The importance of fragmented QRS complexes in prediction of myocardial infarction and reperfusion parameters in patients undergoing primary percutaneous coronary intervention

Primer perkütan koroner girişime giden hastalarda miyokart enfarktüsü ve reperfüzyon parametrelerinin öngörülmesinde fragmante olmuş QRS komplekslerin önemi

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ABSTRACT

Objectives: The QRS complex fragmentations (fQRS) frequently seen on admission electrocardiograms (ECGs) with narrow or wide QRS complex are associated with increased morbidity and mortality. The causative relationship between fQRS and cardiac fibrosis is known, but the relation of fragmented QRS before and after primary percutaneous coronary intervention (p-PCI) with myocardial infarction and reperfusion parameters has not been studied until now.

Study design: The study included 184 consecutive patients with ST elevation myocardial infarction (STEMI) who underwent p-PCI. Presence or absence of fQRS on pre- and post-PCI ECGs and its change following PCI were investigated. In addition, independent predictors of fQRS were also investigated. Patients with significant organic valve disease and patients having any QRS morphology with QRS duration ≥120 ms as well as patients with permanent pacemakers were excluded from the study.

Results: Patients with fQRS on admission ECG had higher leukocyte counts (p=0.001), higher CK-MB (p=0.001) and troponin levels (p=0.005), increased pain to balloon time (p=0.004), higher Killip score (p<0.001), prolonged QRS time (p<0.001), higher Gensini score (p<0.001) and more frequent Q waves on ECG (p<0.001) in comparison to patients with non-fragmented QRS. In addition, these patients usually had an infarction of anterior territory related to a lesion in proximal LAD and wider jeopardized myocardium (p<0.001). fQRS was significantly related to infarction and myocardial reperfusion parameters before and after p-PCI. In the setting of STEMI, absence of fQRS on admission ECG predicted increased ST resolution, higher reduction in QRS duration, and better myocardial reperfusion.

Conclusion: FQRS may be useful in identifying patients at higher cardiac risk with larger areas of ischemic jeopardized or necrotic myocardium.

ÖZET

Amaç: Başvuru elektrokardiyogramlarında (EKG) sıklıkla görülen, dar ya da geniş QRS yapısı olan QRS kompleks fragmantasyonları (fQRS) artmış morbidite ve mortalite ile ilişkilidir. FQRS ve kardiyak fibroz arasındaki sebepsel ilişki bilinmektedir, fakat primer perkütan koroner girişim (p-PKG) öncesi ve sonrası fQRS'nin miyokart enfarktüsü ve reperfüzyon parametreleri ile ilişkisi şimdiye kadar incelenmedi.

Çalışma planı: Çalışmaya p-PKG'ye giden 184 ardışık ST yükselmeli miyokart enfarktüslü (STEMI) hasta alındı. p-PKG öncesi ve sonrası EKG'lerde fQRS varlığı ya da yokluğu ve p-PKG ile fQRS değişimi araştırıldı. Ek olarak, fQRS'in bağımsız öngörücüleri ayrıca araştırıldı. Anlamlı organik kapak hastalığı olan, 120 ms ve üzerinde QRS süresi olan ve de kalıcı kalp pili olan hastalar çalışmadan dışlandı.

Bulgular: Başvuru EKG'sinde fQRS'i olan hastalar olmayan hastalar ile karşılaştırıldığında daha yüksek lökosit sayılarına (p=0.001), daha yüksek CK-MB (p=0.001) ve troponin (p=0.005) düzeylerine, uzamış ağrı balon sürelerine (p=0.004), daha yüksek Killip skorlarına (p<0.001), uzamış QRS süresine (p<0.001), daha yüksek Gensini skoru (p<0.001) ve EKG'de daha sık Q dalgasına sahipti. Ek olarak, bu hastalar proksimal LAD'de bir lezyon ile ilişkili anteriyor bölge enfarktüsü ve daha geniş tehdit altında bir miyokarda sahipti (p<0.001). fQRS, p-PKG öncesinde ve sonrasında enfarktüs ve miyokardiyal reperfüzyon ile anlamlı bir şekilde ilişkiliydi. STEMI seyrinde başvuru EKG'sinde fQRS'in yokluğu artmış ST rezolüsyonunu, QRS süresinde daha belirgin bir azalma ve daha iyi bir miyokart reperfüzyonunu öngördü.

