The Assessment of Relationship between Fragmented QRS Complex and Left Ventricular Wall Motion Score Index in Patients with ST Elevation Myocardial Infarction Who Underwent Primary Percutaneous Coronary Intervention

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Objectives: Fragmented QRS (fQRS) has been found to be associated with high mortality and arrhythmic events in acute coronary syndromes. Regional systolic function using wall motion score index (WMSI) is an alternative to left ventricular ejection fraction (LVEF) for the assessment of left ventricular systolic function. The aim of this study was to investigate the relation between the presence of fQRS on admission electrocardiogram (ECG) and WMSI in ST elevation myocardial infarction (STEMI) underwent primary coronary intervention (PCI). The in-hospital and long-term prognostic significance of persistent fQRS was also evaluated.

Methods: In this retrospective study, 542 patients with a diagnose of STEMI underwent primary PCI were included. Study patients were divided into two groups according to the presence ($n = 153$) or absence ($n = 389$) of a fQRS on admission ECG.

Results: WMSI was found to be significantly higher in fQRS(+) group compared to the fQRS(-) group ($P < 0.001$). In multivariate analysis, WMSI was found to be an independent predictor of fQRS, and fQRS was inversely associated with LVEF. The in-hospital reinfarction ($P = 0.003$), MACE ($P = 0.024$), intraaortic balloon pump use ($P = 0.014$), and advanced heart failure ($P < 0.001$) were found to be significantly more frequent in the fQRS(+) group. The presence of fQRS on admission was found to be associated with an increase in long-term cardiovascular mortality ($P = 0.028$), and long-term all-cause mortality ($P = 0.022$).

Conclusion: WMSI was significantly related with the presence of the fQRS, which reflects the linking between impairment of regional left ventricular systolic function and the presence of severe myocardial injury in STEMI.

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fragmented QRS; left ventricular systolic function; mortality

Despite advances in the diagnosis and treatment with new approaches, ST-segment elevation myocardial infarction (STEMI) remains the most com-

mon cause of cardiovascular mortality and morbidity in developing countries.^{1,2} Electrocardiogram (ECG) and echocardiography are simple, easy to

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apply, and inexpensive diagnostic tools, which are useful for risk stratification and assessment of short- and long-term prognosis following acute myocardial infarction (AMI).

Fragmented QRS, which has been defined as the presence of notched R or S waves without accompanying typical bundle branch block, or the existence of an additional wave like RSR' pattern in the original QRS complex (with a duration of <120 milliseconds),³ arises from impaired ventricular depolarization due to heterogeneous electrical activation of ischemic and/or infarcted ventricular myocardium. It has gained much of interest as a new, easy to assess, and reliable ECG finding in clinical practice. Although the presence of fQRS had been reported to increase the diagnostic performance of ECG in the recognition of previous MI, when added to Q wave analysis,³ the predictive value of fQRS may be change in various patient groups.⁴ It was also reported to be an electrocardiographic sign of nonhomogeneous ventricular conduction delay around myocardial scar tissue.^{5,6} Partial damage of the conducting system inside the ventricle causes the notching of the QRS segment on ECG.⁷ The presence of fQRS was demonstrated to be an independent predictor of decreased myocardial perfusion and functional deterioration, marked left ventricular (LV) dilatation and decreased ejection fraction (EF) in patients with ischemic heart disease.⁸⁻¹⁰ fQRS, which may be widened or narrowed, has been found to be associated with high mortality and arrhythmic events in coronary artery disease (CAD), acute coronary syndromes (ACS),^{11,12} and ischemic and nonischemic cardiomyopathy.^{13,14}

Semiquantitative assessment of regional systolic function using wall motion score index (WMSI) is an alternative to left ventricular ejection fraction (LVEF) for the assessment of LV systolic function. Regional systolic function has been reported to be superior to global assessment in predicting the combined end point of death, congestive heart failure, and unstable angina in patients with STEMI underwent thrombolytic therapy.^{15,16} Moreover, Moller et al. demonstrated the close relationship between global and regional LV systolic function and they reported that both were reliable and important predictors of adverse outcomes after AMI.¹⁷ Also, they presented the preference of early regional systolic function assessment for risk stratification in cases with non-STEMI or in cases with compensatory regional hyperkinesis.¹⁷

The aim of this study was to investigate firstly the relation between the presence of fQRS complex on admission ECG and WMSI in patients with STEMI underwent primary PCI. The in-hospital and long-term prognostic significance of persistent fQRS was also evaluated.

