Short-term Prognosis of Fragmented QRS Complex in Patients with Non-ST Elevated Acute Myocardial Infarction

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Abstract

Background: There remains significant debate as to the relationship between fragmented QRS (fQRS) complexes on electrocardiogram (ECG) and acute myocardial infarction (AMI). Few studies have reported on this relationship in non-ST elevated AMI (NSTEMI), and thus, we attempt to assess this relationship and its potential short-term prognostic value.

Methods: This was a single-center, observational, retrospective cohort study. A total of 513 consecutive patients (399 men, 114 women) with NSTEMI within 24 h who underwent coronary angiography at our department, between January 1, 2014, and December 31, 2014. Patients were divided into 2 groups according to the presence or absence of fQRS complex on the admission ECG. fQRS complexes were defined as the existence of an additional R' or crochetage wave, notching in the nadir of the S wave, RS fragmentation, or QS complexes on 2 contiguous leads. All patients were followed up for 6 months, and all major adverse cardiac events (MACE) were recorded.

Results: In this study, there were 285 patients with fQRS ECG in the 513 patients with NSTEMI. The number of patients with 0–2 coronary arteries narrowed by ≥50% in fQRS group were less while patients with 3 narrowed arteries were more than in the non-fQRS group ($P = 0.042$). There were fewer Killip Class I patients in the fQRS group ($P = 0.019$), while Killip Class II, III, and IV patients were more in the fQRS group than in the non-fQRS group ($P = 0.019$). Left ventricular ejection fraction levels were significantly lower in the fQRS group ($P = 0.021$). Baseline total cholesterol, low-density lipoprotein, creatinine, creatine kinase, homocysteine, high-sensitivity C-reactive protein (CRP), and red blood cells distribution width levels were significantly higher in the fQRS group. Total MACE (MACE, $P = 0.028$), revascularization ($P = 0.005$), and recurrent angina ($P = 0.005$) were also significantly greater in the fQRS group. On final logistic regression analysis, after adjusting for baseline variables, the following variables were independent predictors of fQRS: Coronary artery narrowing ($P = 0.035$), Killip classification ($P = 0.026$), and total cholesterol ($P = 0.002$). The following variables were found to be independent predictors of preoperative MACE: Hemoglobin ($P = 0.000$), gender ($P = 0.026$), fQRS ($P = 0.016$), and time from myocardial infarction to balloon or coronary artery bypasses grafting ($P = 0.013$).

Conclusions: The fQRS complexes are commonly present in NSTEMI and the fQRS complexes are an independent predictor of MACE in NSTEMI patients. The number of narrowed coronary arteries, Killip classification, and total cholesterol are all independent predictors of the fQRS complexes.

Key words: Fragmented QRS Complexes; Major Adverse Cardiac Events; Non-ST Elevated Acute Myocardial Infarction

INTRODUCTION

Acute myocardial infarction (AMI) is characterized by ischemia and necrosis of the myocardium, high mortality, and poor prognosis, especially in non-ST elevated AMI (NSTEMI). Fragmented QRS (fQRS) complexes are special electrocardiographic signals, which reflect altered ventricular conduction around regions of myocardial scaring. fQRS complexes on electrocardiography (ECG) in AMI

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have been associated with adverse cardiac events.[1-7] Several other studies have linked fQRS to underlying structural heart diseases and to poor prognosis.[8-11] Associations between fQRS and increased morbidity and mortality, sudden cardiac death, and recurrent cardiac events have also been previously studied.[3,4,12-15] On the other hand, other studies have found that fQRS on surface ECG is not a reliable predictor of myocardial scaring, angiographic coronary disease, or long-term adverse outcomes.[16-18] However, there is little information in the literature on the correlation between the incidence of major adverse cardiac events (MACE) and fQRS on ECG in NSTEMI. We attempt to analyze this relationship and evaluate its potential for short-time prognosis.

