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REVIEW ARTICLE

The role of fragmented QRS complexes in cardiovascular diseases: Pathophysiology, prognosis, and clinical applications

Lütfü Bekar [1], *Macit Kalçık* [1*], *Abdullah Sarıhan* [2], *Ömer Burak Çelik* [2], *Abdülmelik Birgün* [2], *Muhammet Cihat Çelik* [2], *Mücahit Yetim* [1], *Yusuf Karavelioğlu* [1]

[1] Hitit University, Faculty of Medicine, Department of Cardiology, Çorum, TÜRKİYE

[2] Hitit University, Erol Olçok Education and Research Hospital, Department of Cardiology, Çorum, TÜRKİYE

ABSTRACT

Fragmented QRS (fQRS) is an electrocardiographic marker that reflects conduction abnormalities caused by myocardial scarring, fibrosis, or structural remodeling. Over the past two decades, fQRS has gained increasing attention for its diagnostic and prognostic implications in cardiovascular diseases (CVDs). In ischemic heart disease, fQRS is strongly associated with myocardial infarction, scar burden, and adverse cardiac outcomes, including ventricular arrhythmias and sudden cardiac death. Beyond coronary artery disease, fQRS has also been linked to poor prognosis in non-ischemic cardiomyopathies and heart failure, where it correlates with impaired ventricular function, arrhythmic events, and limited response to cardiac resynchronization therapy. Moreover, fQRS is observed in arrhythmogenic conditions such as Brugada syndrome and in structural disorders including congenital heart disease, myocarditis, and infiltrative cardiomyopathies, serving as a marker of myocardial fibrosis and a predictor of arrhythmogenic risk. The clinical utility of fQRS lies in its simplicity, availability, and low cost, as standard 12-lead electrocardiography is universally accessible. Its incremental prognostic value beyond conventional parameters such as left ventricular ejection fraction highlights its potential to refine risk stratification and guide therapeutic strategies, particularly in identifying candidates for implantable cardioverter-defibrillators. However, widespread clinical adoption is limited by inconsistent definitions, lack of standardization, and variability in interpretation. Future directions include large-scale validation studies, integration with multimodality risk assessment, and the application of artificial intelligence to improve automated detection and predictive accuracy. Overall, fQRS represents a promising, non-invasive tool that could enhance the management of patients across the spectrum of CVDs.

Keywords: fragmented QRS, electrocardiography, myocardial fibrosis, ventricular arrhythmias, sudden cardiac death

Correspondence:
Macit Kalçık, MD.

Address: Department of Cardiology, Faculty of Medicine, Hitit University, Çorum, TÜRKİYE

Email: macitkalcik@yahoo.com

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INTRODUCTION

Cardiovascular diseases (CVDs) remain the leading cause of morbidity and mortality worldwide. According to the World Health Organization, approximately 17.9 million deaths occur annually due to CVDs, representing nearly one-third of all global deaths [1]. In modern cardiology, early diagnosis, risk stratification, and prognostic assessment are essential to improve patient outcomes. Numerous biomarkers and imaging modalities are available for this purpose; however, many of these techniques are either costly, time-consuming, or invasive. Consequently, the identification of easily accessible, non-invasive, and cost-effective markers remains a critical need.

Electrocardiography (ECG) has long been established as one of the most widely used and indispensable tools in cardiovascular medicine. Since its introduction by Willem Einthoven in the early 20th century, ECG has played a pivotal role not only in the diagnosis of rhythm disturbances but also in the evaluation of myocardial ischemia, conduction abnormalities, and structural heart disease

Table 1. Definition and electrophysiological basis of fQRS

Feature	Description
ECG morphology	Additional R', notching in R or S wave, multiple spikes within QRS
Narrow QRS (< 120 ms)	fQRS defined by extra notches/spikes in contiguous leads
Wide QRS (> 120 ms)	Multiple notches within widened QRS (e.g., BBB and pacing)
Underlying mechanism	Myocardial scar, interstitial or replacement fibrosis causing conduction delay and heterogeneity
Electrophysiological correlate	Micro-reentry, zig-zag conduction, fractionated electrograms

Note. QRS: QRS complex & BBB: Bundle branch block

[2]. In recent years, attention has been directed toward subtle ECG findings with potential diagnostic and prognostic value. Among these, the fragmented QRS (fQRS) complex has gained increasing interest.

