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Outcomes of preoperative fragmented QRS detection on operative and postoperative events in patients undergoing elective coronary artery bypass grafting

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ABSTRACT

Objectives: This study aims to investigate the preoperative electrocardiographic data of patients who were candidates for elective coronary artery bypass grafting (CABG) in terms of fragmented QRS (fQRS) presence and to evaluate short-term outcomes of fQRS on operative and postoperative courses.

Patients and methods: Between January 2019 and April 2022, a total of 178 patients (137 males, 41 females; mean age: 61.4±9.3 years; range, 39 to 85 years) who underwent elective CABG were retrospectively analyzed. Preoperative electrocardiographic examinations were performed to detect fQRS. The patients were divided into two groups according to presence of fQRS as the fQRS+ (n=35) and fQRS– (n=143) group. Demographic, clinical, laboratory, operative, and postoperative data of both groups were evaluated.

Results: The mean duration of cardiopulmonary bypass (p=0.017) and number of CABG (p=0.026) in the fQRS group were found to be significantly higher, while the mean preoperative left ventricular ejection fraction values were lower in this group (p<0.001). There was a significant increase in the left ventricular ejection fraction values at the postoperative third month in the fQRS+ group (p<0.001). Mortality encountered in 5.7% in the fQRS+ group, while this rate was 2.7% in the fQRS– group (p=0.336).

Conclusion: Preoperative detection of QRS fragmentations on admission electrocardiograms may have an additional value in predicting postoperative cardiac status and short-term prognosis in patients undergoing CABG.

Keywords: Atrial fibrillation, coronary artery bypass grafting, coronary vessels, myocardial contraction.

Fragmented QRS (fQRS) is a depolarization disorder that can be detected on a 12-lead surface electrocardiography (ECG) and indicates local myocardial fibrosis.[1] The fQRS was first described by Flowers et al.[2] in 1969 as the appearance of an additional R wave (R′) in relation with an important coronary artery region, or notching in the S wave, or the presence of >1 R′ (fragmentation) in two adjacent ECG diversions. In 1973, Boineau and Cox[3] described fragmentary bipolar potentials secondary to coronary ischemia in an animal experiment. In general, the fQRS is defined as a notching in the R wave, a notching in the S wave, RSR′ pattern or more than one R′ in at least two consecutive leads corresponding to the myocardial tissue which is vascularized by the major coronary arteries. Myocardial fibrosis leads to conduction delays which causes non-homogeneous ventricular depolarization, resulting in a notching of the QRS complex on ECG. The fQRS is a finding associated with an increased cardiovascular risk due to coronary artery disease (CAD).[4] Several studies have shown an association between the increase in the number of leads with fQRS and the degree of myocardial fibrosis, cardiovascular morbidity, and mortality.[5]

Coronary artery disease is one of the leading causes of cardiovascular morbidity and mortality. It is responsible for about 30% of mortality over the age of 35 in developed countries.[6] Coronary artery bypass grafting (CABG) is one of the most common procedures to treat CAD.[7] In the present study, we aimed to investigate the effects of fQRS on operative

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and postoperative courses in patients undergoing elective CABG, to identify the cardiovascular risk profiles of the patients, and to identify the need for closer follow-up in post-CABG patients.