Sonuç: FQRS daha büyük tehdit altındaki iskemik ya da nekroze olmuş miyokardı olan yüksek kardiyak riskteki hastaların tanımlanmasında yararlı olabilir.

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QRS complex fragmentations are frequently seen on surface electrocardiograms with narrow or wide QRS complex including paced rhythm, bundle branch block or ventricular premature beats.[1] These fragmentations on surface ECG have been associated with increased adverse cardiovascular events in previous studies.[2-5] Fragmented QRS may be important for stratifying patients at high risk for CVEs on admission and after ST elevation myocardial infarction.

fQRS on a 12-lead resting ECG are defined as various RSR′ patterns (≥1 R′ or notching of S wave or R wave) with or without Q waves without a typical bundle-branch block in 2 contiguous leads corresponding to a major coronary artery territory. Sometimes fQRS may be the only electrocardiographic marker of myocardial damage in patients with non-Q myocardial infarction and in patients with resolved Q wave.[6]

The reasons for documented association between fQRS and increased morbidity and mortality, sudden cardiac death and recurrent adverse cardiac events have been investigated in previous studies.[4,5,7-10] In these studies, the main causative mechanism of fQRS was cardiac fibrosis.[11,12] Additionally, fQRS may represent altered ventricular depolarization, which can be derived from mechanisms such as non-homogeneous activation of ischemic ventricles in the setting of STEMI. The causative relationship between fQRS and cardiac fibrosis is known, but the dynamic effects of primary percutaneous coronary intervention on fQRS and their association with MI and reperfusion parameters have not been studied until now.

In this study, we investigated the effect of p-PCI on fQRS and the relationship between the presence of fQRS on pre- and post-PCI ECG and reperfusion parameters in patients with STEMI.

PATIENTS AND METHODS

Patient population and study protocol

The study was conducted in the cardiology clinics at Rize Education and Research Hospital, Rize, Turkey and Ordu State Hospital in Ordu, Turkey. The sample size of our study was determined by patients admitted to our clinic at diagnosis of STEMI within 1 year. One hundred eighty four patients with STEMI and no history of coronary artery disease, who underwent primary PCI at two institutions between 1 January and 31 December 2010, were enrolled consecutively. All patients were examined by an experienced cardiologist immediately after hospitalization.

Abbreviations:

CAD	*Coronary artery disease*
CVE	*Cardiovascular events*
ECG	*Electrocardiogram*
fQRS	*Fragmented QRS complexes*
MI	*Myocardial infarction*
p-PCI	*Primary percutaneous coronary intervention*
STEMI	*ST Elevation myocardial infarction*

Clinical characteristics, which consisted of multiple descriptors from each patient's history and physical examination, were collected by physicians from cardiology clinics for each patient and were stored in the database of coronary angiography laboratory at each institute. We recorded the baseline characteristics, including hypertension, diabetes mellitus, smoking status, family history for CAD, and lipid parameters. Killip score was used for used for risk stratification.[13]

Patients with significant organic valvular heart disease (3 patients) and bundle branch block (LBBB) (4 patients), incomplete or complete RBBB (3 patients) or duration of QRS ≥120 ms (7 patients with intra-ventricular conduction delay), known history of prior MI (10 patients), and patients with permanent pacemakers (1 patient) were excluded from the study. These exclusion criterions were used in to protect the study data from confounding factors other than STEMI origin and location. In the current study, data was retrospectively collected after exclusion of ineligible patients. Informed consent was obtained from all patients prior to the study. The study was performed in accordance with the principles stated in the Declaration of Helsinki.

Laboratory measurements

Cardiac biomarkers levels including creatine kinase (CK), creatine kinase-MB fraction (CK-MB) and Troponin-I and inflammatory markers including leukocyte counts were measured at our emergency department and used in the analyses as admission values. The lipid samples were drawn by venipuncture to perform routine blood chemistry after fasting for at least 8 hours. Glucose, creatinine, and

lipid profile were determined by standard methods. White blood cell (WBC, leukocyte) counts were obtained using an automated cell counter (Coulter Gen-S, COULTER Corp, Miami, USA).

