62; p = 0.0001) but not all-cause mortality (HR 1.07; p = 0.62).

In a cohort of 879 patients with wide QRS (equal or more than 120 ms, including BBB, PVC, or paced QRS), referred for nuclear stress testing or cardiac catheterization for evaluation of coronary artery disease (CAD), presence of fragmented wide QRS complex was associated with high sensitivity, specificity of myocardial scar and high positive predictive value, negative predictive value (86.8%, 92.5%, 92%, and 87.5%, respectively). When analyzing outcome data, fQRS was associated with an increased risk of all-mortality after adjustment for age, ejection fraction (EF) and history of diabetes mellitus [9].

Pietrasik et al. [11] studied patients with first Q-wave MI and effect of fQRS, resolved Q wave, and persistent Q wave on 2 month follow-up ECG on the risk of recurrent cardiac events defined as unstable angina, recurrent MI or cardiac death. In this study, fQRS was associated with higher risk of recurrent events among the patients who resolved Q wave. It was proposed that fQRS may identify ischemic myocardium [11]. In another cohort of

**Table 1.** Studies assessing fragmented QRS (fQRS) as a predictor for myocardial scar.

Study	N	Patients population	Definition of myocardial scar	Results
Das et al. [8]	479	Consecutive patients with and without prior history of CAD referred for SPECT with QRS < 120 ms	A myocardial scar was defined by a total regional sum stress score and sum rest score $\geq 3$ and a regional sum difference score $\leq 2$ , corresponding to a major coronary artery region	Sensitivity: fQRS = 85.6%; Q wave = 36.3%; fQRS and/or Q wave = 91.4% Specificity: fQRS = 89.4%; Q wave = 99.2%; fQRS and/or Q wave = 89%
Das et al. [9]	879	Consecutive patients with QRS $\geq 120$ ms referred for SPECT or cardiac angiography	Myocardial scar defined as fixed perfusion ( $> 2$ segments) or total occlusion or $> 70\%$ occlusion of major coronary artery with akinesia or dyskinesia of respective left ventricular wall demonstrated by left ventriculogram or echocardiography	Sensitivity for scar fQRS = 86.8% Specificity = 92.5%; PPV = 92; NPV = 87.5
Wang et al. [13]	460	Consecutive patients with or without CAD referred for SPECT	Scar was defined as fixed and mixed viability defects	Sensitivity: fQRS = 31.7%; Q wave = 18.3%; fQRS and Q wave = 1.7% Specificity: fQRS = 83.6%; Q wave = 98.1%; fQRS and Q wave = 98.9%
Carey et al. [14]	138	Patients with ischemic cardiomyopathy evaluated by PET	Infarct volume was quantified by insulin-stimulated 18F-2-fluoro-2-deoxyglucose	Poor correlation between scar on PET and fQRS Sylvester QRS Score better in predicting infarct volume

CAD — coronary artery disease; SPECT — single photon emission computed tomography; PET — positron emission tomography; PPV — positive predictive value; NPV — negative predictive value

56 patients, fQRS seemed to correlate with chronic total coronary occlusion with poorly developed collateral coronary circulation in patients without prior MI [12]. In contrary to those findings, 2 studies failed to show significant association between fQRS and myocardial scar. Wang et al. [13] reassessed sensitivity and specificity of fragmented QRS for detecting myocardial scar. ECG and nuclear perfusion images of 460 consecutive patients with known or suspected CAD were correlated. Q wave has better sensitivity than fQRS in detecting myocardial scar (31.7% vs 1.7%). Similar results were found by Carey et al. [14], in a cohort of 138 patients with severely depressed LV systolic function (mean EF  $27 \pm 9\%$ ) who had infarct volume assessed by positron emission tomography. In this population, fQRS was not predictive for infarct size in both patients with narrow and wide QRS complex [14]. Table 1 summarizes key studies evaluating the association between fQRS and myocardial scar.

