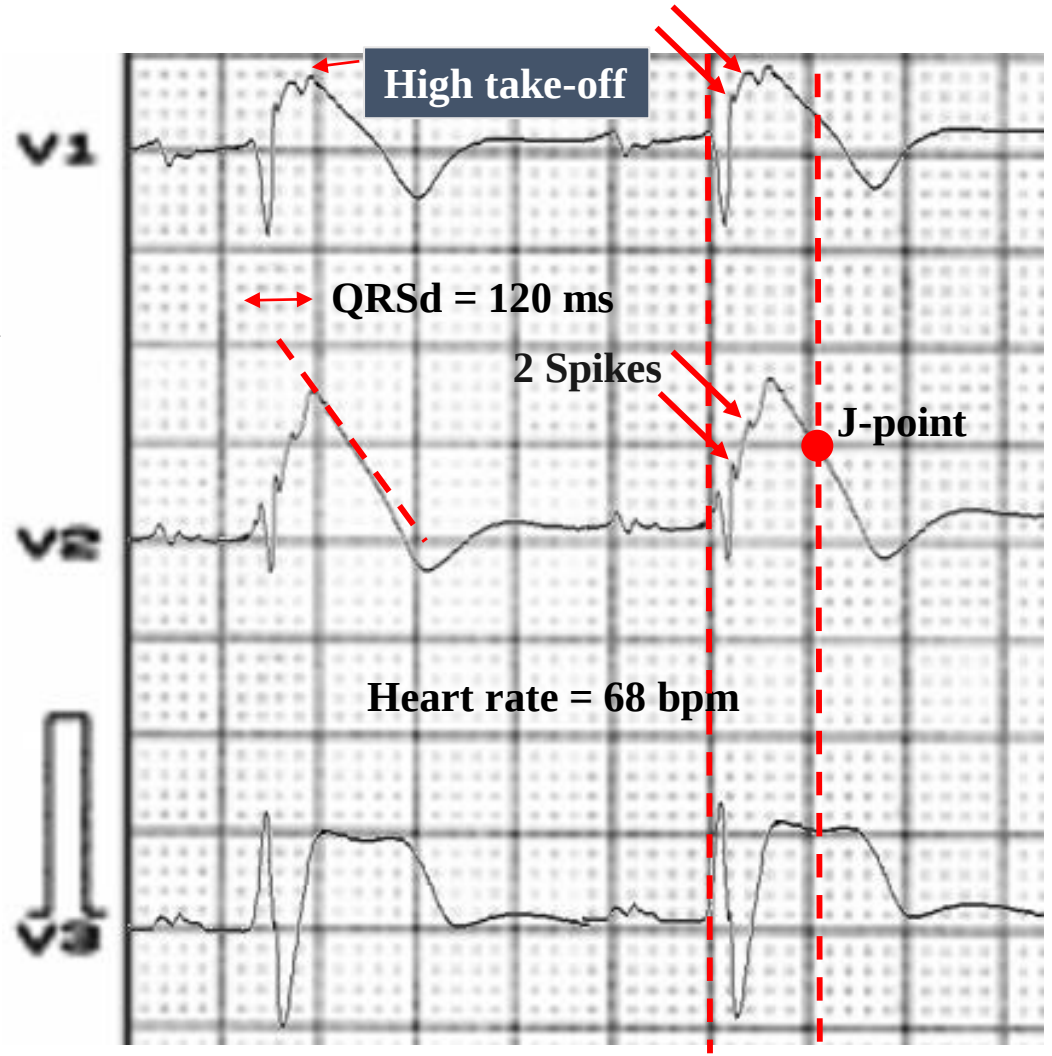
Fragmented QRS

The QRS complex represents the electrical depolarization of ventricular myocardium. In the case of an undisturbed depolarization, the QRS complex has a normal configuration and duration, but abnormal electrical conduction leads to widening of the QRS complex. The block of one of the bundle branches results in a typical bundle branch block pattern. A QRS complex that cannot be classified as bundle branch block due to an atypical configuration is called nonspecipic intraventricular conduction delay or pre-excitation type Wolff-Parkinson-White. If the QRS complex has normal duration and contains notched R or S waveS, various RsR' patterns in at least 2 contiguous ECG leads is called a fragmented QRS(fQRS). If QRS duration is prolonged, the proper nomenclature is wide fragmented QRS (w-fQRS).