METHODS

In this retrospective study, 542 patients admitted to large volume tertiary training and research hospital with a diagnose of STEMI underwent primary PCI between February 2010 and March 2011 were included. The patients were enrolled to the study if they fulfilled the following criteria: (1) they had presented within 12 hours from the onset of symptoms (typically, chest pain lasting for >30 minutes), (2) they had ST-segment elevation ≥ 1 mm in two contiguous electrocardiographic leads or new onset of complete left bundle-branch block, and (3) they had primary PCI (angioplasty and/or stent deployment). The exclusion criteria of the present study was age >85 years, inadequate electrocardiographic and echocardiographic images, history of cardiogenic shock, congenital heart disease, severe organ dysfunction such as liver or kidney failure, malignancy, patients died within the first 48 hours, presence of bundle branch blocks, Wolff-Parkinson-White syndrome, Brugada syndrome, patients with suspected subclinical myocardial involvement such as positive history of chronic inflammatory disease states or acute infective conditions and paced rhythm. A total of 622 patients were screened and 542 patients were found to be eligible for the study after applying the exclusion criteria. Study patients were divided into two groups according to the presence or absence of a fQRS on admission ECG. Presence fQRS group (n = 153) was defined as a fQRS(+), and a absence fQRS group (n = 389) was defined as a fQRS(-) groups. All primary PCI procedures were performed in a single high-volume tertiary care center (>3000 PCI/year) by expert interventional cardiologists, who carry out an average of >75 PCI/year and independent from the study. The demographic informations, cardiovascular risk factors and comorbidities and physical examination data on admission were recorded by systematic review of the patient files. A chewable 300 mg acetylsalicylic acid and

600 mg loading dose of clopidogrel were given to all patients before coronary angiography procedure. The hospital's ethics committee approved the study protocol.

Coronary Angiography, Primary Angioplasty, and Stenting

Primary PCI was performed using the percutaneous femoral approach. During the procedure, nonionic low-osmolality contrast media were used and the artery that was presumed to be unobstructed was injected first. Angiographic data of the patients were evaluated from catheter laboratory records. The coronary artery was confirmed to be clinically significant if its stenosis was more than 50%. Blood flow in the infarct-related artery (IRA) was graded according to the Thrombolysis in Myocardial Infarction (TIMI) classification.¹⁸ Heparin (100 IU/kg) was administered when the coronary anatomy was first defined. An angiographic evaluation was made by visual assessment. Primary angioplasty (including balloon angioplasty and/or stent implantation) was performed only for IRA according to lesion type. For each procedure, procedural success during the acute phase was defined as an obstruction and stenosis of the IRA having been reduced to <30% with TIMI III flow after primary PCI. After PCI procedure, all patients were transferred to the coronary care unit and given standard therapy for STEMI which consisted of 300 mg acetylsalicylic acid, 75 mg clopidogrel, an angiotensin-converting enzyme inhibitor, a beta blocker, a statin, and subcutaneous low-molecular weight heparin (enoxaparin). The use of tirofiban was left to the discretion of the operator.

