ORIGINAL ARTICLE

The Importance of the Number of Leads with fQRS for Predicting In-Hospital Mortality in Acute STEMI Patients Treated with Primary PCI

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Background: Fragmented QRS (fQRS) has been shown to be related to increased cardiovascular mortality and morbidity. However, limited data are available for evaluating the relationship between the number of leads with fQRS and in-hospital all-cause mortality in patients with acute ST segment elevation myocardial infarction (STEMI). The aim of our study is to investigate the prognostic importance of the number of leads with fQRS in acute STEMI patients treated by primary percutaneous coronary intervention (PCI).

Methods: Two hundred ten eligible patients with acute STEMI that underwent primary PCI were enrolled in this study. Each patient's 12-lead electrocardiography (ECG) taken in the first 48 hours was analyzed and the number of leads with fQRS were recorded.

Results: The number derivations with fQRS were significantly higher in patients who developed in-hospital mortality than the patients who did not develop in-hospital mortality (2.6 ± 2.6 vs 0.9 ± 1.3 ; $P = 0.002$). Also, patients with ≥ 3 leads with fQRS had higher rate of in-hospital all-cause mortality (23.5% vs 7.4%, $P = 0.009$), higher frequency of Q wave (67.6% vs 36.9%, $P = 0.001$), and higher frequency of fQRS with Q wave (67.6% vs 15.9%, $P < 0.001$) than those patients with < 3 leads with fQRS. By a multivariate regression analysis, the number of leads with fQRS was found to be an independent predictor of in-hospital all-cause mortality (odds ratio: 1.415, 95% confidence interval: 1.049–1.909, $P = 0.023$).

Conclusions: The number of leads with fQRS on 12-lead ECG is an independent predictor of in-hospital all-cause mortality in patients with acute STEMI treated by primary PCI.

Ann Noninvasive Electrocardiol 2016;21(4):413–419

ST elevated myocardial infarction; fragmented QRS; in-hospital mortality

Fragmented QRS (fQRS) on 12-lead electrocardiography (ECG) is defined by the presence of a single or multiple notches in the R or S wave, without a typical bundle branch block, in ≥ 2 contiguous leads corresponding to major coronary artery territories.¹ Previous studies have shown that it is caused by myocardial scar tissue and appears approximately 24–48 hours after the onset of symptoms or after diagnosis and following myocardial infarction (MI) necrosis.^{2,3} It has also been demonstrated that the presence of fQRS is associated with increased morbidity and mortality,

sudden cardiac death, and recurrent adverse cardiac events.^{4–6}

Although the association between the presence of fQRS and the mortality of patients with acute coronary syndrome (ACS) has been investigated previously,^{7–9} there are limited data regarding the relationship between the number of leads with fQRS and in-hospital all-cause mortality in acute ST segment elevation myocardial infarction (STEMI) patients undergoing primary percutaneous coronary intervention (PCI). The main goal of our study is to investigate the prognostic importance of the

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Financial Support: None.

© 2015 Wiley Periodicals, Inc.
DOI: 10.1111/anec.12329

number of leads with fQRS when predicting in-hospital all-cause mortality in acute STEMI patients undergone primary PCI for the first time.

METHODS

Patients admitted to the Coronary Intensive Care Unit of Dokuz Eylul University Hospital between January 1, 2009 and July 1, 2013 with the diagnosis of first acute STEMI and treated with primary PCI were retrospectively evaluated. The diagnosis of acute STEMI was based on the European Society of Cardiology 2012 guideline of "Third Universal Definition of Myocardial Infarction."¹⁰ The inclusion criteria were as follows: having first acute STEMI and being treated with primary PCI in our clinic. Twenty-three patients with complete bundle branch block or incomplete right bundle branch block were excluded from the study. In addition, patients with pacemaker implantation, known fQRS prior to STEMI, prior history of coronary artery bypass surgery or STEMI, and patients that were at subacute period of STEMI were excluded from the study. As a result, 210 eligible patients whose coronary angiographies were conducted in our clinic were enrolled in our study.