The underlying pathophysiologies are manifold and include myocardial scars induced by ischemic art disease, myocardial fibrosis due to other diseases, primary cardiac pathologies as well as systemic diseases with cardiac involvement. Pathologies on the cellular level, such as ion channel dysfunctions, also correlate with fragmented QRS. Besides the diagnostic relevance, fragmented QRS is known to have prognostic properties, for example in identifying high risk patients with coronary artery disease, cardiomyopathy, Brugada syndrome and acquired long QT syndrome; however, fQRS may also be detected in ECGs of healthy individuals. (**Steger 2015**). fQRS is a novel ECG marker with more sensitivity and less specificity than Q wave. A combination of fQRS with Q wave in a 12-lead ECG results in up to 74% sensitivity and 92% specificity. (**Sadeghi 2016**) fQRS frequency y and QRS duration were found to increase in obstructive sleep apnea syndrome (OSAS) patients. Both parameters are related with increased cardiovascular mortality. Considering the prognostic importance of ECG parameters, it may be reasonable to recommend more detailed evaluation of OSAS patients with fragmented or prolonged QRS complexes with respect to presence of cardiovascular diseases.(**Sayin 2015**). Risk stratification of sudden cardiac death (SCD) is challenging. fQRS is proposed as a non-invasive ECG marker associated with mortality and SCD. Results from individual studies including small numbers of patients are discrepant. Rosengarten et al (**Rosengarten 2015**) performed a meta-analysis of studies evaluating fQRS as a risk stratification tool to predict all-cause mortality and SCD. Electronic databases and bibliographies were systematically searched (1996-2014). Twelve studies (5009 patients) recruiting patients with coronary artery disease or non-ischemic cardiomyopathy were included. fQRS was associated with an all-cause mortality relative risk of 1.71 (CI 1.02-2.85) and a relative risk of SCD of 2.20 (CI 1.05-4.62). Subgroup analysis demonstrated greater mortality and SCD risk in those with LVEF >35% and SCD risk in those with QRS duration <120 ms. Fragmented QRS is associated with all-cause mortality and the occurrence of SCD and may be suited as a marker of SCD risk. The incremental benefit of fQRS should be assessed in a randomized, prospective setting. fQRS on initial presentation with acute coronary syndrome(ACS) is not predictive of subsequent events but, if present 6 months later, could be predictive of an adverse outcome.(**Akbarzadeh 2013**)Regression of fQRS could be a maker of electrical reverse remodeling following CRT.(**Yang 2015**). fQRS complex, as a sign of myocardial scar, predicts non-responsiveness to CRT. fQRS may help selecting of CRT candidates.(**Assadian Rad 2015**)

Fragmented QRS in Brugada Syndrome

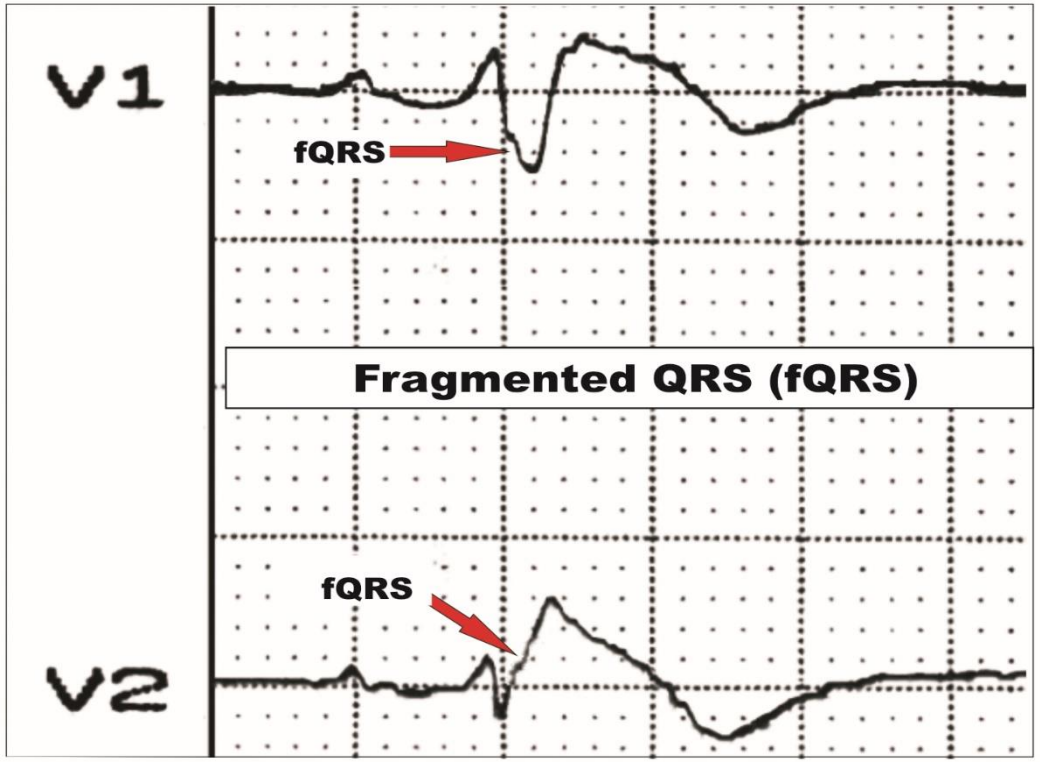
VT/VF inducibility is unable to identify high-risk patients, whereas the presence of a spontaneous type I ECG, history of syncope, ventricular effective refractory period <200 ms, and QRS fragmentation seem useful to identify candidates for prophylactic implantable cardioverter defibrillator.