Analysis of Data

A 12-lead ECG was recorded for each patient immediately after hospital admission, 24th hour and 48th hour. In addition, the MI type was determined from the ECG. All ECGs (Nihon Kohden cardiofax S[ECG-1250K, filter range 0.5–150 Hz, AC filter 60 Hz, at a speed of 25 mm/s, and an amplitude of 10 mm/mV]) were analyzed without using any magnification by two independent clinicians who were blinded to the study design and clinical and angiographic data at first 48th hours. fQRS was defined as the presence of various RSR' patterns, including an additional R wave (R') or notching of the R wave

or S wave, or the presence of more than 1 R' (fragmentation) without typical bundle branch block in two contiguous leads corresponding to a major lead set for major coronary artery territory. A notch on an R or S wave was defined as a definite but transient reversal of direction of the main deflection.¹⁹ The interobserver concordance rate in detection of fQRS was 97%. In case of disagreement, the final diagnosis was achieved by mutual agreement. The intraobserver concordance rate was 98%. The QRS duration was determined by measuring the longest QRS in any lead by both manual readings and digital records obtained by the ECG machine.

All transthoracic echocardiographic (TTE) examinations were performed using a machine (GE vivid S6 Vingmedsystem 5, Horten, Norway) equipped with 2.5–4 MHz transducer. Recordings were taken on patients positioned in the left lateral decubitus position. A quantitative assessment of LV systolic function was carried out using the modified biplane Simpson's method to calculate the LVEF.²⁰ WMSI was calculated using a 17-segment model recommended by the American Echocardiography Association.²¹ Regional wall motion score index (RWMSI) were calculated as sum of wall motion scores divided by number of visualized segment. In this scoring system, higher scores indicate more severe wall motion abnormality (1: normal, 2: hypokinesis, 3: akinesis, 4: dyskinesis, and 5: aneurysmal).

On admission, venous blood was obtained from all patients included in the study before coronary angiography procedure. Within 72 hours after admission, CK-MB was measured daily and the maximum value was recorded. The 12-hour fasting serum levels of triglyceride, total cholesterol, low-density lipoprotein (LDL), and high-density lipoprotein (HDL) cholesterol levels were measured by standard enzymatic methods. Other biochemistry measurements were carried out using standard methods.

DEFINITIONS

Reperfusion time was defined as the time from onset of chest pain to first balloon inflation. Door-to-balloon time was defined as the time between hospital admission and balloon inflation. Advanced heart failure was defined as a New York Heart Association classification of ≥ 3 . Renal

failure was defined as a GFR < 60 mL/min per 1.73 m², which was estimated by the simplified Modification of Diet in Renal Disease (MDRD) equation.²² Diabetes mellitus was defined as a previous history of disease, use of diet, insulin or oral antidiabetic drugs, or fasting venous blood glucose level $\geq$ 126 mg/dL on two occasions in previously untreated patients. Hypertension was diagnosed if systolic arterial pressure exceeded 140 mmHg and/or diastolic arterial pressure exceeded 90 mmHg, or if the patient used antihypertensive drugs. Hyperlipidemia was defined as fasting total serum cholesterol > 200 mg/dL, LDL cholesterol > 130 mg/dL, or serum triglycerides > 180 mg/dL or if the patient used lipid-lowering drugs because of a history of hypercholesterolemia.²³ Smoking was defined as the current regular use of cigarettes.

Study Endpoints and Follow-Up

In-hospital and follow-up data were obtained from hospital records or by interviewing (directly or by telephone) patients, their families, or their family physicians. Major adverse cardiac events (MACE) were defined as cardiovascular death, reinfarction, or repeat target vessel revascularization (TVR) (percutaneous or surgical). Cardiovascular mortality was defined as unexplained sudden cardiac death, death due to acute STEMI, decompensated heart failure, or hemodynamically significant arrhythmia. We set the repeat TVR as the need for PCI or coronary artery bypass grafting surgery because of restenosis or reocclusion of the infarct related artery (IRA). Acute stent thrombosis was defined as the abrupt onset of cardiac symptoms (i.e., an acute myocardial infarction) along with an increase in the levels of biomarkers or electrocardiographic evidence of myocardial injury after stent deployment in the first 24 hours, which was accompanied by angiographic evidence of a flow-limiting thrombus near a previously placed stent. Reinfarction was defined based on universal definition of MI guideline.²⁴

