ORIGINAL ARTICLE

Association of Fragmented QRS Complex with Myocardial Reperfusion in Acute ST-Elevated Myocardial Infarction

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In this study, we aimed to evaluate the relationship between TIMI myocardial perfusion (TMP) grade, as an indicator of myocardial reperfusion, and fragmented QRS (fQRS) in standard 12-lead electrocardiogram. Also, we evaluate fQRS is an additional indicator of myocardial reperfusion. One hundred patients admitted with first STEMI to Coronary Intensive Care Unit and who were used thrombolytic therapy was included in this retrospective study. Standard 12-lead electrocardiogram records of patients simultaneous with coronary angiography (second day) were assessed and analysed for the presence of fQRS. Also, coronary angiography images were analyzed to identify the infarct related artery, TIMI grade of infarct related artery and TMP grade of infarct related artery. The patients with fQRS demonstrated a significantly lower TMP grade, TIMI grade and ejection fraction compared with the non-fQRS patients ($P = 0.004$, $P = 0.003$, $P = 0.02$ respectively). The patients with inadequate myocardial reperfusion demonstrated a significantly higher fQRS compared with the adequate myocardial reperfusion patients. (56.9% versus 23.5%, $P = 0.002$ respectively). On correlation analysis, there was a significant negative correlation between fQRS and left ventricular ejection fraction ($r = -0.232$, $P = 0.02$) TMP grade and adequate myocardial reperfusion (TMP 3) showed significant negative correlation with fQRS ($r = -0.370$, $P = 0.000$; $r = -0.318$, $P = 0.001$ respectively). Presence of fragmented QRS in STEMI patients was associated with inadequate myocardial reperfusion and it can be used as a simple, noninvasive parameter to evaluate myocardial reperfusion.

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Despite new treatment approaches, coronary artery disease remains a major cause of mortality and morbidity worldwide. The main pathophysiological mechanism underlying acute myocardial infarction (AMI) is typically the occlusion of a coronary artery caused by thrombus formation on fissured or disrupted atherosclerotic plaques. In acute ST-segment elevation myocardial infarction (STEMI), it is crucial to start thrombolytic therapy to open the blocked artery and protect the myocardium, as this is associated with short- and long-term prognoses.^{1,2} Patients in whom this treatment

fails may require additional treatments, such as lifesaving percutaneous coronary intervention (PCI). In order to make treatment decisions as quickly as possible, the reperfusion of the affected artery should be evaluated rapidly and accurately using noninvasive methods after thrombolytic treatment. Relief of chest pain, normalization of the ST segment elevation in the electrocardiogram (ECG), and reperfusion arrhythmias are indicators of reperfusion. However, the specificity and sensitivity of these indicators are limited. An additional indicator of reperfusion is an early peak in cardiac

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proteins, such as creatinine kinase myocardial band (CK-MB), troponin, and myoglobin.^{3,4}

The ECG is a simple, easy to apply, and inexpensive diagnostic test that is the gold standard as a first-line investigation for evaluating AMI. Many ECG parameters have been used to determine reperfusion in STEMI. Recently, Das et al. evaluated the fragmented QRS (fQRS) extensively.⁵ It is thought that the presence of an fQRS reflects myocardial scarring and necrotic tissue and many large studies have shown that unwanted cardiac events and mortality are increased in such patients.⁶⁻¹⁰ Moreover, the fQRS is a highly sensitive, independent predictor of mortality.^{11,12}

Although epicardial blood flow is restored after AMI in many patients, reperfusion is inadequate at the tissue level. This problem has been demonstrated using many methods, including myocardial contrast echocardiography, magnetic resonance imaging, scintigraphic methods, and Doppler flow wire measurements.¹³ The thrombolysis in myocardial infarction (TIMI) myocardial perfusion (TMP) grade has been defined in order to evaluate myocardial reperfusion angiographically. The TMP grade effectively reflects myocardial reperfusion and is an independent predictor of long-term mortality.¹⁴

This study evaluated the relationship between the presence of fQRS and TMP grade using the 12-lead ECG in patients admitted with first STEMI who received thrombolytic therapy. The aim of this study was to determine whether fQRS could be used as an additional indicator for evaluating myocardial reperfusion.

METHOD

This study was conducted by retrospectively analysing the records of 100 patients (totally 621 patients, 521 patients excluded who have defined exclusion criteria) admitted with first STEMI to the Coronary Intensive Care Unit during March 2004–June 2006 and who were administered thrombolytic therapy and subjected to angiography to image coronary anatomy.