METHODS

Study population and data collection

We performed a single-center, observational, retrospective cohort study with 513 of 632 consecutive NSTEMI patients admitted to our department between January 1, 2014, and December 31, 2014. Patients with the following criteria included in this study: (1) elevated serum cardiac biomarkers; (2) admission within 24 h of symptom onset; (3) ST-segment depression ≥0.1 mV or T waves tend to be symmetrically inverted; and (4) patients who underwent coronary angiography. Patients were excluded because that they were with severe valve disease; congenital heart disease; pacemaker implantation; other severe organ disease or cancer; bundle branch block in ECG; or they were refused to participate in the investigation and follow-up (n = 119). This study protocol was approved by the human research Ethics Committee at the Beijing An Zhen Hospital, Capital Medical University and was consistent with the *Declaration of Helsinki*. All patients wrote informed consent. Patients with NSTEMI were evaluated and treated according to the guidelines.

Standardized date during hospitalization were analyzed, including demographic information; the present and past history disease; laboratory results; therapy method; complications and we collected information by telephone after patients discharged 6 months about MACE (All Mortality, Cardiac Mortality, Recurrent myocardial infarction (MI), Revascularization, Recurrent Angina, Heart Failure).

Electrocardiography

All patients received 12-lead ECGs. The ECG and supplemental criteria for fQRS complexes were those previously defined by Das.[6] The resting 12-lead ECG filter range: 0.15–100 Hz; AC filter, 60 Hz, 25 mm/s, and 10 mm/mV. After admission, all patients underwent subsequent daily ECG as well as when complaining of discomfort and at discharge.

Coronary angiography

Angiographic data were evaluated from cardiac catheterization records. Coronary angiograms were analyzed by two experienced interventional cardiologists.

Coronary angiography was performed through either the femoral or radial artery by a standard technique. Standard selective coronary angiography was performed with at least 4 views of the left coronary system and 2 views of the right coronary artery. Stenosis diameter of ≥50% with quantitative angiography was considered significant stenosis.

Statistical analysis

Quantitative variables are expressed as mean ± standard deviation (SD) or as median (quartile). Categorical variables were defined as frequencies and percentages and were evaluated using the χ^2 test, Cochran–Armitage trend test, Fisher's exact test, an unpaired Student's t-test, or a Wilcoxon rank sum test. To identify the independent predictors of fQRS and MACE, step-wise multivariate logistic regression analyses were performed and included variables with $P < 0.3$ by univariate analyses. A value of $P < 0.05$ was considered statistically significant. All statistical analyses were performed using SAS 9.1 software (SAS Institute, Inc., Cary, NC, USA).

RESULTS

Baseline characteristics

A total of 513 patients (399 men, 114 women) with NSTEMI were evaluated. fQRS complexes were identified in 285 patients (55.56%). In the analyses of the fQRS and non-fQRS groups, The patients with 0–2 coronary arteries narrowed by ≥50% were significantly less in the fQRS group; while patients with 3 narrowed arteries were more in the fQRS group [P = 0.042, Table 1]. Killip Class I patients were fewer in the fQRS group; while Killip Classes II, III, and IV were more (P = 0.019). Left ventricular ejection fraction (LVEF) levels were lower in the fQRS group (P = 0.021). Their baseline characteristics parameters are shown in Table 1.

Baseline of laboratory examination: Total cholesterol, low-density lipoproteins, creatinine, creatine kinase, homocysteine, C-reactive protein (CRP), and red cell distribution width levels were significantly higher in the fQRS group. Their baseline characteristics parameters are shown in Table 2.

Major adverse cardiac events

Median follow-up time was 5.66 months. 25 patients (4.87%) were lost to follow-up. The incidence of total MACE (21.11% vs. 13.30%), revascularization (9.63% vs. 2.29%), recurrent angina (15.19% vs. 6.88%) were higher in patients with fQRS than those without fQRS [Table 3].

Independent predictors of fragmented QRS

On final logistic regression analysis, after adjusting for baseline variables, the number of narrowed coronary arteries (odds ratio [OR]: 1.236; 95% confidence interval [CI]: 1.015–1.507; P = 0.035), Killip classification (OR: 1.667; 95% CI: 1.062–2.618; P = 0.026), total cholesterol (OR: 1.357; 95% CI: 1.116–1.650; P = 0.002) were all independent predictors of fQRS [Table 4].