Statistical Analysis

Quantitative variables were expressed as mean value $\pm$ standard deviation, and qualitative variables were expressed as a percentage (%). A comparison of parametric values between the two groups was performed by means of two-tailed

Student's *t*-test. Categorical variables were also compared by the likelihood ratio chi-square (χ^2) or Fisher's exact test. Univariate correlations between the fQRS and the other parameters were assessed using Spearman rank correlations test. Multivariate logistic regression analysis was used to identify independent predictors of fQRS. An univariate and backward stepwise multivariate Cox regression analysis, which included variables with P value less than 0.1, were performed to identify independent predictors of cardiovascular mortality. Statistical significance was indicated when a two-sided P value was less than 0.05. All statistical analyses were carried out using the SPSS statistical software, version 16.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

In this study, 542 patients (mean age 55.5 ± 12.8 years, 435 male, 107 female) were enrolled. Patients were classified as fQRS(+) group (n = 153) and fQRS(-) group (n = 389) according to the presence of fQRS on admission ECG. Baseline demographic and angiographic characteristics of the two groups were presented in Table 1. When the two groups were compared, there were no differences with respect to demographic and angiographic characteristics except age and MI localization: the patients in fQRS(+) group were older and had higher prevalence of anterior myocardial infarction at admission as compared to fQRS(-) group.

Laboratory characteristics of fQRS(+) and fQRS(-) groups were summarized in Table 2. Patients in the fQRS(+) group had significantly higher levels of peak creatine kinase-MB, Troponin T, and a lower level of LDL, and total cholesterol levels, compared to the fQRS(-) group. There were no differences between two groups regarding other laboratory characteristics.

Echocardiographic characteristics of fQRS(+) and fQRS(-) groups were presented in Table 3. WMSI, left ventricle end-systolic diameter (LVESD), left ventricle end-diastolic diameter (LVEDD) were found to be significantly higher in fQRS(+) group compared to the fQRS(-) group. However, LVEF was significantly lower in the fragmented group than the nonfragmented group. There was no difference between two groups in terms of left atrium diameter and the degree of mitral regurgitation.

Table 1. Baseline Demographic and Angiographic Characteristics of fQRS (+) and fQRS (–) Groups

	fQRS(+) Group (n:153)	fQRS(–) Group (n:389)	P Value
Age, years	56.88 ± 12.2	54.95 ± 12.8	0.028
Diabetes mellitus, n(%)	39 (25.5)	77 (19.8)	0.146
Hypertension, n(%)	58 (37.9)	144 (37)	0.847
Hyperlipidemia, n(%)	21 (13.7)	63 (16.2)	0.474
Male gender, n(%)	119 (77.8)	316 (81.2)	0.363
Previous CABG, n(%)	2 (1.3)	10 (2.6)	0.368
Previous PCI, n(%)	20 (13.1)	35 (9)	0.160
History of MI, n(%)	25 (16.3)	56 (14.4)	0.568
Current smoker, n(%)	91 (59.5)	227 (58.4)	0.811
Anterior MI, n(%)	90 (58.8)	180 (46.3)	0.009
Reperfusion time, minutes	222.6 ± 133.8	218.9 ± 141.9	0.24
Door-to-balloon time, minutes	35.2 ± 8	34.3 ± 11.6	0.87
Pre-TIMI flow	0.71 ± 1.18	0.83 ± 1.19	0.700
Post-TIMI flow	2.72 ± 0.69	2.73 ± 0.70	0.186
Culprit lesion, n(%) LAD	88 (57.5)	177 (45.5)	0.074
CX	18 (11.8)	53 (13.6)	
RCA	43 (28.1)	150 (38.6)	
Others	4 (2.6)	9 (2.3)	
Stent length, average, mm	23.0 ± 6.7	23.08 ± 6.9	0.680
Stent diameter, average, mm	3.2 ± 0.4	3.2 ± 0.5	0.502
Tirofiban use, n(%)	29 (19)	63 (16.2)	0.441

Mean values (standart deviation) and % (n) were reported for continuous and categorical variables, respectively.
 CABG = coronary artery bypass grafting; MI = myocardial infarction; PCI = percutaneous coronary intervention.