fQRS is defined as the presence of additional R waves (R'), notching in the R or S wave, or the presence of multiple spikes within the QRS complex in at least two contiguous leads corresponding to a major coronary artery territory. It is thought to reflect altered ventricular conduction due to myocardial scar tissue or interstitial fibrosis, leading to heterogeneous ventricular depolarization [3]. First described by Das and colleagues in the early 2000s, fQRS was initially recognized as a marker of myocardial scarring in patients with prior myocardial infarction [4]. Subsequently, its clinical significance has been expanded to a wide spectrum of cardiovascular conditions, including cardiomyopathies, heart failure (HF), arrhythmia, and other structural abnormalities.

The prognostic implications of fQRS have been well documented in multiple studies. In coronary artery disease (CAD), fQRS has been associated with the presence of myocardial scar and has been proposed as a non-invasive alternative to detect myocardial viability [5]. In HF, its presence correlates with disease severity, hospitalization rates, and all-cause mortality. Moreover, fQRS has also been linked to an increased risk of ventricular arrhythmias and sudden cardiac death (SCD), thereby serving as a potential risk stratification tool [6].

Given these findings, fQRS has emerged as a promising, non-invasive ECG marker that may provide clinically valuable information beyond traditional parameters. The aim of this narrative review is to provide a comprehensive overview of the role of fQRS in CVDs, with emphasis on its pathophysiological basis, diagnostic and prognostic implications, and potential clinical applications.

DEFINITION AND ELECTROPHYSIOLOGICAL BASIS OF fQRS

fQRS is an electrocardiographic marker characterized by various alterations in the QRS complex morphology. The classical definition includes the presence of additional R', notching in the nadir of the S wave, notching of the R', or the presence of more than one R' within the QRS complex in at least two contiguous leads corresponding to a major coronary artery territory [7]. These abnormalities may appear in narrow QRS complexes (< 120 ms) or in wide QRS complexes, such as those observed in bundle branch block, ventricular pacing, or pre-excitation syndromes. In these latter settings, fQRS is defined as multiple notches within the widened QRS complex [8] (**Table 1**).

The underlying electrophysiological basis of fQRS is considered to be delayed and heterogeneous ventricular activation, which results from disrupted conduction pathways within diseased myocardium. Histopathological and imaging studies have shown that fQRS corresponds to areas of myocardial scar, interstitial fibrosis, or patchy replacement fibrosis [9]. These pathological substrates cause conduction block, zig-zag conduction pathways, and local areas of slowed activation, which manifest as multiple spikes or notches in the surface ECG [10] (**Table 1**).

Several experimental and clinical studies have demonstrated that fQRS correlates with areas of scar tissue detected by cardiac magnetic resonance (CMR) imaging with late gadolinium enhancement and by nuclear perfusion imaging [11, 12]. Moreover, invasive electrophysiological mapping has revealed that regions showing fQRS often coincide with low-voltage areas, fractionated electrograms, and conduction delay, further confirming the relationship between surface ECG abnormalities and underlying myocardial pathology [13].

It is important to distinguish fQRS from other QRS abnormalities that may arise due to benign variants or technical issues. Small notches or slurring in isolated leads, particularly in young healthy individuals, may represent normal variants rather than pathological fQRS. Similarly, poor electrode contact or baseline noise can mimic fragmentation. Therefore, the definition of fQRS requires careful attention to reproducibility across contiguous leads and correlation with clinical context [14].

From a pathophysiological perspective, the presence of fQRS is thought to reflect micro-reentrant conduction and depolarization abnormalities caused by heterogeneous anisotropic conduction. These conduction disturbances create areas prone to electrical instability, thereby providing a substrate for arrhythmogenesis [15]. Thus, beyond being a marker of myocardial scar or fibrosis, fQRS also represents

an electrophysiological correlation of increased arrhythmic risk.