Table 1: Baseline characteristics of patients with and without fQRS

Characteristics	fQRS group (n = 285)	Non-fQRS group (n = 228)	χ^2/Z	P
Male, n (%)	227 (79.65)	172 (75.44)	1.299*	0.254
Age (years), mean ± SD	62.6 ± 11.5	61.5 ± 11.1	1.080*	0.279
Heart rate on admission (beats/min), median (quartile)	70.0 (15)	70.0 (14)	1.780*	0.075
Dyslipidemia, n (%)	177 (62.11)	128 (56.14)	1.869*	0.172
Chronic renal insufficiency, n (%)	16 (5.61)	21 (9.21)	2.448*	0.117
Hypertension, n (%)	196 (68.77)	157 (68.85)	0.001*	0.983
Diabetes mellitus, n (%)	91 (31.93)	79 (34.64)	0.423*	0.516
Drinking history, n (%)	50 (17. 54)	37 (16.23)	0.156*	0.693
Previous MI, n (%)	69 (24.30)	42 (18.42)	2.571*	0.109
Number of coronary artery narrowed ≥50%, n (%)				
0	4 (1.40)	8 (3.51)	9.874*	0.042
1	89 (31.22)	76 (33.33)		
2	69 (24.22)	69 (30.26)		
3	123 (43.16)	75 (32.89)		
Killip classification, n (%)				
I	210 (73.68)	193 (84.65)	9.984*	0.019
II	47 (16.49)	25 (10.96)		
III	14 (4.91)	6 (2.63)		
IV	14 (4.91)	4 (1.75)		
Treatment, n (%)				
PCI	150 (52.63)	128 (56.14)	2.835*	0.242
Medication	92 (32.28)	77 (33.77)		
CABG	43 (15.09)	23 (10.09)		
LVEF (%), median (quartile)	58.0 (12)	60.0 (10)	2.300†	0.021
SBP on admission (mmHg), median (quartile)	127.0 (18)	125.0 (24)	−0.640†	0.521
DBP on admission (mmHg), median (quartile)	75.0 (10)	71.5 (10)	−1.500†	0.134
Time from MI to balloon or CABG (h), median (quartile)	72.0 (96)	72.0 (72)	−1.510†	0.131

Data are presented as n (%), mean ± SD or median (quartile). *: χ^2 test. †: Wilcoxon rank sum test (Z). Quartile is referred to the interquartile range. fQRS: Fragmented QRS complex; NSTEMI: Non-ST elevated myocardial infarction; MI: Myocardial infarction; LVEF: Left ventricular ejection fraction; PCI: Percutaneous coronary intervention; CABG: Coronary artery bypass grafting; SBP: Systolic blood pressure; DBP: Diastolic blood pressure.

Independent predictors of major adverse cardiac events

On final logistic regression analysis, after adjusting for baseline variables, hemoglobin (OR: 0.965; 95% CI: 0.946–0.984; P = 0.000), gender (OR: 0.378; 95% CI: 0.160–0.892; P = 0.026), fQRS (OR: 0.825; 95% CI: 0.705–0.965; P = 0.016), and time from MI to balloon or coronary artery bypasses grafting (CABG) (OR: 1.031; 95% CI: 0.702–1.513; P = 0.013), were all independent predictors of MACE [Table 5].

DISCUSSION

fQRS complexes are special electrocardiographic signals which reflect altered ventricular conduction around regions of myocardial scaring, although the determinants of this phenomenon are not completely understood. In some studies, patients with nonischemic or ischemic left ventricular dysfunction have shown a relationship between the presence of fQRS and myocardial fibrosis.[19] Pietrasik reported that the presence fQRS could be a good predictor of cardiac events.[20] Furthermore, some clinical trials have indicated that the presence of fQRS on presentation in the emergency department can indicate prognosis and irreversible ischemia in patients with STEMI and NSTEMI.[7,21,22] These studies suggested that the presence of fQRS is noninvasive and easily evaluated maker for cardiac fibrosis and/or ischemia.