Dotted lines show onset and termination of the QRS complex

Two spikes are observed at the upstroke of the S wave in leads V_1 and V_2. f-QRS appears to be a marker for the substrate for spontaneous VF in BS and predicts patients at high risk of syncope.

Fragmented wide QRS complex in a 35-year-old Asian male patient with BrS. f-QRS appears to be a marker for the substrate for spontaneous VF in BrS and predicts patients at high risk of syncope. It is a conduction abnormality within the QRS complex (**Morita 2008**).



Presence of a "notch" within a non-wide QRS complex in two adjacent leads (V_1-V_2.): f-QRS. It is a non-invasive marker of events (Das 2009).

Entities where fQRS is used as a non-invasive marker of events (Das 2009)

- **Coronary artery disease (Das 2007; 2009; 2010)** where it represents a conduction delay of the stimulus and is associated to an increase in mortality and arrhythmic events in these patients.
- **Non-ischemic cardiomyopathies (Das 2010).** In non-ischemic dilated cardiomyopathy with narrow QRS to predict dyssynchrony **(Tigen 2009)**
- **Idiopathic dilated cardiomyopathy.(Sha 2011)**
- **Arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) (Peters 2008)**
- **Hypertrophic cardiomyopathy.** fQRS is associated with HF with hospitalization in HCM patients who had a unique distribution of gene mutations. TNNI3 (**Femenia 2012; Nomura 2015**)
- **Cardiac sarcoidosis (Homsi 2009)**
- **Congenital heart diseases (Moss 2010)**

- **Severe aortic valve stenosis. (Ağaç 2014; Canpolat 2015).**
- **Chagas disease (Baranchuk 2012; 2014 a;b)**
- **Coronary artery ectasia (CAE) (Sem 2014)**
- **Brugada syndrome (Haraoka 2010)**
- **Acquired and congenital long QT syndrome (Yuce 2010;Haraoka2010)** fQRS plays an important role in the appearance of TdP in patients with acquired long QT interval.
- **Myocardial scar** (**Das 2008**)
- **Behçet's disease:** QRS duration is greater and fQRS complexes are more frequent in patients with Behçet's disease. These findings may indicate subclinical cardiac involvement in BD. Given the prognostic significance of ECG parameters, it is reasonable to evaluate patients with BD with prolonged and fQRS complexes more in detail such as late potentials in signal averaged ECG in terms of cardiac involvement.(**Sayin 2013**)
- **Systemic lupus erythematosus(SLE):** A careful cardiovascular evaluation and follow-up is essential to continuously improve survival in SLE. For this purpose, fQRS may be used for the early detection in patients with SLE.(**Demir 2014**)
- **Hypertension:** fQRS is a common electrocardiographic phenomenon in patients with hypertension. Although the diagnostic value for LVH is limited, the presence of fQRS on ECG is associated with a higher risk for worse LVH.(**Zhang 2015**)
- **Radiotherapy:** Radiotherapy for breast cancer induces development of fQRS on ECG. Cardiac radiation dose is independently associated with the development of fQRS.(**Adar 2015**)
- **Nephrotic syndrome(NS): (Tin 2015)** This parameter can be used in the prediction of myocardial functions in this entity.(**Özkan 2014**). An important factor to be concerned in the patient with NS is the medication. In the case of long-term use of steroid, the effect on the QRS can be expected (**Ito 1976**), and this might decrease the utility of fQRS detection.
- **Iron overload in patients with beta-thalassemia major(TM):** Since cardiac involvement is the primary cause of mortality in TM patients, the early diagnosis of cardiac dysfunction is of vital importance. The search for fQRS in the ECGs of these patients, particularly when cardiac T2* values, measured by cardiac MR cannot be determined and followed,is a non-expensive and easy-to-attain method for therapy management.(**Bayar 20115**)
- **Familial Mediterranean fever(FMF):** FMF patients displayed a statistically significant increase in frequency of fQRS. Doppler-derived diastolic index was statistically significantly impaired in FMF patients with fQRS as compared with the patients without fQRS. fQRS might be a new noninvasive marker for cardiac involvement in FMF patients.(**Celik 2015**) **.**