The ECGs of patients were taken on admission, after primary PCI, and at 24th and 48th hours after admission. ECG monitoring was performed with chest leads and leads on the standard extremities with a 0.16–100 Hz filter range, 25 mm/s speed, and 10 mm/mV height. Electrocardiographic examinations were performed with the naked eye by two independent physicians. Percentage of total ST resolution (STR) was calculated by the following formula: $(\text{Sum of ST elevations on Pre-PCI ECG}) - (\text{Sum of ST elevations on Post-PCI ECG}) / (\text{Sum of ST elevations on Pre-PCI ECG}) \times 100$, so total ST segment elevation before and after primary PCI was measured.¹¹ A pathological Q wave was defined as a wave of ≥ 20 milliseconds in duration or a QS complex in leads V₂–V₃ and a wave of ≥ 30 milliseconds in duration and ≥ 0.1 mV deep or QS complex in leads I, II, aVL, aVF, or V₄–V₆ in any two leads of a contiguous lead grouping (I, aVL; V₁–V₆; II, III, aVF).¹⁰ Fragmented QRS was defined as an additional R wave (R'), notching of the R wave, notching of the downstroke or upstroke of the S wave, or more than one R' (fragmentation) without a typical bundle branch block², and the number of

leads with fQRS detected during the first 48 hours were recorded.

The angiographic data were obtained from the catheter laboratory records and evaluated by two expert interventional cardiologists. Coronary angiography and PCI of the patients were performed through the femoral/radial artery. Each lesion in the epicardial coronary artery was classified as proximal, mid, or distal according to coronary segments defined by American College of Cardiology and American Heart Association.^{12,13} The presence of $\geq 50\%$ stenosis in the left main coronary artery and $\geq 70\%$ in the other major epicardial coronary arteries was considered critical stenosis.

STATISTICAL ANALYSIS

Continuous variables were expressed as the mean $\pm$ standard deviation and categorical variables were expressed as percentages. Continuous variables were tested for normal distribution by the Kolmogorov-Smirnov test. Comparisons of continuous variables were based on the Student's *t*-test for parametric variables, and the Mann-Whitney U test for nonparametric variables. Categorical variables were compared with chi-square tests or Fisher's exact chi-square tests. Correlation analysis between continuous variables was carried by the Spearman method. Logistic regression analysis was performed to determine the independent predictors of in-hospital all-cause mortality. A P value of <0.05 was considered to be statistically significant.

RESULTS

A total of 210 patients underwent primary PCI during the study period. The baseline clinical, electrocardiographic, and angiographic characteristics of patients are listed in Table 1. The mean number of leads with fQRS was 1.1 ± 1.6 . Observation of more than one lead with fQRS occurred in 91 (43.3%) patients. In-hospital all-cause mortality developed in 21 (10%) patients. The number of derivations with fQRS was found to be significantly higher in patients who developed in-hospital mortality than in patients who did not develop in-hospital mortality (2.6 ± 2.6 vs 0.9 ± 1.3 ; $P = 0.002$; Fig. 1).

Table 1. The Baseline Clinical, Electrocardiographic, and Angiographic Characteristics of Patients

	(n = 210)
Age (years)	61.6 ± 12.7
Gender M/F	161/49
Hypertension (%)	102 (48.6)
Diabetes mellitus (%)	47 (22.4)
Smoking (%)	125 (59.5)
Chest pain duration on admission (min.)	181.8 ± 204.0
LVEF (%)	41.2 ± 8.2
Maximum CK-MB (ng/mL)	151.8 ± 109.4
Maximum troponin (ng/mL)	36.3 ± 21.4
Number of STE derivations	5.1 ± 1.7
Number of STD derivations	3.0 ± 1.5
QRS duration (msec)	102.7 ± 8.9
Q wave (%)	88 (41.9)
fQRS with Q wave (%)	51 (24.3)
Number of leads with fQRS	1.1 ± 1.6
MI localization	
Anterior (%)	106 (50.5)
Nonanterior (%)	104 (49.5)
Pre-PCI sum of STE (mm)	11.0 ± 7.1
Post-PCI sum of STE (mm)	3.8 ± 3.3
STR ratio (%)	66.2 ± 20.0
Infarct-related artery	
LAD (%)	106 (50.5)
CX (%)	34 (16.2)
RCA (%)	70 (33.3)
Proximal vessel disease (%)	100 (47.6)
Number of vessels with critical stenosis	1.9 ± 0.9
Three-vessel disease (%)	63 (30)
In-hospital mortality (%)	21 (10)