In this study, we investigated the correlation between the incidence of MACE and fQRS on ECG in NSTEMI and found that the presence of fQRS complexes is an important marker for NSTEMI. Additionally, we found that fQRS complexes, low hemoglobin, gender, and time from MI to balloon or CABG were strongly associated with MACE in NSTEMI patients.

We determined that in the fQRS group there were lower levels of LVEF and higher class of Killip Class II, III, and IV patients, similar to previous reports.[1,3] Red cell distribution widths and high-sensitivity CRP were significantly higher in the fQRS group. Red cell distribution width is an indicator of the variability of the circulating red blood cell size and is used to diagnose different types of anemia. Recently, a number of studies have reported on the relationship between red blood cells distribution width and heart failure, coronary artery disease, and stroke.[23-25] Felker et al.,[26] Uyarel et al.,[27] and Ren et al.[28] have all indicated that elevated red cell distribution widths are associated with an increased risk of poor outcomes in patients with heart failure, ST-segment elevation myocardial infarction, and stable angina pectoris. However, the relationship between

Table 2: Baseline of laboratory examination of patients with and without fQRS

Variables	fQRS group (n = 285)	Non-fQRS group (n = 228)	Z	P
Total cholesterol (mmol/L)	4.35 (1.36)	4.08 (1.58)	−2.63	0.009
LDL (mmol/L)	2.60 (1.19)	2.50 (1.25)	−1.99	0.046
HDL (mmol/L)	0.91 (0.29)	0.92 (0.29)	0.06	0.949
Triglyceride (mmol/L)	1.64 (1.19)	1.48 (0.98)	−1.46	0.145
ALT (U/L)	25.00 (21.00)	24.00 (18.00)	−1.24	0.213
AST (U/L)	32.00 (31.00)	29.00 (25.00)	−1.80	0.072
TBIL (μmol/L)	13.00 (7.20)	12.30 (6.50)	−1.06	0.289
DBIL (μmol/L)	2.64 (1.67)	2.63 (1.38)	−0.38	0.707
Urea (mmol/L)	5.40 (2.50)	5.50 (2.40)	0.48	0.630
CREA (μmol/L)	80.60 (23.50)	77.40 (22.30)	−2.00	0.046
FBG (mmol/L)	5.94 (2.26)	5.86 (2.76)	−0.25	0.800
CK (U/L)	142.00 (239.00)	115.00 (167.00)	−1.97	0.049
CK-MB (ng/ml)	6.10 (22.5)	5.00 (16.90)	−1.25	0.210
TNI (ng/ml)	1.96 (6.62)	1.65 (4.69)	−1.24	0.214
HCY (μmol/L)	15.00 (9.80)	14.10 (7.40)	−1.98	0.047
hs-CRP (mg/L)	4.78 (15.61)	3.09 (8.46)	−2.28	0.023
WBC (G/L)	7.47 (2.99)	7.35 (2.64)	−0.09	0.931
Neutrophil (%)	66.10 (12.20)	66.40 (12.50)	−0.17	0.864
Hemoglobin (g/L)	140.00 (23.00)	138.00 (25.00)	−0.83	0.406
RDW (%)	13.10 (0.90)	12.90 (0.80)	−2.41	0.016
PLT (G/L)	211.00 (85.50)	215.00 (82.00)	0.41	0.685
BNP (pg/ml)	176.00 (354.00)	131.00 (297.00)	−1.89	0.058
Platelet agglutination AA (%)	15.00 (3.00)	15.00 (3.00)	−0.65	0.517
Platelet agglutination ADP (%)	52.50 (22.50)	52.50 (23.00)	−0.72	0.474

Data are presented as medians (quartile), used Wilcoxon rank sum test (Z). Quartile is referred to the interquartile range. fQRS: Fragmented QRS complex; LDL: Low-density lipoprotein; HDL: High-density lipoprotein; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; TBIL: Total bilirubin; DBIL: Direct bilirubin; FBG: Fasting blood glucose; CK: Creatine kinase; CK-MB: Creatinine kinase, MB isoenzyme; TNI: Troponin I; HCY: Homocysteine; hs-CRP: High-sensitivity C-reactive protein; WBC: White blood cell; RDW: Red cell distribution width; PLT: Platelet; BNP: Brain natriuretic peptide; CREA: Creatinine; AA: Arachidonic acid; ADP: Adenosine diphosphate.