Table 2. Baseline Laboratory Characteristics of fQRS(+) and fQRS(–) Groups

	fQRS(+)Group (n:153)	fQRS(–) Group (n:389)	P Value
Platelet counts, ×10 ⁹ /L	265.7 ± 90.8	255.6 ± 76.8	0.283
WBC, ×10 ⁹ /L	13.1 ± 4.3	12.7 ± 6.6	0.062
Creatinine, mg/dL	0.90 ± 0.3	0.92 ± 0.6	0.186
GFR(MDRD), mL/min/1.73 m ²	104.3 ± 29.9	107.2 ± 28.7	0.303
Troponin T, ng/mL	3.90 ± 4.97	2.62 ± 2.82	0.006
Peak CK-MB, IU/L	117.4 ± 131.0	91.3 ± 109.3	0.037
Total Cholesterol, mg/dL	185.9 ± 40.1	196.7 ± 46.0	0.029
LDL-Cholesterol, mg/dL	119.6 ± 33.1	129.1 ± 37.5	0.019
HDL-Cholesterol, mg/dL	40.4 ± 10.5	38.8 ± 9.6	0.120
Triglyceride, mg/dl	138.7 ± 125.6	155.7 ± 127.8	0.055
Admission blood glucose, mg/dl	157.4 ± 69.7	156.2 ± 75.2	0.562
Admission blood hemoglobin, g/dl	13.6 ± 1.9	13.9 ± 1.9	0.125
MPV, pL	8.6 ± 1	8.7 ± 0.9	0.456

Mean values (standart deviation) and % (n) were reported for continuous and categorical variables, respectively.
 CK-MB = creatinine kinase-MB; GFR = glomerular filtration rate; HDL = high-density lipoprotein; LDL = low-density lipoprotein;
 MDRD = modification of diet in renal disease; MPV = mean platelet volume; WBC = white blood cell.

In multivariate logistic regression analysis; LVEF (Odds ratio [OR] = 0.933, 95% confidence interval [CI] = 0.909–0.957, $P < 0.001$) and Troponin T (OR = 1.071, 95% = 1.011–1.133, $P = 0.019$) were found to be independently related with fQRS even after adjustment of other parameters such as WMSI, LVEF, age, Troponin T, peak CK-MB, LVEDD, LVESD, which had been found

associated with fQRS in univariate analysis. Because of the interrelation between WMSI and LVEF, multivariate analysis was repeated with the removal of LVEF. WMSI (OR = 7.466, 95% = 3.107–17.936, $P < 0.001$) and Troponin T (OR = 1.078, 95% = 1.017–1.143, $P = 0.012$) were found as independent predictors of fQRS.

Table 3. Echocardiographic Characteristics of fQRS(+) and fQRS(-) Groups

	fQRS(+) Group (n:153)	fQRS(-) Group (n:389)	P Value
WMSI	1.43 ± 0.28	1.29 ± 0.21	<0.001
LVEF, %	45.20 ± 9.40	49.34 ± 8.62	<0.001
LVESD, mm	3.40 ± 0.61	3.23 ± 0.54	0.001
LVEDD, mm	4.91 ± 0.55	4.78 ± 0.47	0.012
Left atrium diameter, mm	3.58 ± 0.44	3.63 ± 0.44	0.291
The degree of mitral regurgitation 0	55	159	0.232
1	65	162	
2	21	36	
3	10	29	
4	2	3	

Mean values (standart deviation) and % (n) were reported for continuous and categorical variables, respectively.

WMSI = wall motion score index; LVEF = left ventricular ejection fraction; LVEDD = left ventricle end-diastolic diameter; LVESD = left ventricle end-systolic diameter.