M = male; F = female; min = minute; LVEF = left ventricular ejection fraction; CK-MB = creatinine kinase-MB; STE = ST elevation; STD = ST depression; msec: milliseconds; fQRS = fragmented QRS; MI = myocardial infarction; PCI = percutaneous coronary intervention; mm: millimeters; STR = ST resolution; LAD = left anterior descending artery; Cx = circumflex artery; RCA = right coronary artery.

When our patient group was divided into two groups (those with ≥ 3 leads with fQRS and those with < 3 leads with fQRS), in-hospital mortality was significantly higher for the group with ≥ 3 leads with fQRS (23.5% vs 7.4%, $P = 0.009$; Fig. 2). Also, patients with ≥ 3 leads with fQRS had a higher rate of nonanterior STEMI (67.6% vs 32.4%, $P = 0.021$), higher maximum troponin levels (54.9 ± 24.7 ng/mL vs 32.7 ± 18.7 ng/mL, $P < 0.001$), a lower left ventricular ejection fraction (LVEF; 34.0 ± 7.2 vs 42.6 ± 7.7 , $P < 0.001$), a higher rate of infarct-related proximal lesions (70.6% vs 43.2%, $P = 0.003$), and a higher rate of three-vessel disease (76.5% vs 21%, $P < 0.001$). These patients had a lower ratio of STR (50.9 ± 22.8 vs 69.1 ± 18.0 , $P < 0.001$), a higher frequency of Q wave (67.6% vs

Figure 1. Mean number of leads with fQRS in mortality (-) and mortality (+) groups. **Figure 2.** In-hospital mortality rate in ≥ 3 leads with fQRS and < 3 leads with fQRS groups.

36.9%, $P = 0.001$), and fQRS with Q wave (67.6% vs 15.9%, $P < 0.001$), a longer QRS duration (108.8 ± 6.2 vs 101.5 ± 8.8 milliseconds, $P < 0.001$) than those with < 3 leads with fQRS (Table 2).

In correlation analysis, as the number of fQRS derivations increased, maximum troponin ($r = 0.490$, $P < 0.001$) and the number of vessels with critical stenosis ($r = 0.495$, $P < 0.001$) increased significantly; conversely, STR ($r = -0.532$, $P < 0.001$) and LVEF ($r = -0.483$, $P < 0.001$) decreased significantly (Fig. 3).

Multivariate logistic regression analyses were performed to determine the independent variables for in-hospital all-cause mortality including age, duration of chest pain on admission, CK-MB and troponin levels, number of ST elevated and ST depressed derivations, QRS duration, Q wave,

Table 2. Comparison of Demographic, Electrocardiographic, and Angiographic Characteristics of Patients with ≥ 3 Leads and Those with < 3 Leads with fQRS

	≥ 3 Leads with fQRS (n = 34)	< 3 Leads with fQRS (n = 176)	P
Age (years)	62.6 $\pm$ 11.7	61.4 $\pm$ 12.9	0.623
Gender M/F	25/9	136/40	0.637
Hypertension (%)	17 (50)	85 (48.3)	0.856
Diabetes mellitus (%)	11 (32.4)	36 (20.5)	0.128
Smoking (%)	19 (55.9)	106 (60.2)	0.637
Chest pain duration on admission (min.)	169.7 $\pm$ 158.9	184.1 $\pm$ 211.9	0.723
LVEF (%)	34.0 $\pm$ 7.2	42.6 $\pm$ 7.7	<0.001
Maximum CK-MB (ng/mL)	236.6 $\pm$ 111.3	135.4 $\pm$ 101.4	<0.001
Maximum troponin (ng/mL)	54.9 $\pm$ 24.7	32.7 $\pm$ 18.7	<0.001
Number of STE derivations	5.3 $\pm$ 2.0	5.0 $\pm$ 1.6	0.630
Number of STD derivations	3.3 $\pm$ 1.5	3.0 $\pm$ 1.5	0.232
QRS duration (msec)	108.8 $\pm$ 6.2	101.5 $\pm$ 8.8	<0.001
Q wave (%)	23 (67.6)	65 (36.9)	0.001
fQRS with Q wave (%)	23 (67.6)	28 (15.9)	<0.001
MI localization (%)			
Anterior MI	11 (32.4)	95 (54)	0.021
Nonanterior MI	23 (67.6)	81 (46)	
STR ratio (%)	50.9 $\pm$ 22.8	69.1 $\pm$ 18.0	<0.001
Proximal vessel disease (%)	24 (70.6)	76 (43.2)	0.003
Number of vessels with critical stenosis	2.7 $\pm$ 0.6	1.7 $\pm$ 0.8	<0.001
Three-vessel disease (%)	26 (76.5)	37 (21)	<0.001