Table 3: The MACE patients with and without fQRS at 6-month follow-up

Variables	fQRS (+) group (n = 270)	fQRS (−) group (n = 218)	χ^2	P
Total MACE	57 (21.11)	29 (13.30)	4.812	0.028
All-cause mortality	2 (0.74)	0 (0)	−	0.505
Cardiac mortality	2 (0.74)	0 (0)	−	0.505
Recurrent myocardial infarction	14 (5.19)	9 (4.13)	0.275	0.600
Revascularization	26 (9.63)	5 (2.29)	10.713	0.001
Recurrent angina	41 (15.19)	15 (6.88)	7.939	0.005
Heart failure	2 (0.74)	2 (0.92)	−	1.000

Data are presented as n (%), Fisher exact test was used where the χ^2 test showed "−". fQRS: Fragmented QRS complex; MACE: Major adverse cardiac events.

Table 4: Multivariate logistic regression analyses for predictors of fQRS

Variables	β	OR (95% CI)	P
Coronary artery narrowing ≥50%	0.119	1.236 (1.015–1.507)	0.035
Killip classification	0.141	1.667 (1.062–2.618)	0.026
Total cholesterol	0.184	1.357 (1.116–1.650)	0.002

fQRS: Fragmented QRS complex; OR: Odds ratio; CI: Confidence interval.

Table 5: Multivariate logistic regression analyses of predictors of MACE

Variables	β	OR (95% CI)	P
Hemoglobin	−0.473	0.965 (0.946–0.984)	0.000
Gender	−0.216	0.378 (0.160–0.892)	0.026
fQRS	−0.106	0.825 (0.705–0.965)	0.016
Time from MI to balloon or CABG	0.013	1.031 (0.702–1.513)	0.013

MACE: Major adverse cardiac events; MI: Myocardial infarction; CABG: Coronary artery bypass grafting; fQRS: fragmented QRS complex; OR: Odds ratio; CI: Confidence interval.

red cell distribution width and adverse outcomes in these patients has not been fully explained. Cengiz et al.[29] reported a correlation between red cell distribution width and advanced fibrosis in nonalcoholic steatohepatitis. All these studies found that inflammation may be a factor of increased red cell distribution width, and they may be factors to increase the risk of poor outcomes in coronary artery disease. In this study, we found significantly higher red cell distribution widths and CRP levels in the fQRS group.

This study also showed that the fQRS group had higher rates of patients with 3 narrowed (≥50%) coronary arteries, MACE, recurrent angina, and recurrent angina. This suggests that the presence of fQRS might be strongly correlated with a higher incidence of cardiovascular events and/or serious coronary artery disease. Additionally, we found the fQRS group to be associated with more numbers of narrowed coronary arteries; higher Killip classifications, higher total cholesterol levels, and increased rates of recurrent angina. Thus, we believe more attention should be paid to patients with fQRS on ECG at initial presentation and can help determine prognosis.

In addition, we found that hemoglobin levels, male, fQRS, and time from MI to balloon or CABG were independent predictors of preoperative MACE. Therefore, male patients with low hemoglobin and positive fQRS complexes should be considered high risk and treated with balloon or CABG as quickly as possible. From this study, we concluded that the fQRS complexes are common present in NSTEMI and the fQRS complexes is an independent predictor of MACE in NSTEMI patients. The number of narrowed coronary arteries, Killip classification, and total cholesterol are all independent predictors of the fQRS complexes.

Study limitations

This study is limited by its retrospective design and the small patient population analyzed. Larger clinical studies are necessary to confirm these findings.

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Conflicts of interest

There are no conflicts of interest.

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