Fragmented QRS

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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.

High take-off

QRSd = 120 ms

2 Spikes

Two spikes are observed at the upstroke of the S wave in leads V1 and V2. f-QRS appears to be a marker for the substrate for spontaneous VF in BS and predicts patients at high risk of syncope.

Heart rate = 68 bpm

Dotted lines show onset and termination of the QRS complex

ragmented 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 n BrS and predicts patients at high risk of syncope. It is a conduction abnormality within the QRS complex (**Morita 2008**).

J-point

F i

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)**

Presence of a "notch" within a non-wide QRS complex in two adjacent leads (V1-V2.): f-QRS. It is a non-invasive marker of events (Das 2009).

- ➢ **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**) **.**

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