



EDITORIAL COMMENT

Stratification of patients for coronary angiography: Fragmented QRS complexes – a marker of severity?☆



Estratificação de doentes para angiografia coronária: QRS fragmentado – um marcador de gravidade?

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The possibility that particular alterations on a standard electrocardiogram (ECG) can reveal the existence of areas of myocardial fibrosis could be of clinical interest, not only for non-invasive detection of obstructive coronary disease, but also as an easily accessible risk marker that can be assessed without the need for more complex and costly exams.

The presence of pathological Q waves on the ECG has long been used in clinical practice to identify scarring from previous transmural myocardial infarction (MI). However, this sign has low sensitivity, since it may not initially appear (non-Q-wave MI) or may sooner or later disappear, and so the absence of Q waves does not exclude the possibility of fibrous scarring of the myocardium.

There have therefore been efforts for many years to discover alterations in the morphology of the QRS complex that can reliably identify the presence of myocardial scarring. Examples include the investigation by Flowers et al.¹ in the 1960s of high-frequency components of the QRS, which the authors discovered to be more common in patients with previous MI, a finding subsequently confirmed by Das et al.² in single-photon emission computed tomography

studies of myocardial perfusion demonstrating that fragmented QRS complexes (fQRS) on the 12-lead ECG were a marker of previous MI, with significantly superior sensitivity and comparable negative predictive value to Q waves.

Various clinical trials confirmed the potential value of fQRS, defined by Das et al. as the presence of an additional R wave (R') or notching in the nadir of the S wave, or the presence of more than one R' in contiguous leads, corresponding to a major coronary artery territory. A search then began to establish these signs as risk markers in coronary patients, in order to confirm the relationship between fQRS and cardiac events. The relationship was investigated in acute coronary syndromes (ST- and non-ST-elevation MI and unstable angina),³ after primary percutaneous coronary intervention,⁴ and following MI as a predictor of sudden death or heart failure.⁵

The risk of arrhythmic events in patients with fQRS has also been investigated in various other conditions,⁶ including ischemic and non-ischemic cardiomyopathy, Brugada syndrome, acquired long QT syndrome and arrhythmogenic right ventricular dysplasia, as well as for screening of cardiac involvement in diseases such as rheumatoid arthritis, fibromyalgia and sarcoidosis.

Taken together, these studies suggest that fQRS may be associated with myocardial fibrosis and hence with prognosis, thus functioning as a possible risk marker in different populations. However, these associations have not been definitively proven and published studies show that the sensitivity of this sign varies considerably. For example, in

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studies on stable coronary disease or MI, fQRS seem to be reasonably good predictors of cardiac events, but not of mortality, while in non-ischemic cardiomyopathy they appear to be related to the degree of fibrosis and dyssynchrony, and in patients with left ventricular dysfunction no association has been shown between fQRS and arrhythmic events.

The study by Eyuboglu et al. in this issue of the *Journal*⁷ appears to be of some clinical interest. It assumes that the presence of fQRS is a risk marker in patients with ischemic heart disease and seeks to identify subpopulations with more severe disease among those undergoing a first diagnostic coronary angiography by analyzing the relationship between disease severity and the ECG leads (anterior or inferior) in which these complexes are observed. Disease severity in the two groups is assessed by means of an internationally used angiographic measure of the complexity of coronary artery disease, the SYNTAX score.

In accordance with the study hypothesis, differences were found: it was concluded that coronary disease was more severe when fQRS were detected in the anterior rather than the inferior leads.

Although the scope of the study was limited, we consider that it is of some interest, particularly in its potential to contribute to improved stratification of patients about to undergo coronary angiography.

Besides the limitations pointed out by the authors, such as the relatively small study population and the lack of data about coronary hemodynamics and microvascular dysfunction, it should also be noted that the relationship between fQRS and coronary disease severity is taken as proved, which is not in line with the available evidence. This assumption is mainly based on retrospective studies, but it conflicts with the results of at least two trials cited in the review by Pietrasik and Zaręba,⁶ which found no association between this sign and mortality or arrhythmic events, and the authors concluded that fQRS were not useful for risk stratification in ischemic heart disease. The present study could have helped clarify the situation if it had included a third arm of patients from the same cohort who did not present fQRS, to be compared with the other two groups.

In the systematic review of fQRS mentioned above,⁶ the authors point out some of the controversial aspects concerning the value of this finding, including the fact that its sensitivity and predictive ability vary with different study populations, persistent doubts as to whether it really can identify myocardial scarring in coronary patients, its inability to predict mortality or arrhythmic events in these patients, and the fact that it has not been shown to predict response to ventricular resynchronization. However, Pietrasik and Zaręba believe that the main factor limiting the use of fQRS is the subjective nature of how they are defined and that there is a need for a more objective assessment of inhomogeneity in ventricular activation.

One point that could have been dealt with more thoroughly in the study by Eyuboglu et al. is the relationship between the localization of fQRS and the coronary territories affected. As the authors had access to details of each patient's coronary lesions, they could have sought to relate them to the leads in which the fragmented pattern were detected, which would help to identify the coronary territories with more significant lesions before coronary angiography. Das et al.² deduced from the leads in which fQRS were observed which segments of the myocardium (anterior, lateral, or inferior) were scarred and which vascular territories were affected (anterior descending, circumflex, or right coronary). In the present study, group 2 had fQRS in the anterior leads, associated with the territories of the anterior descending and circumflex arteries, which may explain the greater severity of coronary disease in this group.

Finally, it should be pointed out that the endpoints in this study are only surrogates for more clinically important outcomes such as mortality or hospitalization. We hope that the authors' investigation will continue and that some light can be shed on these questions, which will help to increase our understanding of the ability of fQRS to predict cardiovascular events, and thus to improve risk stratification in coronary patients.

Conflicts of interest

The author has no conflicts of interest to declare.

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