According to ACC/AHA/ESC 2007 criteria, patients were diagnosed as having STEMI (the presence of ischemic chest pain with >2 mm ST segment elevation in at least two contiguous chest leads or >1 mm ST segment elevation in extremity lead). Demographic features and

routine laboratory parameters of all patients were recorded. Electrocardiographic records of the patients admitted with first STEMI and who were administered thrombolytic therapy were obtained and assessed along with the records of coronary angiographies performed simultaneously (first 4 days). ECGs performed after 48 hours of thrombolytic therapy for defining the fQRS. Standard extremity and chest lead ECGs were performed at a 0.16–100 Hz frequency range, 25 mm/s speed and amplitude of 10 mm/Mv. fQRS were defined as QRS morphologies containing different RSR' patterns on two contiguous leads of a major coronary artery territory. Presence of fQRS in ≥ 2 contiguous anterior leads (V₁ to V₅) were assigned to myocardial scar and necrosis in anterior segments or left anterior descending territory. Presence of fQRS in ≥ 2 contiguous lateral leads (I, aVL, and V₆) was assigned to myocardial scar and necrosis in the lateral segments or left circumflex territory. Similarly, presence of fQRS in ≥ 2 contiguous inferior leads (II, III, and aVF) was to myocardial scar and necrosis in inferior segments or right coronary artery territory. These various morphologies were defined as an additional R wave or notching in the nadir of S wave or >1 R' (fragmentation) (Fig. 1). ECGs of the patients were analysed for fQRS independent of the presence of Q wave. Moreover, MI localization and presence of pathologic Q wave were determined. Complete resolution was defined as 70% or higher resolution compared to admission in ST segment, as determined by an ECG performed 90 minutes after thrombolytic therapy.

Inclusion criteria were to have acute STEMI for the first time. Although fQRS were found among patients having a wide QRS in ECG, only those having a normal QRS duration were included in the study for homogeneity. Patients having complete branch block (QRS > 120 ms), incomplete right branch block, pacemaker rhythm, left ventricular hypertrophy voltage criteria, using digoxin, having electrolyte disorder (hyperkalemia, hypocalcemia), hypertrophic, and dilated cardiomyopathy was excluded from the study.

Infarct related artery, initial TMP grade of infarct related artery and initial TIMI grade of infarct related artery were determined by assessing the coronary artery images obtained by using Judkin's method and through the femoral artery puncture and standard 6F Judkins right and left catheters.

Figure 1. ECG record 2 days after thrombolytic therapy in an anterior MI patients in our study (fQRS in fragmented QRS pattern on v_3 , v_4 lead).

TIMI 3 flow was regarded as an adequate TIMI flow grade. In patients having a TMP grade of 3, myocardial reperfusion was regarded as adequate while it was regarded as inadequate in patients having a TMP grade of 0/1/2. Results were expressed as average+standard deviation and percentage. Significance of the statistical difference between the groups was evaluated by chi-square and independent sample *t*-test. Correlation analysis between the groups was carried by Pearson method. Statistical package program SPSS (Statistical Package from the Social Sciences Program for windows 15.0, SPSS, Chicago, IL) was used for statistical calculations. $P < 0.05$ was regarded as statistical significance in all the analysis.

RESULTS

A total of 100 patients admitted with first acute STEMI and who were administered thrombolytic therapy was included in the study. Demographic clinical and laboratory characteristics of the patients are summarized in Table 1. When evaluated in terms of the localization of MI, 54% of the patients had anterior MI while 46% had inferior MI. In 64.2% of the patients administered, thrombolytic therapy was t-PA. The other 35.8% of the patients, thrombolytic therapy was streptokinase. As a result of the thrombolytic

Table 1. Basic Clinical and Laboratory Characteristics of the Patients

	Acute STEMI Patients (n = 100)
Age(year)	54.6 ± 10.1
Gender(M/F)	83/17
Hypertension	35 (35%)
Diabetes Mellitus	16 (16%)
History of smoking	72 (72%)
Family history	33 (33%)
SBP/DBP	111 ± 4/70 ± 3
Left ventricular EF (%)	47.2 ± 8.6
Administered thrombolytic therapy	
(t-PA/Streptokinase)	52 (64.2%)/29 (35.8%)
Admission plasma blood glucose (mg/dl)	134 ± 49
Hemoglobin (gr/dl)	14.6 ± 1.7
White blood cell (per mm ³)	11666 ± 4007
BUN (mg/dl)	21.57 ± 10.28
Creatinin (mg/dl)	1.1 ± 0.70
Total Cholesterol (mg/dl)	198.8 ± 40.5
HDL (mg/dl)	41.7 ± 8.7
LDL(mg/dl)	128.2 ± 35.4
CK peak (μ/dl)	2496 ± 1531
CK MB peak (μ/dl)	276 ± 218

