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Editorial Comment
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Usefulness of Fragmented QRS Complex for Diagnosis and Outcome Prediction in Patients with Coronary Artery Disease

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Resting electrocardiogram (ECG) is a useful tool for detecting coronary artery disease (CAD) and predicting outcomes in patients with CAD.[1,2] Common ECG abnormalities in patients with CAD include ST-segment deviation (ischemic-appearing ST depression or elevation), T-wave inversion (≥ 1 mm), ventricular arrhythmia, and pathologic Q wave (≥ 40 ms or ≥ 25% of R-wave amplitude).[2-5] The pathologic Q wave is a marker of a prior myocardial infarction (MI).[5] However, it has a low sensitivity for an old MI, and there is no specific marker for a prior non-Q-wave MI.[6] The presence of a fragmented QRS complex (fQRS) on a 12-lead ECG is a marker of ventricular conduction abnormality due to myocardial scar, which may serve as a better ECG sign of an old MI than the Q wave.[6,7] In a cohort of 479 patients who were referred for nuclear stress tests, myocardial scar, Q waves, an fQRS, and an fQRS and/or a Q wave were present in 39%, 15%, 35%, and 42% of patients, respectively.[6] In that study, fQRS was defined 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 two contiguous leads, corresponding to a major coronary artery territory.[6] Sensitivity, specificity, and the negative predictive value for myocardial scar, defined by fixed perfusion defects, were 36.3%, 99.2%, and 70.8%, respectively, for the Q wave alone; 85.6%, 89%, and 92.7%, respectively, for the fQRS alone; and 91.4%, 89%, and 94.2%, respectively, for the fQRS and/or Q wave.[6] Compared to the Q wave, fQRS has a significantly higher sensitivity and negative predict value for detection of myocardial scar.

fQRS is not only useful for identifying myocardial scar in patients with CAD or suspected CAD but also valuable for distinguishing MI from non-MI and predicting mortality or major adverse cardiac events in patients with acute coronary syndrome (ACS).[6,8,9] In a study of 896 patients with ACS (441 MI and 455 unstable angina) who underwent cardiac catheterization, serial ECGs were obtained every six to eight hours during the first 24 hours and the next day (< 48 hours), fQRS was present in a significantly larger number of patients in the MI [or non-ST-segment elevation MI (NSTEMI)] group compared to the unstable angina group (51% vs. 3.7% and 50% vs. 3.7%, both $p < 0.001$).[8] Seventy-four percent of patients developed fQRS within 24 hours of presentation.[8] Kaplan-Meier survival analysis showed a higher mortality risk in the fQRS group than the non-fQRS group.[8] Univariate ECG predictors of mortality were Q wave, fQRS, ST-segment depression, T-wave inversion, and QRS duration.[8] After adjusting for clinical variables, fQRS, ST-segment depression, and T-wave inversion were independent predictors of mortality, whereas Q wave and QRS duration were not.[8] The presence of fQRS is a moderately sensitive and highly specific sign for MI, including ST-segment elevation MI (STEMI) and fQRS has a significantly higher sensitivity and comparable specificity to Q waves for identifying MI. In a retrospective study of 513 patients with NSTEMI, fQRS was present within 24 hours of the symptom onset in 55.6% of patients.[9] fQRS was an independent predictor of six-month major adverse cardiac events. Patients with fQRS were more likely to have recurrent angina and coronary revascularization than patients without fQRS.[9]

In this issue of Acta Cardiologica Sinica, Liang et al. conducted a retrospective study to evaluate the usefulness of fQRS for diagnosis and outcome prediction in 302 ACS patients.[10] The present study enrolled 62 pa-

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tients (20.5%) with unstable angina, 53 patients (17.5%) with NSTEMI, and 187 patients (61.9%) with STEMI.[8] fQRS was present in a significantly greater percentage of patients in the MI groups (NSTEMI 37.7%, STEMI 35.8%) compared to the unstable angina group (19.4%) (both $p < 0.05$).[10] For MI patients (n = 240), patients with fQRS had a higher mortality risk compared to those without fQRS.[10] They concluded that fQRS within 48 hours of presentation may be used to differentiate unstable angina from NSTMI, and predict mortality in patients with acute MI.[10] Similarly to prior studies,[8,9] the usefulness of fQRS for diagnosis and outcome prediction in ACS was confirmed again.[10] However, there are several issues that need to be addressed. First, the percentage of non-ST-elevation ACS (unstable angina and NSTEMI) in the whole ACS cohort was only 38%, which was much smaller than the prevalence in the general population (approximately 70%, according to the 2013 Heart Disease and Stroke Statistics).[10,11] Second, the difference in fQRS incidences between unstable angina and MI (STEMI or NSTEMI) was smaller compared to the study by Das et al.[8,10] A higher incidence of fQRS in unstable angina (19.4% vs. 3.7%) and lower incidences of fQRS in NSTEMI and STEMI were observed (NSTEMI 37.7%, STEMI 35.8%) compared to the studies by Das et al. (NSTEMI 50%, STEMI 55%) and Li et al. (NSTEMI, 55.6%).[8-10] Different settings of a low-pass filter for ECG recordings might explain the observed differences.[12] Increasing the cutoff frequency of the low-pass filter will unmask additional spikes within the QRS complex and increase the detection rate of fQRS.[12] In the present study, the setting of low-pass filter for ECG recordings was not reported.[10] In addition, different time intervals for serial ECG recordings and different cutoff values of cardiac isoenzyme may change the diagnosis of unstable angina and NSTEMI, and indirectly influence the incidence of fQRS in patients with unstable angina and NSTEMI.

fQRS is a simple, inexpensive, and readily obtainable ECG sign that can be identified easily by clinicians. The potential role of fQRS in diagnosis and outcome prediction in patients with CAD has been shown several times in previous studies. It is possible that the predictive value of fQRS (a marker of depolarization abnormality) for outcome prediction can be improved further by combining an ST-deviation, T-wave inversion, or marker of repolarization abnormality, which needs further evaluation.

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