ECG

A 12-lead surface ECG was obtained from all patients in the supine position immediately after their admission to the coronary care unit (CCU). The 12-lead ECG (Nihon Kohden - cardiofax S ECG-1250K, filter range 0.5 Hz to 150 Hz, AC filter 60 Hz, 25 mm/s, 10 mm/mV) was analyzed by two independent clinicians who were blinded to study design and data. A repeat ECG was obtained 90 minutes after p-PCI.

The fQRS was defined by the presence of various RSR' patterns (QRS duration <120 ms) with or without Q wave, which include an additional R wave (R' prime) or notching of the R wave or S wave, or the presence of more than one R prime (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. The presence of fQRS was detected by inspection of tracings with the naked eye. Analysis of the standard 12-lead ECG was performed without using any magnification. In case of disagreement, the final diagnosis was achieved by mutual discussion. Fragmentations were considered to be present if a visually identifiable signal was demonstrated in all complexes of a particular lead. In this case, for statistical analysis, fQRS was defined to be present if found in ≥2 contiguous leads in anterior, lateral or inferior derivations. We also determined the number of fQRS representing a number of fQRS ≥2 and one fQRS complex alone not accepted as indicating the presence of fQRS.

The QRS time was measured by manual and digitalized methods and significant difference was not found between the two methods. QRS time was determined by the longest QRS in any lead.[6] There was a 99% concordance for ECG interpretation of the presence of fQRS and non-fQRS.

The diagnosis of acute STEMI was made as previously described.[14] The diagnosis of acute STEMI was also confirmed by demonstrating the culprit lesion by coronary angiography.[15]

Pathologic Q wave: Any Q wave in lead V2 or V3 ≥0.02 seconds or QS complex in leads V2 and V3 Q wave ≥0.03 seconds and ≥0.1 mV deep or QS complex in lead I, II, aVL, aVF, or V4 to V6 in any 2 leads of a contiguous lead grouping (I, aVL, and V6; V4 to V6; and II, III, and aVF), and R wave ≥0.04 seconds in lead V1 or V2 and R/S ratio ≥1 with a concordant positive T wave in the absence of a conduction defect was considered as pathologic.[14]

Jeopardized myocardium was determined by the sum of ST elevations (in mm) on each ST elevated derivation on pre- and post-PCI ECGs (Total ST elevation score). Percentage of total ST resolution was calculated by the following formula: (Sum of ST elevations on Pre-PCI ECG) - (Sum of ST elevations on Post-PCI ECG) / (Sum of ST elevations on Pre-PCI ECG) x 100.

Delta QRS time was calculated by the following formula: (Pre-PCI QRS duration) - (Post-PCI QRS duration).

Coronary angiography and primary PCI

All of the patients took 300 mg aspirin and 600 mg clopidogrel prior to the procedure. At the start of the procedure, 10.000 IU intravenous heparin was administered. Coronary stenting directly, or followed by balloon angioplasty, was performed where eligible. Diameters of vessel and stent and dilatation procedure were recorded during PCI. Glycoprotein IIb-IIIa inhibitor (tirofiban) was administered at the preference of the operator. After the procedure, patients were followed in the intensive coronary unit (ICU) until stabilization. All of the patients were treated according to the recommendations of ACC/AHA Guidelines for the Management of Patients with STEMI.[16]

Selective coronary angiography was performed urgently at the hemodynamic laboratory using Standard Judkins technique through the femoral artery. Multiple views were obtained in all patients, with visualization of the left anterior descending and left circumflex coronary in at least 4 views, and the right coronary artery in at least

2 views. Atherosclerotic coronary involvement was assessed by the number of vessels involved (vessel score) and by a severity score. Significant stenosis was determined visually and defined as ≥50% reduction in lumen diameter in any view compared with the nearest normal segment. Vessel score ranged from 0 to 3, depending on the vessels involved (0: <50% luminal narrowing, 1, 2 and 3: number of luminal narrowed vessels of ≥50%). Coronary atherosclerotic burden was assessed using the Gensini score.[17] The TIMI (Thrombolysis In Myocardial Infarction) Flow Grade was used to scale coronary flow.[18] The TIMI Myocardial Blush grade score was used to evaluate microvascular perfusion.[19]