### QRS fragmentation and cardiac events in coronary artery disease

Significance of the appearance of fQRS in the patients with acute coronary syndrome has been

investigated. In the cohort of 896 patients with acute coronary syndrome, 2 groups were identified: 337 patients with MI (both STEMI and NSTEMI), and a control group of 445 patients with unstable angina. Fragmented QRS developed in 224 patients with MI and 17 with unstable angina (51% vs 3.7%;  $p < 0.001$ ) and new Q waves developed in 122 (28%) with STEMI, 76 (23%) with NSTEMI, and 2 (0.4%) with unstable angina [15]. In the multivariate Cox regression analysis, presence of fQRS was associated with a 68% higher risk of all-cause death (HR 1.68;  $p = 0.003$ ) during mean follow-up period of  $34 \pm 16$  months [15]. In a cohort of 85 patients with no prior history of CAD who underwent primary percutaneous coronary intervention (PCI) for acute MI, 48 hour post-procedure ECG were analyzed for the presence of fQRS and predictive value for major adverse cardiac events (MACE) was assessed [16]. However, there was no clear definition of MACE in this study. During follow-up of  $6.6 \pm 2.3$  years, there was significantly higher frequency of MACE among the patients with fQRS as compared to those who did not have fQRS (29.4% vs 5.9%;  $p = 0.003$ ). In the multivariate Cox regression analysis, fQRS was an independent predictor of MACE (HR 7.16; 95% CI 3.17–20.11;  $p = 0.006$ ). Q wave and Q wave

**Table 2.** Studies evaluating prognostic value of fragmented QRS (fQRS) in coronary artery disease.

Study	N	Study population	Frequency of fQRS	Follow-up time	Study end-points
Das et al. [10]	998	Patients with QRS < 120 ms who were referred for nuclear stress test	27.35%	57 ± 23 months	All-cause mortality: HR = 1.07; p = 0.62 Cardiac events: HR 1.62; p = 0.0001
Das et al. [9]	879	Patients referred for nuclear stress test or cardiac catheterization with QRS ≥ 120 ms	47.20%	29 ± 18 months	All-cause mortality: HR = 1.41; p = 0.017 Most predictive of mortality in patients with f-LBBB
Das et al. [15]	896	Patients with acute coronary syndrome	51% among patients with MI, 17% in control group	34 ± 16 months	All-cause mortality: HR = 1.68; p = 0.003
Pietrasik et al. [11]	350	Patients with first Q-wave MI	53% on 2-month follow-up ECG	23 ± 9 months	fQRS was not associated with increased risk of cardiac event: cardiac death, non-fatal MI or unstable angina. Only in patients who Q wave, fQRS resolved was associated with increased risk of event: HR = 2.68; p = 0.04
Ari et al. [16]	85	Patients with no prior CAD who presented with acute MI (STEMI vs NSTEMI)	40%	6.6 ± 2.3 years	MACE: HR = 7.16; p = 0.006
Torigoe et al. [17]	170	Patients with prior MI assessed for number of leads with fQRS	≥ 3 leads w/fQRS 34%	6.4 ± 2.9 years	Cardiac death or hospitalization for heart failure: HR = 1.33; p = 0.002

HR — hazard ratio; MACE — major adverse cardiac events; MI — myocardial infarction; CAD — coronary artery disease; LBBB — left bundle branch block

distortion were not significant predictors. This study demonstrated that presence of fQRS at the 48<sup>th</sup> hour post-PCI is a strong and significant predictor of MACE among patients with STEMI [16].

Another approach to evaluate significance and importance of fQRS in patients with CAD was used by Toriqoe et al. [17]. The association between the number of leads with fQRS and the risk of cardiac death or hospitalization for heart failure was assessed in patients with prior MI. During mean follow-up of 6.4 ± 2.9 years, there were 37 primary events among 170 patients. In the multivariate Cox proportional hazard model, only age and a number of leads with fQRS complex were significant predictors of the cardiac death or heart failure hospitalization. It was demonstrated that the presence of ≥ 3 leads with fQRS complex was the most useful predictor of primary event [17]. Table 2 provides data regarding prognostic significance of fQRS in CAD.