Table 4. The Comparison of fQRS(+) and fQRS(-) Groups in Terms of In-Hospital and Follow-Up Adverse Cardiovascular Events

	fQRS(+) Group (n:153)	fQRS(-) Group (n:389)	P Value
Cardiovascular mortality, n (%)	8 (5.2)	8 (2.1)	0.05
Reinfarction, n (%)	16 (10.5)	15 (3.9)	0.003
TVR, n (%)	10 (6.5)	17 (4.4)	0.297
MACE, n (%)	24 (15.7)	35 (9.0)	0.024
Stroke, n (%)	2 (1.30)	6 (0.4)	0.886
CPR, n (%)	7 (4.6)	7 (1.8)	0.067
VT/VF, n (%)	9 (5.9)	14 (3.6)	0.235
Advanced heart failure, n (%)	27 (17.6)	27 (6.9)	<0.001
IABP, n (%)	7 (4.6)	4 (1.0)	0.014
Atrial fibrillation, n (%)	5 (3.3)	14 (3.6)	0.850
Major bleeding, n (%)	6 (3.9)	14 (3.6)	0.858
All-cause mortality (follow-up), n (%)	20 (13.1)	27 (6.9)	0.022
Cardiovascular mortality (follow-up), n (%)	18 (11.8)	24 (6.2)	0.028
Follow-up time, days	566.1 ± 160.2	563.7 ± 168.7	0.533

Mean values (SD) and % (n) are reported for continuous and categorical variables, respectively.

CPR = cardiopulmonary resuscitation; IABP = Intraaortic balloon pump; MACE = major adverse cardiac events (cardiovascular death, reinfarction, target vessel revascularization); TVR = target vessel revascularization; VT = ventricular tachycardia; VF = ventricular fibrillation.

The comparison of the two groups in terms of in-hospital and follow-up adverse cardiovascular events were reported in Table 4. The in-hospital reinfarction, MACE, intraaortic balloon pump use and advanced heart failure were observed to be significantly more frequent in the fQRS(+) group. The in-hospital mortality noted more often in the fQRS(+) group than in the fQRS(-) group ($P = 0.05$). The mean durations of follow-up for the occurrence of clinical endpoints in fQRS(+) and fQRS(-) groups were 563.7 ± 168.7 and 566.1 ± 160.2 days, respectively. When endpoints were evaluated in relation to the presence of fQRS on admission ECG, 18 patients (11.8%) died in the fQRS(+) group and 24 patients (6.2%) died in the fQRS(-) group

($P = 0.028$). Moreover, the rate of total mortality was found to be significantly higher in the fragmented group than in the nonfragmented group ($P = 0.022$).

We performed a univariate and multivariate analysis to determine the factors associated with long term all-cause deaths (Tables 5 and 6). HT, fragmented QRS, WMSI, LVEF, post TIMI flow, age, and GFR were analyzed using the multivariate cox regression model. Multivariate Cox analyses with three different models were done by using backward selection for predicting long-term death. When all parameters, which were found to be significant in univariate analysis, were included into model 1, age was found to

Table 5. Univariate Analysis for Possible Predictors of Long Term All-Cause Mortality

Variables	OR	CI(%95)	P
HT	1.824	1.029–3.234	0.040
DM	1.279	0.664–2.464	0.462
Fragmented QRS	1.967	1.102–3.511	0.022
WMSI	35.208	13.216–93.792	<0.001
LVEF	0.902	0.877–0.983	<0.001
Post-TIMI flow	0.703	0.502–0.983	0.039
Unsuccessful procedure	2.186	0.855–5.591	0.103
GFR(MDRD)	0.983	0.974–0.991	<0.001
Age	1.053	1.030–1.076	<0.001
Gender (male)	0.683	0.357–1.328	0.265

OR = odds ratio; CI = confidence interval; WMSI = wall motion score index; LVEF = left ventricular ejection fraction; GFR = glomerular filtration rate; MDRD = modification of diet in renal disease; TIMI = thrombolysis in myocardial infarction.