Statistical analysis

Continuous variables were reported as mean ±

Table 1. Baseline characteristics of the study population

Pre-PCI Parameters (admission)	Fragmentation on admission ECG				
	Non-fragmented QRS (n=94)		Fragmented QRS (n=90)		
	%	Mean±SD	%	Mean±SD	*p*
Age (years)		61±12		62±13	0.56
Gender (male)	80		82	0.75	
Body mass index (kg/m^2)		27.2±3.9		27.1±4.3	0.95
Hypertension	31		33		0.73
Diabetes mellitus	52		49		0.72
Smoking	37		38		0.93
Hyperlipidemia	54		60		0.33
Family history of CAD	21		20		0.89
Heart rate (bpm)		82±18		86±19	0.16
Systolic blood pressure (mmHg)		130±24		131±28	0.82
Diastolic blood pressure (mmHg)		82±11		81±13	0.46
Plasma blood glucose (mg/dl) (Adm.)		155±66		161±73	0.61
Creatinine (mg/dl)		1.0±0.3		1.1±0.4	0.26
Total cholesterol (mg/dl)		177±34		192±42	0.07
LDL (mg/dl)		114±28		126±35	0.12
HDL (mg/dl)		38±8		38±8	0.75
Triglyceride (mg/dl)		140±80		148±84	0.65
Leukocytes (10^3/mm^3)		12±3.3		13.8±4.0	**0.001**
Neutrophils (/mm^3)		7946±2891		9885±3541	**<0.001**
Lymphocyte (/mm^3)		2527±1724		2327±1169	0.38
Monocyte (/mm^3)		683±488		845±476	0.031
Hemoglobin (mg/dl)		14±1.9		14±2.2	0.57
Gensini score		52±23		67±27	**<0.001**
CK (U/L) (Adm.)		410±523		905±1147	**<0.001**
CK-MB (U/L) (Adm.)		61±59		106±87	**0.001**
AST (U/L) (Adm.)		64±112		88±93	0.014
LDH (U/L) (Adm.)		394±288		512±427	0.039
Troponin I (ng/mL) (Adm.)		2.4±6.0		7.7±14.5	**0.005**

CAD: Coronary artery disease; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; NS: Not significant; Adm.: Admission value; PCI: Percutaneous coronary intervention; CK: Creatinine kinase; CK-MB: Creatinine kinase muscle/brain; LDH: Lactate dehydrogenase.

standard deviation; categorical variables were defined as percentages. Continuous variables were compared by Student's t-test and the chi-squared test was used for the categorical variables between two groups. The Pearson's correlation coefficient was used for correlation analyses. Mean values were compared by ANOVA using Tukey's post hoc test among different groups. Logistic regression analysis was used for multivariate analysis of independent variables. All tests of significance were two-tailed. Statistical significance was defined as $p<0.05$. The SPSS statistical software (SPSS 15.0 for Windows, Chicago, IL, USA) was used for all statistical calculations.

RESULTS

The baseline clinical characteristics are shown in Table 1. Mean number of fQRS was 3±1 in patients with fQRS. Patients with fQRS on admission ECG had higher leukocyte counts ($p=0.001$), and especially neutrophil counts ($p<0.001$), higher

Table 2. Infarction related parameters and their association with fragmentations on pre-PCI ECG

Pre-PCI (n)	nfQRS (n=94)		fQRS (n=90)		
	%	Mean±SD	%	Mean±SD	*p*
Pain to balloon time (hours)		4±2		5±3	**0.004**
Killip score (3/4)	3		23		**<0.001**
IRA					
LAD	38		64		
Cx	35		20		**0.002**
RCA	27		16		
Territory of STEMI (Anterior)	38		64		**<0.001**
Number of ST elevated derivations		3.7±1.3		4.9±1.7	**<0.001**
Total ST elevation on Pre-PCI ECG (mm)		8.9±5.9		12.8±7.6	**<0.001**
Number of obstructed vessels ≥50%		1.9±0.7		1.8±0.8	0.32
Total occlusion in IRA	79		82		0.62
Q wave on ECG	27		41		0.039
Gensini score		52±23		67±27	**<0.001**
QRS duration (ms) Pre-PCI (Adm.)		88±13		96±14	**<0.001**
Tirofiban use	27		41		0.039
Location (segment) of lession (LAD)					
Proximal	17		39		
Mid	75		61		0.012
Distal	8		0		
Location (segment) of lession (Cx)					
Proximal	7		7		
Mid	57		75		0.12
Distal	38		0		
Location (segment) of lession (RCA)					
Proximal	9		32		
Mid	62		68		**0.004**
Distal	29		0		

IRA: Infarct related artery; nfQRS: Non-fragmented QRS; fQRS: Fragmented QRS; TIMI: Thrombolysis in myocardial infarction coronary flow grade; LAD: Left anterior descending artery; Cx: Circumflex coronary artery; RCA: Right coronary artery; STEMI: ST elevated myocardial infarction; PCI: Percutaneous coronary intervention.

