ACTA CARDIOLOGICA
2019, VOL. 74, NO. 3, 185–187
https://doi.org/10.1080/00015385.2019.1600827

EDITORIAL

# Fragmentation of the QRS complex: the latest electrocardiographic craze?

## Background, definition of terms, pathophysiology

The wording « fragmentation of the QRS complex » or « fragmented QRS » (fQRS) indicates the presence of high frequency potentials (spikes) inside the QRS complex. The term was first coined in 1973 in the report of an experimental study of canine hearts where coronary occlusion provoked the appearance of fragmented electrograms which were a source of reentrant activity [1]. Previously, it had already been suggested that a high frequency « notching » of the QRS complex could be a marker for cardiac structural diseases causing biventricular enlargement [2]. The appearance of fQRS can be provoked by any condition interfering with the normally homogeneous depolarisation process within the myocardium and leading to local conduction slowing, e.g. ischemia, scar, fibrosis, myofiber disarray, inflammation, and microvascular abnormality.

The popularity of this term « fragmentation » was greatly enhanced by the early publication of Das et al. who showed in patients with coronary artery disease (CAD) a good correlation between fQRS and the presence of myocardial scar detected by single photon emission tomography [3]. Their definition of fQRS was as follows: QRS duration $<$120 ms, an additional R wave (R′) or notching in the nadir of S wave, or $>$1 R′ (fragmentation) in 2 contiguous leads corresponding to a major coronary territory (Figure 1). Later on, the definition was extended to cases where QRS duration was $\geq$120 ms [4] and the grouping of leads was also considered, i.e. anterior (V1–V5), lateral (I, aVL, V6), and inferior (II, III, and aVF).

Following the publication of Das, an avalanche of papers generally enthusiastic, with few discordant voices, showed up in the literature [5]. Someone even dubbed fQRS « the hidden talisman »! [6]. The usefulness of fQRS was primarily investigated in CAD patients, but also in a host of various cardiac abnormalities [7].

## Diagnostic and predictive value of fQRS

In *CAD patients*, as compared with the presence of a Q wave, fQRS had higher sensitivity (85.6%) and negative predictive value (92.7%) for detecting myocardial scar [3]. Subsequent publications reported the same kind of positive findings in patients with a wide QRS complex [4]. One single study failed to show significance of fQRS for detecting myocardial scar [8]. Numerous studies have shown the relationship between fQRS and prognosis in CAD patients [5]. A multivariate analysis revealed that fQRS was an independent predictor for cardiac events (HR = 1.62) [9]. Several studies have identified fQRS as an independent predictor of ventricular arrhythmias and sudden cardiac death [10]. Recently, in a series of 452 patients with anterior STEMI undergoing primary PCI, fQRS was associated with target vessel failure but did not correlate with infarct size [11]. In the same kind of population (PCI in acute coronary syndrome), a systematic review and meta-analysis showed that fQRS was associated with higher (up to 2.6 fold) overall mortality [12]. Another recent meta-analysis confirmed that in STEMI patients, fQRS was associated with reperfusion failure and in-hospital mortality [13].

In patients with various types of *cardiomyopathies*, with a few exceptions [14], fQRS had also good diagnostic and prognostic value. Its usefulness was demonstrated in various structural heart diseases, e.g. dilated cardiomyopathy, both ischaemic and non-ischaemic; hypertrophic cardiomyopathy [15]; cardiac sarcoidosis; arrhythmogenic right ventricular dysplasia [5,10]. Even subclinical left ventricular dysfunction assessed by echocardiography has been shown to be associated with fQRS in type-2 diabetic patients [16].

Clinical value of fQRS was also investigated in patients with *primary electrical diseases* such as Brugada syndrome and acquired long QT syndrome, as well as in *miscellaneous conditions* (congenital heart disease, mitral stenosis caused by rheumatic fever, rheumatoid arthritis, etc.) [5,7].