Table 6. Multivariate Analysis for Possible Predictors of Long Term All-Cause Mortality

	Variables	OR	CI(%95)	P
Model 1	HT	1.063	1.032–1.094	0.331
	Fragmented QRS	1.833	0.885–3.930	0.095
	WMSI	5.015	0.505–49.831	0.169
	LVEF	0.96	0.885–0.952	0.188
	Post -TIMI flow	0.868	0.586–1.285	0.479
	GFR(MDRD)	0.993	0.980–1.006	0.313
	Age	1.059	1.026–1.094	0.001
Model 2	Fragmented QRS	1.850	0.918–3.728	0.085
	Age	1.068	1.040–1.098	<0.001
	WMSI	19.270	6.216–59.770	<0.001
Model 3	Fragmented QRS	1.859	1.042–3.314	0036
	Age	1.052	1.029–1.076	<0.001

OR = odds ratio; CI = confidence interval; WMSI = wall motion score index; LVEF = left ventricular ejection fraction; GFR = glomerular filtration rate; MDRD = modification of diet in renal disease; TIMI = thrombolysis in myocardial infarction.

be a significant predictor of long term all-cause mortality ($P = 0.001$). Moreover, model 2 was consisted of parameters such as age, WMSI, and fQRS. Age ($P < 0.001$) and WMSI ($P < 0.001$) were found to be independent significant predictor of long term all-cause mortality. Model 3, which was consisted of age and fQRS, showed that both the age ($P < 0.001$) and fQRS ($P = 0.036$) were independent significant predictors of long term all-cause mortality in patients with STEMI underwent primary PCI. In Kaplan-Meier survival analysis, the all-cause deaths rate was 13.1% in the fragmented QRS group versus 6.9% in the nonfragmented QRS ($P = 0.022$; Fig. 1).

DISCUSSION

The main findings of this study were as follows: (1) WMSI was found to be significantly higher in fQRS(+) group compared to the fQRS(-) group;

(2) WMSI was found as an independent predictor of fQRS, and fQRS was inversely associated with LVEF; (3) the in-hospital reinfarction, MACE, intraaortic balloon pump use, advanced heart failure were found to be significantly more frequent in the fQRS(+) group; (4) the presence of fQRS on admission was found to be associated with an increase in long-term cardiovascular mortality and long term all-cause mortality; and (5) when multivariate Cox analyses with different models were done for predicting long-term death; WMSI and fragmented fQRS were found as independent significant predictors of long term all-cause mortality in patients with STEMI underwent primary PCI. To the best of our knowledge, the relation between fragmented QRS and WMSI, which is the indicator of regional systolic function, was investigated for the first time according to the literature in patient with STEMI underwent primary PCI.

The frequency of fQRS on ECG has been previously presented to be ranging from 34.9%

Figure 1. Kaplan-Meier curve for long term all-cause mortality according to fQRS(+) and fQRS(-) groups in the entire population of patients (P = 0.024 by log-rank test).

to 60.1% in ACS.^{3,5,25} fQRS may occur due to nonhomogeneous activation of ischemic or infarcted ventricles. The possible reason of cardiac arrhythmias and conduction disturbances seems to be related to myocardial inflammation, focal fibrosis, and ischemia within the conduction system.²⁶ Cetin et al. demonstrated that fQRS was independently related to increased C-reactive protein, which is one of the reliable indicator of inflammation.²⁷ fQRS, that may result as an end effect of inflammation at cellular level, can represent an increased cardiac risk by different causative mechanisms in ACS. In our study, consistent with the previous studies, inflammation and myocardial infarction were thought to be responsible for the formation of fQRS and impairment of LV function.