Table 3. Change of fQRS by p-PCI and its relationship with infarction and reperfusion parameters

Perfusion parameters (n)	Pre-PCI (–) Post-PCI (–) (n=71) Group 1	Pre-PCI (+) Post-PCI (–) (n=23) Group 2	Pre-PCI (–) Post-PCI (+) (n=23) Group 3	Pre-PCI (+) Post-PCI (+) (n=67) Group 4	*p*
Percentage of total ST resolution (%)	64±29	62±27	56±35	41±52†	**0.008**
Total ST elevation on Pre-PCI ECG (mm)	8.6±5.2	13.1±7.6	9.6±7.8	13.0±7.7†	**0.001**
Total ST elevation on Post-PCI ECG (mm)	3.5±3.5	5.3±4.8	4.7±6.2	7.4±6.5†	**<0.001**
QRS duration (ms) Pre-PCI	89±14	97±14†	87±10	96±14†	**<0.001**
QRS duration (ms) Post-PCI	80±12	91±14†	88±11†	91±12†	**<0.001**
Delta QRS time (ms)	-7±13	-5±13	1±9†	-5±11	**0.039**
Post-PCI TIMI score (2 and 3) (%)	87	100	96	82	0.13
Post-PCI Blush score (2 and 3) (%)	79	44†	87	49†	**<0.001**
CK (U/L) (Adm.)	394±505	1031±1384†	474±603	909±1112†	**0.004**
CK-MB (U/L) (Adm.)	62±60	111±90†	62±61	109±86†	**0.001**
Troponin I (ng/mL) (Adm.)	2.5±6.9	7.6±13.3	2.3±3.7	8.4±15.3†	**0.032**
Neutrophils (/mm^3)	7897±2808	8223±2896	8164±3281	10481±3585†	**<0.001**

Absence (–) and presence (+) of FQRS; CK: Creatinine kinase; CK-MB: Creatinine kinase muscle/brain; TIMI: Thrombolysis in myocardial infarction coronary flow grade; STEMI: ST elevated myocardial infarction; PCI: Percutaneous coronary intervention.
† When compared with group 1 (pre and post-PCI fQRS negative) by post-hoc Tukey test, p<0.05.

CK-MB (p=0.001) and troponin levels (p=0.005), increased pain to balloon time (p=0.004), higher Killip score (p<0.001), prolonged QRS duration (p<0.001), higher Gensini score (p<0.001) and more frequent Q waves on ECG (p<0.001) in comparison to patients with non-fragmented QRS. Additionally, these patients usually had an infarction on anterior territory often related to a lesion in proximal LAD and wider jeopardized myocardium (p<0.001) (Table 2) and fQRS on post-PCI ECG was correlated with decreased ST segment resolution (p=0.008) (Table 3). In Table 3 the study parameters are presented in groups determined by the presence or absence of fQRS on pre-PCI and post-PCI ECGs. Four groups were formed according to the changes in fQRS status after PCI. While patients in Group 4 (fQRS both present on admission and after PCI) had the lowest percentage in ST segment resolution and lower post-PCI blush score compared to patients in Group 1 (No fQRS).

Table 4. Correlations of number of fQRS complexes with myocardial infarction and reperfusion parameters

Variables	Pre-PCI		Post-PCI	
Percentage of total ST resolution	r=-0.211	p=0.004	r=-0.268	p<0.001
Total ST elevation on Pre-PCI ECG (mm)	r=0.285	p<0.001	r=0.165	p=0.03
Total ST elevation on Post-PCI ECG (mm)	r=0.334	p<0.001	r=0.259	p=0.001
Delta QRS time (reduction in ms)	r=-0.044	p=0.6	r=-0.211	p=0.005
QRS duration (ms) Pre-PCI	r=0.308	p<0.001	r=0.178	p=0.02
QRS duration (ms) Post-PCI	r=0.314	p<0.001	r=0.330	p<0.001
Post-PCI TIMI score	r=-0.089	p=0.2	r=-0.088	p=0.2
Post-PCI Blush score	r=-0.387	p<0001	r=-0.187	p=0.01
Gensini score	r=0.279	p<0.001	r=0.025	p=0.8

TIMI: Thrombolysis in myocardial infarction coronary flow grade; PCI: Percutaneous coronary intervention.