References

1. Adar A, Canyılmaz E, Kiris A, et al.Radiotherapy Induces Development of Fragmented QRS in Patients with Breast Cancer.Breast Care (Basel). 2015;10(4):277-80.
2. Ağaç MT, Korkmaz L, Bektas H, Acar Z, Erkan H, Kurt IH, Adar A, Celik S.Increased frequency of fragmented QRS in patients with severe aortic valve stenosis.Med Princ Pract. 2014;23(1):66-9.
3. Akbarzadeh F, Pourafkari L, Ghaffari S,et al.Predictive value of the fragmented QRS complex in 6-month mortality and morbidity following acute coronary syndrome.Int J Gen Med. 2013;6:399-404.
4. Assadian Rad M, Tabarzan Baboli N, Barzigar A, et al.The role of the fragmented QRS complexes on a routine 12-lead ECG in predicting non-responsiveness to cardiac resynchronization therapy.Anatol J Cardiol. 2015; 15 (3): 204-8.
5. Baranchuk A, Miranda R, Femenia F FECHA Investigators. Chagas' cardiomyopathy and Fragmented QRS. Re: QRS fragmentation as a marker of arrhythmias in coronary artery disease, in cardiomyopathies and ion channel diseases. Int J Cardiol. 2012;160:151–152.
6. Baranchuk A.Fragmented QRS and Chagas' disease.Indian Pacing Electrophysiol J. 2014;14(6):309-10. (a)
7. Baranchuk A, et al. Fragmented Surface ECG was a Poor Predictor of Appropriate Therapies in Patients with Chagas' Cardiomyopathy and ICD Implantation (Fragmented ECG in CHAgas' cardiomyopathy Study) Ann Noninv Electrocardiol. 2014;19:43. (b)
8. Bayar N, Kurtoğlu E, Arslan Ş, Erkal Z, Çay S, Çağırcı G, Deveci B, Küçükseymen Assessment of the relationship between fragmented QRS and cardiac iron overload in patients with beta-thalassemia major.S.Anatol J Cardiol. 2015;15(2):132-6.
9. Canpolat U, Akboga K, Özeke Ö, et al.Fragmented QRS complex as an emerging risk indicator in severe aortic stenosis.Med Princ Pract. 2015;24(2):200.
10. Celik MM, Buyukkaya E, Ustun N, et al.Relation of fragmented QRS to tissue Doppler-derived parametersin patients with familial Mediterranean fever.Wien Klin Wochenschr. 2015 ;127(5-6):185-90.
11. 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.Heart Rhythm. 2007; **4**: 1385–1392.
12. Das MK, Suradi H, Maskoun W, et al. Fragmented wide QRS on a 12-lead ECG: a sign of myocardial scar and poor prognosis. Circ Arrhythm Electrophysiol. 2008;1:258–268.
13. Das MK, Zipes DP. Fragmented QRS: a predictor of mortality and sudden cardiac death. Heart Rhythm. 2009;6(3 Suppl):S8–S14