WMSI, which is derived by dividing the sum of the wall motion scores by the number of visualized segments, represents the extent of regional wall motion abnormalities. While, a ventricle with completely normal wall motion would have score index of 1.0, higher score representing progressively greater degrees of ventricular dysfunction. When two-dimensional echocardiography was performed simultaneously with sestamibi single-

photon emission computed tomography (SPECT), the correlation was found between the WMSI and myocardial perfusion defect in patients with acute STEMI. Patients with a WMSI higher than 1.7 had a perfusion defect greater than 20%.²⁸

Mahenthiran et al. reported the fQRS as a marker of elevated stress myocardial perfusion abnormalities and functional deterioration of left ventricle.⁹ Erdem et al. demonstrated a significant negative correlation between fQRS and LVEF in patients with acute STEMI.¹² Das et al. found that the fQRS group had a significantly lower LVEF than the non-fQRS group in patients with CAD.²⁹ Stavileci demonstrated this inverse relation between fQRS and LVEF in STEMI.¹¹ Similar findings have been reported in the study by Angue et al., which LVEF was evaluated with cardiac MRI in patients with AMI. In this study, the presence of fQRS was found to be associated with significant decrease in LVEF.³⁰ In our study, we demonstrated the inverse relation between fQRS and LVEF in STEMI underwent primary PCI, similar to previous studies. Furthermore, our study is the first to present the significant relation between fQRS and WMSI in patient with STEMI underwent primary

PCI. In our study, cardiac enzymes (Troponin T, peak CK-MB) were significantly higher in fQRS(+) group compared to the fQRS(-) group. Patients with fQRS(+) had lower EF and higher WMSI which could be related to the size of myocardial infarction in STEMI. The regional and global LV dysfunctions, which were represented by WMSI and LVEF, respectively, may be due to severe and extensive myocardial injury in fQRS(+) group in STEMI.

Recent studies have demonstrated that fQRS is a predictor of MACE in patients with CAD and ACS.^{13,31} Stavileci et al. reported the relation of persistent fQRS on admission ECG with poor prognosis in acute STEMI. Also, there was a lack of expected mortality benefit of reperfusion therapy, particularly that of fibrinolytic therapy, in STEMI patients with fQRS.¹¹ Moreover, the potential predictive role of the fQRS for MACE and all-cause mortality has been reported in stable CAD and non-STEMI in previous studies.^{6,13,25} Recent studies were also presented that fQRS had been form within 24–48 hours of the symptom onset and persist thereafter and predicted MACE in CAD patients.^{32,33} The positive correlation between presence of the fQRS and MACE demonstrated not only in AMI but also in ischemic cardiomyopathy who had a cardioverter defibrillator implanted.^{29,34} However, Lorgis et al. did not demonstrate the fQRS as an important predictor of MACE in their study, while they were significantly more frequent in fragmented group. In the same study, persistent fragmentation of the QRS had an incremental prognostic value after AMI beyond traditional risk markers.³⁵ In our study, fQRS was found to be significantly related with long term all-cause mortality and long-term cardiovascular mortality and MACE in STEMI underwent primary PCI, consistent with previous studies. Moreover, in our study, not only age but also fQRS and WMSI were found as independent significant predictors of long term all-cause mortality in different models of multivariate Cox analyses. The independent predictive value of fragmented QRS in this setting may be different in various studies. This different result may be due to patient's or culprit lesion characteristics.

Study Limitations

The main limitation of the present study includes retrospective and single-center design, probably

leading to significant referral bias. Also, we did not perform analyses based on the number of leads with fQRS on admission ECG, which may have decreased the predictive value of fQRS. Myocardial perfusion scanning, or magnetic resonance imaging should be used to identify a possible correlation between fQRS and myocardial changes due to ischemia or necrosis. We did not assess a relation between fQRS and long-term MACE except cardiovascular mortality in this study.

CONCLUSION

WMSI was significantly related with the presence of the fQRS, which reflects the linking between impairment of regional LV systolic function and the presence of severe myocardial injury in this setting. Moreover, a significant inverse relation between fQRS and LVEF was reported in this study, in accordance with most of the previously presented studies. We demonstrated that the presence of fQRS on admission ECG was related with higher in-hospital adverse events and long-term cardiovascular mortality in patients with STEMI undergoing primary PCI. The predictive value of fQRS for long term all-cause mortality was also reported with this study.

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