In summary, fQRS is a surface ECG marker that indicates underlying myocardial conduction abnormalities, most commonly due to scar or fibrosis. Its detection requires standardized criteria and careful interpretation, yet it offers a simple, non-invasive method to identify patients with structural and electrophysiological substrates that predispose to adverse cardiovascular outcomes.

fQRS AND CAD

CAD represents the most common underlying pathology associated with fQRS. Myocardial ischemia and infarction lead to irreversible structural alterations, including necrosis, fibrosis, and scar formation, which subsequently produce delayed and heterogeneous ventricular conduction. These conduction disturbances manifest on the surface electrocardiogram as fQRS complexes. Thus, the presence of fQRS in patients with CAD reflects the underlying substrate of myocardial scarring or non-homogeneous conduction within ischemic territories [16].

fQRS in Acute Coronary Syndromes

In the setting of acute coronary syndromes, the detection of fQRS has been proposed as an early and sensitive marker of myocardial injury. Studies have shown that fQRS may appear in the early phase of acute myocardial infarction (AMI), even before the development of Q waves, thereby providing incremental diagnostic information [17]. It was shown that fQRS had higher sensitivity than Q waves in detecting prior myocardial infarction, especially in patients with non-Q-wave AMI [18]. This finding highlights the potential role of fQRS as a more reliable marker of myocardial damage compared to traditional Q-wave criteria.

Moreover, fQRS has been linked to infarct size and the extent of myocardial damage. Patients with extensive fQRS abnormalities on admission ECG are more likely to have larger infarcts, lower left ventricular ejection fraction (LVEF), and adverse in-hospital outcomes [12]. The persistence of fQRS following reperfusion therapy has also been associated with incomplete myocardial recovery, suggesting that fQRS may serve as a marker of failed reperfusion or ongoing ischemia [19].

fQRS in Chronic Ischemic Heart Disease

In patients with stable CAD or prior myocardial infarction, fQRS has been consistently correlated with myocardial scar detected by advanced imaging modalities, including single-photon emission computed tomography and CMR with late gadolinium enhancement [11, 12]. Importantly, fQRS provides additional diagnostic value over conventional Q waves, particularly in patients with small or non-transmural infarctions, where Q waves may be absent or non-diagnostic.

The prevalence of fQRS in patients with prior myocardial infarction has been reported to range between 40% and 50%, depending on the criteria used and the population studied [5]. Its presence has been independently associated with reduced LVEF, higher rates of recurrent ischemic events, and adverse long-term outcomes, including all-cause and cardiovascular mortality [20]. These associations suggest that fQRS is not merely an epiphenomenon but a clinically meaningful marker of myocardial pathology.

Prognostic Significance of fQRS in CAD

A large body of evidence supports the prognostic significance of fQRS in patients with CAD. The presence of fQRS has been shown to predict major adverse cardiovascular events, including recurrent myocardial infarction, hospitalization for HF, and SCD [21]. It was reported that in patients with Q-wave myocardial infarction, fQRS predicted recurrent cardiac events independently of other risk markers such as LVEF and QRS duration [6]. Similarly, it was shown that fQRS was associated with increased mortality in post-MI patients, even after adjusting for traditional risk factors [22].

Another important clinical implication is the role of fQRS in risk stratification for SCD. Myocardial scar tissue forms a substrate for reentrant arrhythmias, and fQRS as a non-invasive marker of scar may help identify patients at higher risk. Several studies have shown that patients with CAD and fQRS are more likely to develop ventricular tachyarrhythmias and may benefit from closer monitoring or prophylactic implantable cardioverter-defibrillator (ICD) therapy [23, 24].

Limitations in CAD Populations

Despite the strong evidence base, several limitations should be acknowledged. The diagnostic accuracy of fQRS may be affected by interobserver variability and differences in the applied diagnostic criteria. Furthermore, fQRS is not specific to CAD, as it may also be observed in non-ischemic cardiomyopathies and other structural heart diseases [14]. Standardization of definitions and integration with other diagnostic modalities are necessary to enhance its utility in clinical practice.

In summary, fQRS represents a valuable non-invasive marker of myocardial scar and conduction abnormalities in patients with CAD. Its presence in acute and chronic ischemic settings is associated with larger infarct size, impaired ventricular function, increased risk of recurrent events, and higher mortality. As such, fQRS offers incremental diagnostic and prognostic information and may play an important role in risk stratification, particularly for SCD (**Table 2**).

fQRS and Cardiomyopathies

Cardiomyopathies represent a heterogeneous group of myocardial disorders that are frequently associated with structural remodeling, fibrosis, and scarring. These