SBP = systolic blood pressure; DBP = diastolic blood pressure; EF = ejection fraction; t-PA = tissue plasminogen activator; BUN = blood urea level; HDL = high-density lipoprotein; LDL = low-density lipoprotein; CK peak = creatinine kinase peak; CK-MB peak = creatinine kinase-myocardial band peak.

Table 2. Comparison of Characteristics between Two Groups

	fQRS group(n = 45)	Non-fQRS group(n = 55)	P value
Age (year)	54.62 ± 10.53	54.56 ± 9.97	N.S
Gender (M/F)	40/5	43/12	N.S
Hypertension	16 (35.6%)	19 (34.5%)	N.S
Diabetes Mellitus	6 (13.3%)	10 (18.2%)	N.S
History of smoking	32 (71.1%)	40 (72.7%)	N.S
Left ventricular EF (%)	45 ± 8.4	49 ± 8.5	0.02
Admission plasma blood glucose (mg/dl)	135.1 ± 46.4	133.2 ± 51.9	N.S
Total Cholesterol (mg/dl)	202.5 ± 45.1	195.8 ± 37.0	N.S
LDL (mg/dl)	132.5 ± 39.2	124.7 ± 32.3	N.S
CK MB peak (μ/dl)	306 ± 187.5	246 ± 246.4	N.S
MI localisation (Anterior/Inferior)	24/21	30/25	N.S
Complete ST resolution	27 (60%)	34 (61.8%)	N.S
Q wave (%)	35 (77.8%)	40 (72.7%)	N.S
Duration (day)	1.6 ± 3.6	2.4 ± 2.1	N.S
PCI	29 (70.7%)	31 (57.7%)	N.S

therapy, complete resolution was detected in 61% of the patients. The average duration between AMI and coronary angiography was 2.1 ± 1.8 days. Pathological Q wave was detected in 75% of the patients. When coronary angiographies of the patients were evaluated, infarct related artery was found to be LAD in 56 patients, RCA in 36 patients and CX in eight patients. PCI was performed in 60% of the patients.

fQRS was detected in a total of 45 patients while it was not detected in 55 patients. Patients were divided into two groups based on the presence of fQRS. In patients where fQRS was detected, left ventricular ejection fraction was lower (45 ± 8.4 against 49 ± 8.5) and statistically significant ($P = 0.02$). There was no difference between two groups other clinical and laboratory characteristics. (Table 2)

Pathologic Q wave was present in 77.8% of the patients in fQRS group and in 72.7% non-fQRS group ($P > 0.05$). In the groups (fQRS/non-fQRS), number of patients having TIMI 3 flow were 16/36, number of patients having TIMI 0/1/2 flow were 29/18, respectively and the difference was statistically significant ($P = 0.003$). Again in the groups, number of patients having a TMP grade of 3 was 8/26 and number of patients having a TMP grade of 0/1/2 was 37/28, respectively and the difference was statistically significant ($P = 0.004$). There was no difference between the group's complete resolution and other parameters.

Patients were also divided into two groups in terms of having an adequate myocardial

reperfusion and inadequate myocardial reperfusion. Myocardial reperfusion was found to be adequate (TMP 3) in 34 patients. In 65 patients, myocardial reperfusion was inadequate. In the groups having inadequate myocardial reperfusion, history of smoking was high, and the difference was statistically significant (88.2% and 64.6% respectively, $P = 0.012$). There was no difference between two groups in terms of other clinical and laboratory parameters. PCI rate was found to be statistically significant different between group (50% and 72.6%, respectively, $P = 0.033$). In the group having inadequate myocardial reperfusion, fQRS was detected in 56.9% of the patients while only 23.5% of those in the group having adequate myocardial reperfusion had fQRS. In terms of presence of fQRS, the difference between the groups was statistically significant ($P = 0.002$). There was no statistically significant difference between the groups in terms of other electrocardiographical and angiographical parameters. As a result of the correlation analysis of variables, there was a mildly significant negative correlation between fQRS and left ventricular ejection fraction ($r = -0.232$, $P = 0.02$). There was no correlation between fQRS and full ST segment resolution. TIMI flow grade and adequate TIMI flow (TIMI 3 flow) showed a significant negative correlation with fQRS ($r = -0.347$, $P = 0.000$; $r = -0.318$, $P = 0.002$, respectively). TMP grade and adequate myocardial reperfusion (TMP 3) also showed a significant negative correlation with fQRS ($r = -0.370$, $P = 0.000$; $r = -0.318$, $P = 0.001$, respectively).