M = male; F = female; min = minute; LVEF = left ventricular ejection fraction; CK-MB = creatinine kinase-MB; STE = ST elevation; STD = ST depression; msec: milliseconds; fQRS = fragmented QRS; MI = myocardial infarction; STR = ST resolution.

fQRS with Q wave, proximal vessel disease, MI localization, number of affected lesion narrowness $> 70\%$, number of leads with fQRS, and ST segment resolution score. Number of leads with fQRS (odds ratio [OR]: 1.415, 95% confidence interval [CI]: 1.049–1.909, $P = 0.023$), number of ST elevated derivations (OR: 1.330, 95% CI: 1.002–1.764, $P = 0.048$), number of vessels with critical stenosis (OR: 2.235, 95% CI: 1.019–4.902, $P = 0.045$), and age (OR: 1.069, 95% CI: 1.024–1.116, $P = 0.003$) were found to be independent predictors of in-hospital all-cause mortality (Table 3).

DISCUSSION

The main finding of our study was that the number of fQRS derivations was significantly higher in acute STEMI patients treated with primary PCI and those who developed in-hospital mortality. In addition, the presence of a greater number of fQRS derivations was associated with lower LVEF and STR ratios, higher troponin levels, and a higher number of vessels with critical stenosis in coronary angiography.

The presence of fQRS is traditionally defined as the presence of different RSR' patterns at two

consecutive derivations corresponding to the major coronary arteries regardless of the Q wave while QRS duration is below 120 milliseconds in 12-lead ECG.¹ Therefore, the prognostic value of the number of fQRS derivations ≥ 2 has usually been investigated in studies and it has been found to predict mortality significantly in patients with ACS.^{9,14} In addition, a higher number of fQRS derivations has been shown to be associated with worse left ventricular functions, elevated troponin levels, and lower STR ratios.^{8,15,16} Therefore, in acute STEMI patients with the presence of a higher number of fQRS derivations, myocardial scar tissue can be expected to be larger and these patients can be expected to be at higher risk.

The number of fQRS derivations was found to be significantly higher in cases with in-hospital mortality in our study. In addition, the ratio of in-hospital mortality was significantly higher in patients with fQRS number ≥ 3 compared to patients with fQRS number < 3 (23.5% vs 7.4%, $P = 0.009$). Similar to our study, Yildirim et al.¹⁷ determined that as the number of fQRS derivations increased, particularly in patients with ≥ 4 fQRS derivations, major adverse cardiac events (MACE) also increased significantly. The most

Figure 3. Correlation analysis between number of leads with fQRS and maximum troponin, LVEF, number of vessels with critical stenosis, ST resolution ratio.