Table 2. Prevalence and clinical relevance of fQRS in CVDs

Condition	Prevalence (%)	Clinical significance
Acute myocardial infarction	40-50	Marker of myocardial injury and infarct size
Chronic ischemic heart disease	~40	Indicates scar, associated with recurrent ischemia
Dilated cardiomyopathy	25-50	Associated with reduced LVEF, higher HF admissions
Hypertrophic cardiomyopathy	30-40	Correlates with fibrosis and arrhythmic risk
Arrhythmogenic right ventricular cardiomyopathy	High	Identifies RV structural disease, VT risk
Heart failure (all types)	30-50	Reflects disease severity, higher mortality
Brugada, congenital heart disease, sarcoidosis, amyloidosis	Variable	Predictor of arrhythmias and sudden cardiac death

Note. RV: Right ventricle

pathophysiological alterations result in non-homogeneous ventricular conduction, which can be detected on surface electrocardiography as fQRS. Multiple studies have demonstrated that fQRS is prevalent among patients with dilated cardiomyopathy (DCM), hypertrophic cardiomyopathy (HCM), restrictive cardiomyopathy, and arrhythmogenic right ventricular cardiomyopathy (ARVC), with significant implications for diagnosis, prognosis, and arrhythmic risk stratification [14].

DCM

In DCM, progressive myocardial remodeling and interstitial fibrosis form the structural substrate for conduction abnormalities. fQRS has been observed in a substantial proportion of patients with non-ischemic DCM, with prevalence rates ranging from 25% to 50% depending on the diagnostic criteria applied [25]. The presence of fQRS in DCM patients has been linked to reduced left ventricular ejection fraction, increased New York Heart Association (NYHA) functional class, and higher rates of hospitalization for HF [26].

From a prognostic perspective, fQRS serves as a predictor of adverse outcomes in DCM. It has been associated with increased risk of ventricular arrhythmia, SCD, and poor response to pharmacological therapy [23]. Furthermore, in patients undergoing cardiac resynchronization therapy (CRT), fQRS has been proposed as a marker of non-response, reflecting extensive fibrosis and disrupted conduction pathways that hinder effective biventricular pacing [27].

HCM

HCM is characterized by myocyte disarray, interstitial fibrosis, and abnormal conduction. fQRS has been detected in up to 40% of patients with HCM, and its presence correlates strongly with the burden of myocardial fibrosis as documented by late gadolinium enhancement on CMR imaging [28]. Patients with fQRS tend to have more extensive hypertrophy, more severe diastolic dysfunction, and a higher risk of ventricular arrhythmias [29].

Importantly, fQRS has emerged as a valuable tool for risk stratification in HCM. Studies have reported that HCM patients with fQRS exhibit an increased incidence of sustained ventricular tachycardia (VT), appropriate ICD shocks, and SCD events [30]. Thus, incorporation of fQRS into existing risk models may enhance the identification of high-risk HCM patients who may benefit from ICD implantation.

Restrictive and Infiltrative Cardiomyopathies

Restrictive and infiltrative cardiomyopathies, such as amyloidosis and sarcoidosis, are frequently associated with conduction disturbances due to diffuse interstitial infiltration and fibrosis. In cardiac amyloidosis, fQRS has been reported as a common finding, reflecting severe myocardial involvement [31]. Similarly, in cardiac sarcoidosis, fQRS correlates with the presence of granulomatous inflammation and scarring as confirmed by CMR or positron emission tomography imaging [32]. Importantly, in both conditions, the presence of fQRS has been linked to higher arrhythmic risk and adverse prognosis, underscoring its potential role in guiding clinical management.

ARVC

ARVC is another cardiomyopathy in which fQRS plays a significant role. The pathogenesis of ARVC involves fibrofatty replacement of the right ventricular myocardium, leading to conduction abnormalities and reentrant arrhythmias. fQRS has been identified as a sensitive ECG marker of ARVC, frequently appearing in the right precordial leads (V1-V3) [33]. Its presence has been associated with extensive structural disease, reduced right ventricular function, and higher incidence of ventricular arrhythmias [34].