DISCUSSION

Many studies have shown that thrombolytic therapy for STEMI prevents death and adverse cardiovascular events.¹⁵⁻¹⁸ Thrombolytic therapy is the most frequently used reperfusion treatment worldwide. The clinical evaluation of coronary reperfusion in STEMI patients that have undergone thrombolytic therapy is important in terms of modifying the treatment strategy depending on the results. Patients in whom this treatment fails may require additional treatments, such as lifesaving PCI. In order to make a decision as quickly as possible, the reperfusion of the affected artery should be evaluated rapidly and accurately after thrombolytic treatment using noninvasive methods. The resolution of chest pain, 50% resolution of the ST segment elevation at 90 minutes compared to baseline, and reperfusion arrhythmias indicate reperfusion. However, the specificity and sensitivity of these indicators are limited. Consequently, studies have sought new myocardial reperfusion indicators.^{19,20} Therefore, we evaluated the importance of fQRS as an additional indicator of myocardial reperfusion.

In coronary artery patients, fQRS is regarded as an indicator of myocardial scarring and necrotic tissue. In 200 patients with AMI, Micheal et al. showed that fQRS had a high specificity, but moderate sensitivity.¹² In 896 acute coronary syndrome (ACS) patients (337 non-STEMI, 104 STEMI, and 455 unstable angina), Das et al. found that fQRS had a higher specificity and sensitivity when compared to the pathological Q wave.⁸ Another study found that adverse cardiac events and all-cause mortality rates were significantly higher in the fQRS group.⁷ Similarly, a study of AMI patients found that ST depression, T-wave inversion, and fQRS were independent predictors of mortality.¹¹ Consequently, there is consensus that fQRS is an independent predictor of adverse cardiac events.^{8,10} A positive correlation was found between the presence of fQRS and events in patients with ischemic cardiomyopathy who had a cardioverter-defibrillator implanted.^{5,12} Torigoe et al. showed that the number of leads with fQRS, especially ≥ 3 leads, was an independent predictor of cardiac death or hospitalization for heart failure in patients with a prior MI.²¹

The TMP grade can be used to describe the effectiveness of myocardial reperfusion and is an independent predictor of long-term mortality.¹⁴ The TMP grade indicates myocardial perfusion

independent of epicardial blood flow, yielding prognostic information beyond epicardial flow.²² The relationship between the presence of fQRS and TMP grade had not been previously examined, making this study the first to evaluate this. Of our patients, 34 had adequate myocardial reperfusion, while 65 had inadequate myocardial reperfusion. The group with adequate myocardial reperfusion had lower fQRS compared to the group with inadequate myocardial reperfusion and the difference between the groups was significant. A correlation analysis of the variables showed significant negative correlations between fQRS and TMP grade and adequate myocardial perfusion (TMP 3).

Das et al. found that the fQRS group had a significantly lower ejection fraction than the non-fQRS group.⁵ Similarly, we found that the left ventricular ejection fraction was significantly lower in the fQRS group. In addition, there was a significant negative correlation between the fQRS and left ventricular ejection fraction, which is consistent with previous studies.^{5,23}

We found no significant correlation between the presence of fQRS and ST segment resolution showing myocardial reperfusion. This unexpected result was thought to be due to the limited number of patients and defining full ST resolution as $\geq 70\%$ resolution of the ST segment elevation.

Limitations

One of the major limitations of this study was to have a limited number of patients. Second, myocardial reperfusion was assessed by angiography in this study. Using other methods such as MR imaging and myocardial contrast echocardiography could have additional advantages.

Conclusions

According to these findings, fQRS imaged in 12 lead ECG can be used as an additional parameter in evaluating myocardial reperfusion in STEMI patients receiving thrombolytic therapy. This may help determine the subpatient group having an inadequate myocardial reperfusion who may benefit from an early invasive intervention after thrombolytic therapy. However, this result should be supported by large-scale studies in the future.

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