Table 5. Independent predictors for pre and post PCI fQRS

	Logistic regression				
Model 1	Presence of fQRS (Admission, pre-PCI)				
Independent variables	β	SE	Wald	OR 95% CI	*p**
QRS duration (ms) (admission)	0.1	0.02	11.2	1.067 (1.028-1.107)	**0.001**
Total ST elevation score on Pre-PCI ECG (mm)	0.1	0.04	6.9	1.115 (1.028-1.210)	**0.009**
Number of ST elevated derivations (Adm.)#	0.6	0.2	11.3	1.876 (1.300-2.708)	**0.001**
Territory of STEMI (Anterior)#	1.9	0.6	11.1	6.703 (2.188-20.538)	**0.001**
Gensini score	0.03	0.01	6.9	1.028 (1.007-1.049)	**0.009**
Leukocytes (mg/dl)	0.1	0.07	1.9	1.107 (0.958-1.279)	0.17
Neutrophils (mg/dl)#	0.07	0.08	0.8	1.073 (0.917-1.256)	0.38
Troponin I	0.05	0.03	3.6	1.056 (0.998-1.117)	0.05
CK-MB#	0.01	0.003	4.7	1.006 (1.001-1.012)	0.03
Q wave on ECG	0.6	0.5	1.1	1.756 (0.607-5.079)	0.29
Model 2	Presence of fQRS (90. minute, post-PCI)				
QRS duration (ms)					
Post-PCI	0.04	0.02	4.9	1.040 (1.005-1.076)	0.03
Total ST elevation on Post-PCI ECG (mm)	0.1	0.05	3.7	1.095 (0.998-1.202)	0.05
Territory of STEMI (Anterior)#	0.9	0.4	5.3	2.488 (1.141-5.425)	0.02
Percentage of total ST resolution#	-0.01	0.01	3	0.998 (0.975-1.002)	0.08
Leukocytes (mg/dl)	0.1	0.05	3.9	1.112 (1.000-1.236)	0.04
Neutrophils (mg/dl)#	0.1	0.06	3.7	1.129 (0.997-1.277)	0.06
Troponin I	0.03	0.02	2.5	1.035 (0.992-1.079)	0.12
CK-MB#	0.003	0.002	1.3	1.003 (0.998-1.008)	0.25
Post PCI Blush score (0/1)	0.3	0.5	0.5	1.379 (0.536-3.545)	0.51

STEMI: ST elevation myocardial infarction; CK-MB: Creatinine kinase muscle/brain; OR: Odds Ratio; CI: Confidence Interval; β: βeta Coefficient; SE: Standard error; * Logistic regression analyses with step wise method were used for the multivariate analysis of independent variables which were included if they were significantly different in the univariate analyses. # When included as an independent variable in the analysis.

Patients without fQRS achieved increased ST resolution (p=0.008), higher reduction in QRS duration (p=0.039) and better myocardial reperfusion (p<0.001) in comparison to patients with fQRS on any ECG (Table 3).

The relationship of the number of fQRS with reperfusion parameters are presented in Table 4. The number of fQRS correlated negatively with percentage of total ST resolution and myocardial reperfusion score and correlated positively with QRS duration, the extent of coronary involvement and total ST elevation on admission and after PCI.

We performed logistic regression analysis to determine the independent variables for the presence of fQRS on admission and after PCI (Table 5). Independent predictors were QRS duration, total ST elevation score, Gensini score, CK-MB levels, anterior MI for fQRS on admission, and QRS duration and anterior MI for post-PCI ECG respectively. In these analyses, presence of fQRS before and after PCI was related to wider jeopardized myocardium and infarction, but presence of fQRS after PCI was not directly related to myocardial reperfusion.

DISCUSSION

In this study, we evaluated the relationship between the presence of fQRS on admission and post-PCI

ECGs and myocardial reperfusion parameters in patients with STEMI. We found that fQRS was related to higher inflammatory state, prolonged QRS time, greater extent of infarction and jeopardized myocardium and myocardial perfusion before and after primary PCI. Patients without fQRS achieved increased ST resolution, higher reduction in QRS duration and better myocardial reperfusion in comparison to patients with fQRS.