14. Das MK, et al. Fragmented qrs on twelve-lead electrocardiogram predicts arrhythmic events in patients with ischemic and nonischemic cardiomyopathy. Heart Rhythm. 2010;7:74.
15. Demır K, Avcı A, Yılmaz S, et al.Fragmented QRS in patients with systemic lupus erythematosus.Scand Cardiovasc J. 2014;48(4):197-201.
16. Femenia F, Arce M, Arrieta M, Baranchuk A. Surface fragmented QRS in a patient with hypertrophic cardiomyopathy and malignant arrhythmias: is there an association? J Cardiovasc Dis Res. 2012;3:32–35.
17. Haraoka K, Morita H, Saito Y, et al. Fragmented QRS is associated with torsades de pointes in patients with acquired long QT syndrome. Heart Rhythm. 2010;7:1808–14.
18. Ito T, Su KM, Murata M, Koizumi T, Matsumoto S, Ito Y, et al. Experimental studies on the effect of glucocorticoids on cardiac muscle. Recent Adv Stud Cardiac Struct Metab. 1976;12:203–10.
19. Morita H1, Kusano KF, Miura D, Nagase S, Nakamura K, Morita ST, Ohe T, Zipes DP, Wu J.Fragmented QRS as a marker of conduction abnormality and a predictor of prognosis of Brugada syndrome. Circulation. 2008 Oct 21;118(17):1697-704.
20. Nomura A, Konno T, Fujita T, et al.Fragmented QRS predicts heart failure progression in patients with hypertrophic cardiomyopathy.Circ J. 2015;79(1):136-43.
21. Özkan G, Adar A, Ulusoy S, et al. Presence of fragmented QRS and its correlation with myocardial performance index in patients with nephrotic syndrome. Anatolian J Cardiol. 2014;14:450–5
22. Priori SG, Gasparini M, Napolitano C, et al Risk stratification in Brugada syndrome: results of the PRELUDE (PRogrammed ELectrical stimUlation preDictive valuE) registry. J Am Coll Cardiol. 2012 Jan 3;59(1):37-45.
23. Rosengarten JA, Scott PA, Morgan JM.Fragmented QRS for the prediction of sudden cardiac death: a meta-analysis.Europace. 2015;17(6):969-77
24. Sadeghi R, Dabbagh VR, Tayyebi M, et al.Diagnostic value of fragmented QRS complex in myocardial scar detection: systematic review and meta-analysis of the literature.Kardiol Pol. 2016;74(4):331-7.
25. Sayin MR, Akpinar I, Gursoy YC, et al.Assessment of QRS duration and presence of fragmented QRS in patients with Behçet's disease. Coron Artery Dis. 2013;24(5):398-403.
26. Sayin MR, Altuntas M, Aktop Z, et al.Presence of Fragmented QRS Complexes in Patients with Obstructive Sleep Apnea Syndrome.Chin Med J (Engl). 2015;128(16):2141-6.

27. Sen F, Yılmaz S, Kuyumcu MS, et al .The Presence of Fragmented QRS on 12-Lead Electrocardiography in Patients with Coronary Artery Ectasia.Korean Circ J. 2014;44(5):307-11.
28. Sha J, Zhang S, Tang M, Chen K, Zhao X, Wang F. Fragmented QRS is associated with all-cause mortality and ventricular arrhythmias in patient with idiopathic dilated cardiomyopathy. Ann Noninvasive Electrocardiol. 2011;16:270–275.
29. Steger A, Sinnecker D, Berkefeld A, Müller A, Gebhardt J, Dommasch M, Huster KM, Barthel P, Schmidt G.Fragmented QRS. Relevance in clinical practiceHerzschrittmacherther Elektrophysiol. 2015;26(3):235-41.
30. Tin SS, Wiwanitkit V.Fragmented QRS and myocardial performance index in nephrotic syndrome.Anatol J Cardiol. 2015;15(2):161.
31. Yang XW, Hua W, Wang J, et al.Regression of fragmented QRS complex: a marker of electrical reverse remodeling in cardiac resynchronization therapy.Ann Noninvasive Electrocardiol. 2015;20(1):18-27.
32. Zhang B, Zhen Y, Shen D, Zhang G.Significance of fragmented QRS complexes for identifying left ventricular hypertrophy in patients withhypertension.Ann Noninvasive Electrocardiol. 2015;20(2):175-80.