Table 3. Multivariate Logistic Regression Analysis Showing the Independent Predictors of In-Hospital All-Cause Mortality

	β	SE	Wald	OR (95% CI)	P
Age	0.067	0.022	9.132	1.069 (1.024-1.116)	0.003
Number of STE derivations	0.285	0.144	3.897	1.330 (1.002-1.764)	0.048
Number of leads with fQRS	0.347	0.153	5.181	1.415 (1.049-1.909)	0.023
Number of vessels with critical stenosis	0.804	0.401	4.026	2.235(1.019-4.902)	0.045

β = β coefficient; SE= standard error; OR= odds ratio; CI= confidence interval (variables: age, duration of chest pain on admission, CK-MB, troponin, number of ST elevated and ST depressed derivations, QRS duration, Q wave, fQRS with Q wave, proximal vessel disease, MI localization, number of affected lesion narrowness >70%, number of leads with fQRS, ST segment resolution score).

important difference in our study from this study is evaluating in-hospital mortality instead of MACE and presenting the number of fQRS derivation to be an independent variable in predicting in-hospital mortality (OR: 1.415, 95% CI: 1.049–1.909,

P = 0.023). Torigoe et al.¹⁸ observed similar findings in patients with prior MI history. They found that the fQRS derivation number as an independent predictor for cardiac death or hospitalization due to heart failure. The most important difference

between our study and this study was that we investigated acute STEMI patients.

In our study, the frequency of Q wave and fQRS with Q wave were significantly higher and QRS duration was significantly longer in patients with ≥ 3 leads with fQRS. However, in multivariate logistic regression analyses, they were not found to be an independent predictor of in-hospital all-cause mortality. Similar to our study, Ari et al.¹⁹ demonstrated that fQRS is an independent predictor of MACE in patients with STEMI who have undergone primary PCI, whereas Q wave and fQRS with Q wave at 48th hour did not predict MACE. Moreover, Das et al.¹⁴ demonstrated that fQRS is an independent predictor of mortality in patients with ACS, whereas Q wave and QRS duration did not predict mortality.

The association between the presence of fQRS and three-vessel disease has been shown in previous studies.^{8,20} It has been shown in our study that the number of vessels with a critical stenosis increases as the number of derivations with fQRS increases, and three-vessel disease is present in 76.5% of patients with three or more fQRS derivations. In addition, proximal vessel disease was detected more frequently in patients with ≥ 3 fQRS leads. The possible underlying mechanism for the relationship between the number of leads with fQRS and a higher incidence ratio of three-vessel diseases might be a more severe ischemia in the infarct-related artery territory, which is probably subject to poorer collateral circulation in these patients.

Coronary angiography is the gold standard method to demonstrate the epicardial coronary artery patency. However, epicardial coronary artery patency may not always indicate nutritive tissue reperfusion at the cellular level. Recent data suggest that STR may predict cardiovascular outcomes better than angiographic infarct-related artery patency.^{21,22} Consistent with previous studies,^{8,16} we found a negative correlation between number of leads with fQRS and STR ratio. Therefore, it can be stated that elevated fQRS derivation numbers would result in a poorer reperfusion indicator at the cellular level in acute STEMI patients and that outcomes would be worse in these patients.

In our study, patients with ≥ 3 leads with fQRS had a higher incidence rate of nonanterior location of STEMI compared to patients with non-fQRS. Although some previous studies have found no

relationship between the presence of fQRS and MI localization^{8,15} anterior MI has been found more frequently in other studies.²³ Sheng et al.²⁴ demonstrated that fQRS develops more frequently at inferior segment leads free from MI localization in one of their recent studies. Moreover, Das et al.² demonstrated that the sensitivity of fQRS at inferior segment leads in showing myocardial scar tissue is higher than fQRS at anterior and lateral leads (82.7%, 72.7%, and 62.9%, respectively). Studies with larger patient series investigating myocardial segment with fQRS according to MI localization are necessary in order to explain more clearly the relationship between leads with fQRS and MI localization.

LIMITATIONS

One of the most important limitations of our study is the lack of a long-term follow-up. We evaluated only the in-hospital mortality of the patients. Second, our findings cannot be generalized to all acute STEMI patients since we included only the first acute STEMI patients who were treated with primary PCI.

CONCLUSIONS

The number of leads with fQRS provides useful prognostic information for patients with acute STEMI treated by PCI. The presence of increased numbers of leads with fQRS, especially ≥ 3 leads, reflect a greater extent of ischemia and predicts a higher risk of patients with increased in-hospital mortality. Considering it is a noninvasive and easily applicable method, fQRS derivation number should be considered for prognostic assessment in all patients presenting with acute STEMI.

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