Although fQRS is defined as unexpected deviation in the QRS morphology, the exact cause of QRS complex fractionations on surface ECG is not entirely known. FQRS predicts cardiac events in different populations. Pathophysiologically, fQRS is generally due to regional myocardial fibrosis or scarring and data suggest that ischemia might cause fQRS via nonhomogeneous myocardial electrical activation.[20-24] In patients with ischemic or non-ischemic left ventricular dysfunction, fQRS correlated with myocardial fibrosis.[25] In previous studies in which Gadolinium delayed enhancement on cardiac magnetic resonance imaging was used to determine myocardial structure, fQRS has shown a correlation with extensive myocardial scar.[11,12] FQRS was also found to be a marker of a prior MI, demonstrated by regional perfusion abnormalities with scintigraphic evaluation, which has a substantially higher sensitivity and negative predictive value compared to the Q wave.[6,26] Regional fQRS patterns denote the presence of a correspondingly greater focal regional myocardial scar on stress myocardial perfusion imaging.[27] Additionally, chronic ischemia may cause patchy myocardial fibrosis without prior MI.[28]

Myocardial ischemia is a well-known cause of heart failure and ventricular arrhythmias due to development of scar tissue, which is related to increased mortality and morbidity.[6,20,27,29] Non-homogenous depolarization of myocardium caused by ischemia and infarction may be the main determinant for increased arrhythmic events during the course of hospitalization in the setting of STEMI. The extent of infarcted myocardium on admission was assessed by admission cardiac biomarkers in our study and fQRS independently correlated with the extent of infarcted myocardium at admission. This relationship was significant for CK and CK-MB especially, but not for Troponin I. This may be related to late increases in Troponin levels in the setting of STEMI. On the other hand, we did not use peak troponin levels, a potential study limitation. Additionally, we also found a significant relationship between fQRS and the extent and severity of CAD. This may be due to increased jeopardized ischemic myocardium that may in turn also contribute to non-homogenous conduction in the myocardium.[2,23]

In patients with STEMI, prolonged QRS time was associated with increased long term mortality due to increased incidence of heart failure, arrhythmia and ischemia.[30-32] In our study, prolonged QRS time was related to fQRS even in a relatively normal range of QRS (<120 ms). This observed relationship may have two possible explanations. Either fragmentation on QRS complex is induced by prolongation in QRS time or fragmentation on QRS increases the duration of the QRS complex. However, we can only speculate as to the cause or results of QRS fragmentation. This interaction should be studied further to clarify causal relationship in an electrophysiological study.

Although post-PCI TIMI myocardial reperfusion grade was significantly related to the presence of fQRS on admission, this relationship was not valid at post-PCI ECG. In our opinion, myocardial stunning and hibernation concepts may explain this conflict. At the cellular level, electrical homogeneity can be restored slowly in these situations despite sufficient myocardial reperfusion. We speculate that in some patients, fragmentations were related to presence of stunned myocardium that may resolve in the course of disease and in other situations cannot be resolved due to presence of myocardial scar.

Fragmented QRS, which may be derived from the effects of the individual risk factors, MI, and perfusion related factors on myocardial electricity at cellular level, can represent increased cardiac risk by different causative mechanisms in patients with STEMI. Twelve-lead surface ECG, which is an inexpensive, non-invasive, and easily apprehensible method, is presently the gold standard in differential diagnosis, determining treatment methods, and performing risk stratification of STEMI. fQRS

may be useful for identifying patients at higher cardiac risk with larger areas of ischemic jeopardized or necrotic myocardium, and it can provide information about the presence of enhanced heterogeneity of myocardial conduction and cardiac electrical instability in an individual patient.

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Key words: Coronary artery disease; electrocardiography; heart failure/diagnosis; myocardial infarction; myocardial reperfusion; primary coronary intervention; prognosis; risk factors; ST elevation myocardial infarction.

Anahtar sözcükler: Koroner arter hastalığı; elektrokardiyografi; kalp yetersizliği/tanı; miyokart enfarktüsü; miyokart reperfüzyonu; primer koroner girişim; prognoz; risk faktörü; ST yükselmeli miyokart enfarktüsü.