Taken together, the evidence suggests that fQRS is a common and clinically relevant finding in various forms of cardiomyopathy. Its presence reflects underlying myocardial fibrosis and conduction abnormalities, and it is consistently associated with impaired functional status, arrhythmic events, and adverse outcomes. As such, fQRS represents an important, non-invasive marker for diagnosis, risk stratification, and therapeutic decision-making in patients with cardiomyopathies (**Table 2**).

fQRS and Arrhythmias

The arrhythmogenic potential of fQRS is well established across multiple cardiac conditions. Because fQRS reflects regions of conduction slowing and non-uniform ventricular activation due to myocardial fibrosis or scarring, it provides an electrocardiographic marker of arrhythmogenic substrate. Numerous studies have demonstrated a robust association between fQRS and both ventricular and supraventricular arrhythmias, with important implications for risk stratification and therapeutic decision-making [4].

fQRS and Ventricular Arrhythmias

VT and ventricular fibrillation frequently originate from regions of myocardial scar. These areas harbor reentrant circuits caused by patchy fibrosis and heterogeneous conduction, which manifest on surface ECG as fQRS complexes. Clinical and electrophysiological mapping studies have demonstrated that fQRS correlates with regions of low-voltage electrograms, late potentials, and fractionated signals within the scar, thereby identifying arrhythmogenic regions non-invasively [13].

Several clinical studies have confirmed that the presence of fQRS predicts ventricular arrhythmias in patients with ischemic cardiomyopathy, non-ischemic DCM, and HCM. In patients with prior myocardial infarction, fQRS was associated with a significantly higher incidence of sustained VT and appropriate ICD therapies compared to those without fQRS [20]. Similarly, in non-ischemic cardiomyopathy, the presence of fQRS predicted ventricular tachyarrhythmic events independently of left ventricular ejection fraction [25].

Meta-analyses have further reinforced these findings, demonstrating that fQRS significantly increases the risk of ventricular arrhythmias and SCD across diverse populations [23]. This evidence highlights the potential role of fQRS as a readily available risk stratification tool to guide decisions regarding ICD implantation.

fQRS and SCD

The prediction of SCD remains a major clinical challenge, particularly in patients with preserved or moderately reduced ejection fractions who do not otherwise meet conventional ICD criteria. fQRS has emerged as a potential marker of SCD risk in such populations. For example, in the MADIT II and other large ICD trials, fQRS was independently associated with increased risk of mortality and appropriate ICD therapies [22]. Importantly, fQRS may provide additive prognostic value beyond left ventricular ejection fraction, helping refine current guidelines for ICD implantation [5].

fQRS and Supraventricular Arrhythmias

Although the majority of research has focused on ventricular arrhythmias, several studies have investigated the relationship between fQRS and supraventricular arrhythmias, particularly atrial fibrillation (AF). In patients with CAD and HF, fQRS has been associated with a higher prevalence of AF, suggesting that conduction abnormalities reflected in ventricular depolarization may coexist with atrial conduction disturbances [35]. Furthermore, the burden of fQRS has been reported to predict the recurrence of AF following catheter ablation, possibly due to the presence of diffuse myocardial fibrosis and conduction heterogeneity (36).

fQRS in Risk Stratification for Ablation and Device Therapy

The ability of fQRS to identify arrhythmogenic substrates has implications for guiding therapeutic interventions such as catheter ablation and device therapy. In patients with scar-related VT, mapping studies have shown that regions displaying fQRS correspond closely to ablation targets, and their elimination may improve procedural outcomes [8]. Likewise, the presence of fQRS in patients with ICDs has been associated with higher rates of appropriate shocks, highlighting its potential role in predicting device therapy burden [24].

In summary, fQRS is strongly associated with both ventricular and supraventricular arrhythmias. By reflecting myocardial scar and conduction heterogeneity, it serves as a powerful non-invasive marker of arrhythmogenic substrate. The presence of fQRS is predictive of ventricular tachyarrhythmias, SCD, and atrial arrhythmias, and may help refine patient selection for ICD implantation, ablation, and closer rhythm monitoring (**Table 2**).

fQRS and HF

HF is a complex clinical syndrome characterized by impaired cardiac structure and function, often accompanied by myocardial remodeling, fibrosis, and electrical conduction abnormalities. These pathophysiological changes create the substrate for both mechanical dysfunction and arrhythmia. As a surface electrocardiographic marker of intramyocardial conduction delay and scarring, fQRS has emerged as a relevant parameter in the context of HF, providing diagnostic and prognostic insights that extend beyond conventional measures such as ejection fraction and QRS duration [14].