### Fragmented QRS complex and ischemic and non-ischemic cardiomyopathy

The fragmented complex QRS and the risk of arrhythmic events was evaluated in the cohort of

361 patients with ischemic and non-ischemic cardiomyopathy who received implantable cardioverter-defibrillator (ICD) either for primary or secondary prevention of sudden cardiac death. Both narrow and wide complex fQRS was associated with higher risk of arrhythmic events defined as ICD shock or anti-tachycardia pacing; however, there was no association between fragmentation and mortality [18]. In a cohort of 128 patients with idiopathic dilated cardiomyopathy with EF equal or less than 40%, Sha et al. [19], demonstrated that presence of fQRS was a strong univariate predictor of all-cause mortality and arrhythmic events (HR 7.90, p = 0.015). However, since hazard ratios from multivariate Cox regression were not reported, it cannot be established whether fQRS was an independent risk factor for mortality or arrhythmic events in this study [19].

In the MADIT II (Multicenter Automatic Defibrillation Implantation Trial) trial, study evaluating the effect of ICD in the patients with severe LV ischemic dysfunction (LVEF ≤ 30%), the presence of fQRS was not associated with increased risk of sudden or all-cause mortality in this population [20]. However, there was significant increase in the risk of sudden cardiac death and all-cause death, in

**Table 3.** Studies evaluating prognostic value of fragmented QRS in ischemic and nonischemic cardiomyopathy.

Study	N	Study population	Frequency of fQRS	Follow-up time	Study end-points
Das et al. [18]	361	Patients with ischemic and non-ischemic CM who received ICD for either primary or secondary prevention	23%	16.6 ± 10.2 months	Increased risk of arrhythmic events defined as appropriate ATP (150–188) or appropriate shock (> 181): HR = 7.62; p < 0.001 No effect on mortality: HR = 1.18; p = 0.74
Brenyo et al. [20] Pietrasik et al. [21]	1188/209 with LBBB	Patients with ischemic CM (EF ≤ 30%) who received ICD for primary prevention	27%	19 ± 12 months	No effect in total population. Increased risk of death only among patients with LBBB and inferior fQRS: HR = 2.30; p = 0.001
Cheema et al. [22]	846	Patients with ischemic and non-ischemic CM (EF ≤ 35%)	33%	40 ± 17 months	All-cause mortality: HR = 0.63; p = 0.43. Arrhythmic mortality: HR = 0.49; p = 0.38
Forleo et al. [23]	394	Patients with ischemic and non-ischemic CM (EF ≤ 35%) implanted with ICD for primary prevention	26%	26 ± 18 months	Death or ICD therapy — no difference in frequency of end-points in patient with and without fQRS
Rickard et al. [26]	233	Patients with LVEF ≤ 40% and NYHA class II–VI undergoing implantation of CRT device		4.4 ± 1.9 years	All-cause mortality — no difference (44% vs 37%, p = 0.31) No difference in response to CRT (LVEF, LVEDV, LVESV)

HR — hazard ratio; CM — cardiomyopathy; EF — ejection fraction; CRT — cardiac resynchronization therapy; ICD — implantable cardioverter-defibrillator; LBBB — left bundle branch block; LVEF — left ventricular ejection fraction; LVEDV — left ventricular end-diastolic; LVESV — left ventricular end-systolic volume; ATP — anti-tachycardia pacing

MADIT II patients with LBBB and inferior wide QRS complex fragmentation, indicating regional variability in the risk [21].