## Methodological and technical problems, future directions

Many authors have advocated the use of fQRS as a simple, easy-to-do measurement, taken from the old good 12-lead ECG, which could be a marker of myocardial scar and which could predict cardiac events and mortality in various cardiac diseases. However, we can ask the question: is not it too simple to be really useful?

One problem is the influence of recording and filtering techniques on the electrocardiographic aspects of fQRS. For instance, a low-pass filter of 35 Hz instead of 150 Hz will mask several small spikes within the QRS [5]. Some authors remind us that visual inspection of the ECG is often the cause of poor reproducibility and that fQRS definition is hampered by intra and inter-observer variability. The counting of the leads with fQRS is also a

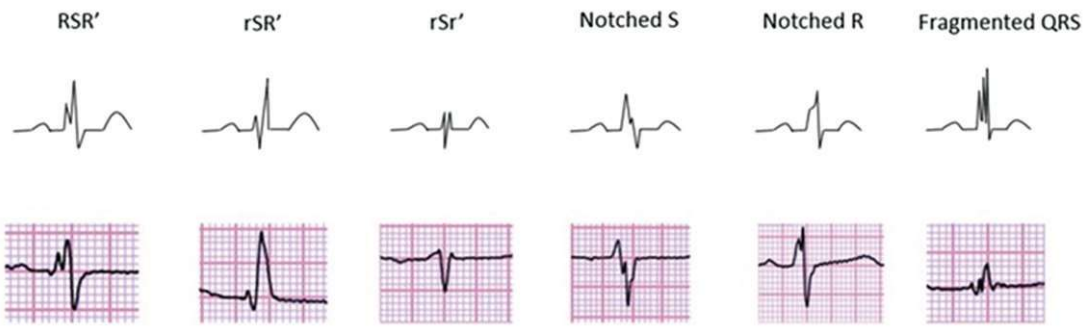


**Figure 1.** Different morphologies of fQRS on 12-lead ECG as described by Das et al. [3]. Reprinted from the article « QRS fragmentation patterns representing myocardial scar need to be separated from benign normal variants: hypotheses and proposal for morphology based classification » » by Haukilahti A. et al. [10], with permission.

**Figure 2.** An example of the measurement of amplitude changes and location of the fragmentation in QRS complex. The amplitude will be measured between three points: one is tagged to fQRS notch, the second is tagged to fQRS peak, and the third is tagged to the peak of the wave where fQRS occurs. Reprinted from the article « QRS fragmentation patterns representing myocardial scar need to be separated from benign normal variants: hypotheses and proposal for morphology based classification » by Haukilahti A. et al. [10], with permission.

problem because of the redundance and interdependence of the limb leads [17].

Future directions have been suggested by several authors.

A new and more precise classification of the various patterns of fQRS aiming at the differentiation between myocardial scar and benign normal variants is currently under investigation [10] (Figure 2).

Some have advocated the use of a more quantitative approach of fQRS, for instance the derivative of dV/dT [5]. One could also figure out to perform a high precision analysis, sort of signal-averaged processing as for the search of late potentials, but inside the whole QRS complex [17]. Magnetocardiography has also been suggested, but it is not in routine use to-day. However, vectorcardiography can be utilised: a study with the quantitative assessment of vector loop morphology (roundness, planarity, thickness, rotational, and dihedral angles) showed that fQRS detected from the 12-lead ECG had low sensitivity (31%) for detecting QRS loop folding on the VCG [18].

Finally, attempts are being made to design special algorithms for the automatic detection of fQRS [19] and even a machine learning approach for the detection and quantification of QRS fragmentation has been proposed [20].

In conclusion, the real value of fQRS as a diagnostic and prognostic tool cannot be assessed by using a subjective visual judgment based on the standard 12-lead ECG. A more quantitative, observer independent approach, and a better characterisation of this phenomenon of fragmented depolarisation are clearly needed.

## Disclosure statement

No potential conflict of interest was reported by the authors.

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Received 14 March 2019; revised 19 March 2019; accepted 22 March 2019