Prevalence of fQRS in HF

The prevalence of fQRS among HF patients is notably high, with studies reporting rates ranging from 30% to 50%, depending on etiology, disease severity, and the criteria used for fQRS definition [37]. Ischemic cardiomyopathy, in particular, demonstrates a higher prevalence due to the presence of post-infarction scarring, whereas non-ischemic DCM may exhibit fQRS as a result of diffuse interstitial fibrosis [23]. Importantly, fQRS can appear in both narrow and wide QRS complexes, which underscores its value across different HF phenotypes.

fQRS and Disease Severity

Several investigations have demonstrated that the presence of fQRS correlates with markers of disease severity in HF. Patients with fQRS tend to have lower LVEF, larger left ventricular dimensions, and more advanced NYHA functional class compared with those without fQRS [24]. Moreover, fQRS has been linked to higher circulating levels of biomarkers of myocardial stress and fibrosis, such as brain natriuretic peptide and galectin-3, suggesting a close association between ECG findings and molecular markers of disease progression [38].

Prognostic Implications of fQRS in HF

The prognostic role of fQRS in HF has been consistently documented. The presence of fQRS has been associated with higher rates of hospitalization for worsening HF, all-cause mortality, and SCD [20]. In ischemic cardiomyopathy, fQRS predicts adverse outcomes even after adjustment for traditional risk factors and echocardiographic parameters [39]. Similarly, in non-ischemic HF, fQRS has been reported as an independent predictor of mortality and arrhythmic events [25].

The number of leads exhibiting fQRS also appears to have prognostic relevance. Patients with fQRS in multiple contiguous leads demonstrate significantly worse outcomes than those with isolated fragmentation, reflecting the extent of underlying myocardial disease [5].

fQRS and CRT

CRT has become an established treatment for selected patients with HF and wide QRS complexes, particularly those with left bundle branch block morphology. However, approximately 30% of patients are non-responders to CRT. fQRS has been investigated as a predictor of CRT response, with mixed results. Some studies have suggested that the presence of fQRS is associated with a poor response to CRT, reflecting diffuse fibrosis and impaired conduction that hinder effective resynchronization [40]. Conversely, other reports have indicated that fQRS might help identify patients who would benefit most from CRT by marking extensive conduction abnormalities [41]. Further research and standardized criteria are necessary to clarify this relationship.

fQRS in HF with Preserved Ejection Fraction (HFpEF)

While most research has focused on HF with reduced ejection fraction, emerging data suggest that fQRS may also be relevant in HFpEF. In this population, fQRS has been associated with diastolic dysfunction, left atrial enlargement, and increased risk of AF [42]. Given the rising prevalence of HFpEF and the lack of robust prognostic markers in this group, fQRS may provide additional insights into disease characterization and risk stratification.

In summary, fQRS is a prevalent finding in patients with HF, irrespective of etiology. Its presence correlates with more advanced disease, reduced functional capacity, and adverse outcomes, including hospitalization, mortality, and SCD. The potential role of fQRS in guiding CRT selection and predicting response further emphasizes its clinical relevance. As a non-invasive, low-cost ECG marker, fQRS has significant potential to complement existing diagnostic and prognostic tools in HF management (**Table 2**).

fQRS IN OTHER CARDIAC CONDITIONS

Although fQRS has been most extensively studied in the contexts of ischemic heart disease, arrhythmias, and HF, its significance extends to several other cardiac conditions. Because fQRS reflects localized or diffuse myocardial conduction abnormalities, it has diagnostic and prognostic implications across a variety of structural and genetic heart diseases.

fQRS in Brugada Syndrome

Brugada syndrome is an inherited arrhythmia disorder characterized by ST-segment elevation in the right precordial leads and an increased risk of SCD. fQRS is frequently observed in patients with Brugada syndrome, particularly in leads V1-V3. Electrophysiological mapping has revealed that these fragmented signals correspond to regions of conduction delay in the right ventricular outflow tract [43]. Clinical studies have shown that fQRS is significantly associated with a history of syncope, ventricular arrhythmias, and appropriate ICD therapies in Brugada patients [44]. Thus, fQRS may serve as a non-invasive risk marker in this high-risk population, complementing other clinical and electrocardiographic features.