Cheema et al. [22] evaluated the association between fQRS complex and primary end-point of all-cause mortality and secondary end-points specific cause mortality and appropriate ICD shocks in the cohort of 842 patients with LV dysfunction (LVEF ≤ 35%), both ischemic and non-ischemic etiology. Fragmented QRS was present in 32.5% of patients. Mean follow-up of the study was 40 ± 17 months for entire cohort. There was no significant difference in event-free survival between patients with fQRS and without fQRS. Fragmented QRS was not associated with increased risk of all-cause mortality, arrhythmic mortality and non-arrhythmic mortality. There was no significant association between study end-point, when the presence of fQRS complex was stratified by ICD status, the etiology of LV dysfunction, QRS duration or by individual territories. In conclusion, this study demonstrated no associated between fQRS, and mortality and arrhythmic events; and fQRS was not proven to be useful factor in risk stratification of patients eligible for ICD therapy [22]. Similar conclusions were drawn from study by Forleo et al. [23] in which consecutive 394 patients from a single center in Italy were assessed for presence or absence of fQRS prior to the implantation of ICD.

The end-point of the study was all-cause death or appropriate ICD therapy defined as appropriate shock or appropriate anti-tachycardia therapy. During mean 26.3 ± 17.5 months of follow-up, the event-free survival was similar between patients with and without fQRS, indicating no significant role of this parameter in risk stratification for ICD therapy [23]. Table 3 shows key studies assessing QRS fragmentation in ischemic and non-ischemic cardiomyopathy.

### Fragmentation of QRS complex and dyssynchrony and cardiac resynchronization therapy

Basaran et al. [24] correlated fQRS complexes with cardiac dyssynchrony and myocardial fibrosis in patients with non-ischemic cardiomyopathy and narrow QRS complex. Cardiac dyssynchrony was assessed in 25 patients by echocardiography based time to peak myocardial contraction (TS) and standard deviation of TS (TS-SD) in all 12 LV segments, previously described by Yu et al. [25]. Myocardial fibrosis was assessed in 20 patients, based on late gadolinium enhancement (LGE) on cardiac magnetic resonance (CMR). Nineteen (76%) patients had significant dyssynchrony. Out of them, 14 (74%) patients had fQRS complex either in the most delayed segment or one of the dyssynchronous segment. In

patients evaluated by CMR, 17 (85%) patients had LGE and out of them, 13 (76%) patients had fQRS complexes at the concordant segments. This study suggested close correlation between fibrosis, dyssynchrony and the presence of fQRS in patients with narrow QRS and non-ischemic cardiomyopathy.

Effect of fQRS on the efficiency of cardiac resynchronization therapy (CRT) was assessed by Rickard et al. [26] in the cohort of 233 patients with LVEF  $\leq 40\%$  and NYHA class II–VI undergoing implantation of CRT device. Presence of fQRS was assessed on 12-lead standard ECG prior to the implantation. The end-points of the study were LVEF, LV end-diastolic and LV end-systolic volumes and all-cause mortality. During mean follow-up of  $4.4 \pm 1.9$  years, there was no difference in all-cause mortality between patients with and without fQRS (44% vs 36.8%;  $p = 0.31$ ). In conclusion, this study showed no significant association between fQRS and response to CRT, and no effect of fQRS complex on the all-cause mortality among the patients on CRT [26].

### Brugada syndrome

Morita et al. [27] assessed the presence of fQRS complex among 115 patients with Brugada syndrome type I. Thirteen patients had prior ventricular fibrillation (VF), 28 had syncope, and 74 were asymptomatic. Fragmented QRS was assessed in pre-cordial leads:  $V_1$ ,  $V_2$  and  $V_3$ . To exclude the patients with normal RBBB with additional spikes within QRS complex, abnormal QRS fragmentation was defined as  $\geq 4$  spikes in one or  $\geq 8$  spikes in all of  $V_1$ ,  $V_2$  and  $V_3$  leads. Fragmented QRS was present in 43% of patients, and more frequently in the VF group. Among the patients from the study who received ICD, patients with fQRS had frequent recurrence of syncope due VF during first 4 years of follow-up. Syncope due to ventricular tachycardia was rare among the patients without fQRS. This study suggested that multiple spike within QRS complex indicates the presence of an arrhythmogenic substrate with multiple areas of conduction slowing in a relative large tissue mass [27].

### Arrhythmogenic right ventricular dysplasia

Peters et al. [28] analyzed ECG of 360 arrhythmogenic right ventricular dysplasia (ARVD) diagnosed patients and 52 control patients for the presence of fQRS in either 1 right precordial lead or in more than 1 lead including all standard leads. Fragmented QRS was found in 306 (85%) ARVD patients

and only in 2 (4%) control subjects. There was no significant association between presence of fQRS in any leads and cardiac events; however, presence of fQRS complex in right precordial leads seemed to be an important screening tool to evaluate ECG suspicious for ARVD [28].

### Acquired long QT syndrome

Frequency of fQRS was assessed in 70 patients with acquired severe QT prolongation ( $QTc \geq 550$  ms). Thirty-two patients had syncope or torsades de pointes (TdP) and 38 did not have any event. Frequency of fQRS was significantly higher in a syncope/TdP group than in asymptomatic group (81% vs 21%;  $p < 0.01$ ). In addition, syncope/TdP group had longer QT, longer TpTe and higher U wave than asymptomatic group. This study suggested that fragmentation of QRS complex might be a predisposing factor for developing TdP among the patients with acquired prolongation of QT [29].

### Miscellaneous diseases

There has been an interest in fQRS as a screening tool in a systemic disease with cardiac involvement. Kadi et al. [30] assessed the frequency of fQRS complexes in patients with rheumatoid arthritis (RA) and in control group of patients with fibromyalgia rheumatica. Patients with BBB and cardiovascular disease were excluded. Fragmented QRS were more often found among the patients with RA than a control group (37.5% vs 5.7%;  $p = 0.001$ ). Duration of a disease was significantly associated with a presence of fQRS [30].

In a cohort of 112 patients with biopsy-proven sarcoidosis, baseline ECG were evaluated for presence of fQRS [31]. Fifty two patients were diagnosed with cardiac sarcoidosis and 60 did not have cardiac involvement. Among individuals with cardiac involvement, fQRS was more prevalent than those without cardiac involvement (75% vs 33.9%;  $p < 0.01$ ). Similarly BBB were more common in patients with cardiac involvement. Study concluded that the presence of fQRS or BBB in patients with sarcoidosis should raise suspicion for cardiac involvement and prompt further evaluation [31].

### Summary

Presence of fragmented QRS represents distortion of signal conduction and depolarization process within ventricles which is related to myocardial scar/myocardial ischemia or myocardial fibro-

sis. The meaning/predictive value of this ECG marker seems to be different in different populations. Still there is dispute if it can predict the presence of myocardial scarring in patients with CAD. Two major studies demonstrated different degree of sensitivity of fragmented QRS [8, 13]. In patients with stable CAD and patients with acute MI, QRS fragmentation seems to be good predictor of cardiac events, however, does not affect mortality [10]. In patients with non-ischemic cardiomyopathy, fragmentation of narrow QRS complex seems to correlate with degree of fibrosis and dyssynchrony and importantly may influence the response for CRT [24]. However, based on clinical studies with larger number of patients with current indications for cardiac resynchronization, fragmentation is not affecting the therapy response [26]. In patients with LV dysfunction, there is no clear evidence that presence of fragmented QRS could predict arrhythmic events [20–23].

Major factor limiting utility of fragmentation is a subjective assessment of significant fQRS. Since fQRS represents alternation and inhomogeneity in ventricular activation, which based on studies quoted in this review, may have significant clinical diagnostic and prognostic value in different cardiovascular diseases, there is a need for more objective evaluation of depolarization alternation process. One of the future directions of more objective analysis of depolarization process is an analysis of high frequency QRS components. HyperQ is a novel technology allowing measurement of QRS signal amplitude and morphology and seemed to be more sensitive than ST-T changes during exercise stress testing for detecting ischemia [32].

**Conflict of interest:** none declared

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