fQRS in Congenital Heart Disease

In patients with repaired congenital heart disease, such as tetralogy of fallot (TOF), conduction abnormalities are common due to surgical scars and chronic right ventricular remodeling. fQRS has been observed in a high proportion of TOF patients and correlates with right ventricular dilation, fibrosis, and reduced exercise capacity [45]. Importantly, the presence of fQRS in TOF survivors is associated with an increased risk of ventricular arrhythmias and SCD, making it a potential marker for identifying patients who may benefit from prophylactic ICD implantation [46].

fQRS in Myocarditis and Infiltrative Cardiomyopathies

Acute and chronic myocarditis often produce patchy myocardial scarring that disrupts normal conduction. Several studies have shown that fQRS is prevalent in myocarditis and may persist even after the resolution of acute inflammation, reflecting residual fibrosis [47]. In infiltrative cardiomyopathies such as cardiac sarcoidosis and amyloidosis, fQRS is a frequent finding and has been associated with arrhythmias, conduction block, and poor outcomes [48]. In sarcoidosis, fQRS correlates with areas of late gadolinium enhancement on CMR and predicts

Table 3. Prognostic implications of fQRS

Prognostic domain	Evidence
Ventricular arrhythmias	Strong predictor in ischemic and non-ischemic cardiomyopathies
Sudden cardiac death	Independent risk factor across multiple populations
Heart failure outcomes	Higher hospitalization and mortality rates
Cardiac resynchronization therapy	Associated with poor response in some cohorts
Implantable cardioverter-defibrillator	Useful for refining ICD candidacy beyond LVEF

ventricular arrhythmic events [49]. These observations suggest that fQRS could serve as a valuable, inexpensive screening tool in infiltrative cardiomyopathies where advanced imaging modalities may not always be available.

fQRS extends beyond ischemic and non-ischemic cardiomyopathies to provide clinically meaningful information in several other cardiac disorders, including Brugada syndrome, congenital heart disease, myocarditis, and infiltrative cardiomyopathies. In each of these conditions, fQRS correlates with structural abnormalities such as fibrosis or conduction delay and identifies patients at elevated risk for ventricular arrhythmias and SCD. Its role as a low-cost, non-invasive marker makes it an attractive complement to more advanced imaging and invasive diagnostic modalities (**Table 2**).

CLINICAL IMPLICATIONS AND FUTURE DIRECTIONS

The identification of fQRS on the surface electrocardiogram provides a simple, inexpensive, and widely available method to evaluate myocardial conduction abnormalities. Its presence across a wide spectrum of CVDs raises important considerations for clinical practice. Although its prognostic significance has been demonstrated in ischemic heart disease, HF, arrhythmia, and other conditions, translation into routine clinical decision-making remains an evolving area.

One of the most clinically relevant applications of fQRS is its utility in risk stratification for ventricular arrhythmias and SCD. Multiple studies have demonstrated that the presence of fQRS identifies patients at higher risk of major adverse cardiac events independent of traditional markers such as LVEF [3]. This is particularly valuable in patients with preserved or moderately reduced LVEF, where conventional risk stratification tools may fail to detect individuals at risk. Integrating fQRS into clinical practice may thus complement existing criteria for selecting candidates for ICD implantation or intensified surveillance.

fQRS correlates with myocardial scar and fibrosis as documented by advanced imaging modalities, especially CMR with late gadolinium enhancement [11]. Given the limited availability and high cost of CMR, fQRS can serve as an accessible screening tool to detect structural abnormalities in resource-limited settings. Furthermore, fQRS may guide clinicians in identifying patients who require more advanced diagnostic evaluation, including imaging or electrophysiological testing (**Table 3**).

Recent observational data suggest that fQRS may retain independent prognostic value even when combined with contemporary imaging biomarkers such as myocardial strain parameters and extracellular volume (ECV) quantification [28, 42]. Although strain imaging and T1/ECV mapping provide detailed characterization of diffuse myocardial fibrosis, fQRS continues to identify patients with higher arrhythmic and adverse event risk after adjustment for these markers [32]. This indicates that electrical fragmentation reflects complementary electrophysiological information beyond structural abnormalities detected on CMR.

Beyond ICD implantation, fQRS may provide insights into the response to CRT. Several studies have suggested that patients with fQRS demonstrate worse outcomes and less favorable responses to CRT compared to those without fQRS [20]. Identifying such patients before device implantation could optimize patient selection and improve cost-effectiveness of therapy.

The prognostic implications of fQRS could be enhanced by integrating traditional electrocardiographic analysis with novel digital health technologies. Artificial intelligence (AI) and machine learning algorithms have been increasingly applied to ECG interpretation, and the inclusion of subtle QRS fragmentation patterns may enhance predictive accuracy for adverse cardiac outcomes [50]. These technologies may allow automated, high-throughput recognition of fQRS in large populations, improving screening efficiency and consistency across clinical centers (**Table 4**).

Despite the promising data, several limitations must be considered before widespread adoption of fQRS in clinical algorithms. First, the definition and diagnostic criteria for fQRS vary across studies, leading to inconsistency in prevalence and prognostic associations [14]. Standardization of fQRS criteria is essential for reproducibility and integration into guidelines. Second, fQRS is not specific to a single pathology and may be observed in a wide range of cardiac conditions, limiting its diagnostic specificity. Lastly, interobserver variability in ECG interpretation remains a challenge, although automated detection algorithms may reduce this concern in the future.

Table 4. Clinical applications and future directions of fQRS

Application	Clinical Utility
Risk stratification	Provides incremental prognostic value beyond LVEF
Diagnostic marker	Surrogate for myocardial scar/fibrosis when imaging is unavailable
Therapeutic guidance	Helps in selecting ICD/CRT candidates
Research and innovation	Standardization of criteria, integration with multimodal risk scores
Artificial intelligence	Automated ECG detection and improved predictive accuracy

Several areas warrant further investigation to fully establish the role of fQRS in clinical cardiology. Large, prospective, multicenter studies are needed to confirm their incremental prognostic value across diverse populations and disease states [20]. Research should also focus on clarifying whether therapeutic decisions guided by fQRS, such as earlier ICD implantation or closer follow-up, lead to improved outcomes. Moreover, combining fQRS with biomarkers, imaging, and genetic testing may create a more comprehensive and individualized risk assessment strategy.

fQRS represents a promising, accessible, and non-invasive marker with broad clinical implications across cardiovascular medicine. While it has demonstrated diagnostic and prognostic value in multiple conditions, its integration into clinical practice will require standardization, validation in large cohorts, and demonstration of utility in guiding therapeutic decisions. Future research integrating ECG-based markers such as fQRS with advanced technologies and multimodality risk assessment may significantly improve the management of patients at risk of adverse cardiac outcomes.

CONCLUSION

fQRS has emerged as a valuable electrocardiographic marker that reflects underlying myocardial conduction abnormalities due to fibrosis, scarring, or structural remodeling. Since its initial description, fQRS has been shown to hold diagnostic and prognostic significance across a wide spectrum of cardiovascular conditions, ranging from CAD and HF to arrhythmias, congenital heart disease, myocarditis, and infiltrative cardiomyopathies. Its presence consistently correlates with adverse outcomes, including ventricular arrhythmias, SCD, and progression of HF.

The major strength of fQRS lies in its accessibility. Electrocardiography is universally available, inexpensive, and non-invasive, making fQRS an attractive marker in both high-resource and resource-limited settings. Moreover, fQRS often provides incremental prognostic information beyond traditional parameters such as left ventricular ejection fraction, allowing clinicians to identify high-risk patients who may otherwise be overlooked by conventional tools. This feature is particularly relevant for guiding device therapies, including ICD and CRT.

Nonetheless, several challenges remain before fQRS can be fully integrated into routine clinical practice. The lack of standardized diagnostic criteria, variability in definitions across studies, and interobserver differences in ECG interpretation limit the reproducibility of findings. Furthermore, while fQRS is a sensitive marker of myocardial abnormality, it is not specific to a single pathology, necessitating complementary diagnostic evaluations.

Future research should focus on large-scale, multicenter studies to validate the prognostic utility of fQRS across diverse populations and disease states. The incorporation of fQRS into multimodal risk assessment strategies, combining biomarkers, advanced imaging, and genetic testing, may offer a more comprehensive approach to individualized patient care. In addition, the integration of AI and automated ECG analysis holds promise for enhancing the accuracy, consistency, and clinical applicability of fQRS assessment.

In summary, fQRS is a promising non-invasive marker with broad implications for diagnosis, prognosis, and risk stratification in cardiovascular medicine. While further work is needed to standardize definitions and validate its role in guiding therapeutic decisions, current evidence supports its potential as a cost-effective and widely applicable tool in the management of patients with CVD.

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