PATIENTS AND METHODS

This single-center, retrospective study was conducted at Medicana International Istanbul Hospital, Department of Cardiovascular Surgery between January 2019 and April 2022. A total of 178 patients (137 males, 41 females; mean age: 61.4±9.3 years; range, 39 to 85 years) who underwent elective CABG during the study period were included. Exclusion criteria were as follows: having pacemakers, undergoing emergent CABG, and previous valve surgery. A 12-lead ECG was performed preoperatively in all patients with a filtration rate of 0.15 to 100 Hz, AC filtration of 60 Hz, 25 mm/h speed, 10 mm/mV amplitude settings in the supine position. All ECGs were evaluated for the presence of QRS by two cardiologists who were blinded to the study design. The QRS fragmentation was defined on a 12-lead ECG as an additional R wave (R′), notching on a R or S wave, RSR pattern or multiple R′s on two adjacent leads with or without a Q wave on the QRS wave. According to the presence of fQRS on surface ECG, the patients were divided into two groups as the fQRS+ (n=35) and fQRS− (n=143) group. Demographic characteristics of the patients such as age, sex, body mass index (BMI) and clinical data such as comorbidities were recorded. Both groups were compared in terms of high-sensitivity C-reactive protein (hs-CRP), lipid profile, complete blood count parameters, left ventricular ejection fraction (LVEF) values on transthoracic echocardiography, cardiopulmonary bypass (CPB) duration, number of CABG, aortic clamp time (ACT), duration of intubation, length of intensive care unit (ICU) stay and hospital stay, postoperative new-onset atrial fibrillation (POAF), and mortality rates.

Statistical analysis

Statistical analysis was performed using the R version 4.2.0 software (R Core Team; R Foundation for Statistical Computing, Vienna, Austria). Continuous data were presented in mean ± standard deviation (SD) or median (min-max), while categorical data were presented in number and frequency. The compatibility of quantitative data with normal distribution was examined using the Shapiro-Wilk test. In terms of quantitative data, the Student t-test or Mann-Whitney U test was used for the comparisons of the groups. In terms of categorical data, the chi-square test or Fisher exact test was used to compare the groups. To predict the presence of fQRS, area under curve (AUC), sensitivity and specificity values and 95% confidence intervals (CIs) under the receiver operating characteristics (ROC) curve were used and the diagnostic accuracy of significant variables in the univariate analysis was examined. The most optimal cut-off value was determined, as the value corresponding to the maximum Youden index (J=Sensitivity+Specificity-1). Postoperative risk factors for the presence of fQRS were determined in the univariate logistic regression model and multiple logistic regression model was further applied. The odds ratio (OR) values obtained from the models and the corresponding 95% CI values were presented. The "pROC" library was used in the *R* program (by Xavier Robin, Switzerland) for ROC analysis. A *p* value of <0.05 was considered statistically significant.

RESULTS

Of a total of 178 patients included in the study, the fQRS was detected in 35 (19.6%) patients. Demographic, clinical, laboratory, operative and postoperative data of both groups are summarized in Table 1. On transthoracic echocardiography performed before elective CABG, the mean left LVEF values of the patients with fQRS+ were 41.51±10.96% (range, 28 to 60%) (p<0.001). The mean neutrophil/lymphocyte ratios were found 2.73±2.32 (range, 0.71 to 20.8), whereas the mean platelet/lymphocyte ratios were 126.89±124.32 (range, 39.19 to 1481.2) and the mean eosinophil/lymphocyte ratios were 0.09±0.08 (range, 0.002 to 0.578), respectively.

All patients in the study received a standard CABG anesthesia. Sternotomy was performed in all patients. Left internal mammary artery and great saphenous vein grafts were prepared. The patients were operated under CPB and under cardioplegic arrest. The mean number of CABG in the fQRS+ group was 4.71±0.99 (range, 1 to 8) (p=0.026). The mean CPB duration was 135.46±27.64 (range, 28 to 192) min and the mean ACT was 67.2±17.94 (range, 20 to 109) min. The diagnostic accuracy of the variables in predicting the presence of fQRS is summarized in Table 2 and Figures 1 and 2. Five (14%) patients needed inotropic support

Table 1
Demographic, clinical, laboratory, operative, and postoperative data of patients

	fQRS + (n=35)				fQRS – (n=143)				
	n	%	Mean±SD	IQR	n	%	Mean±SD	IQR	*p*
Age (year)			60.94±9.37	39-85			61.8±9.18	43-83	0.625‡
Sex									0.069†
Male	31	88.5			106	74.1			
Female	4	11.5			37	25.9			
BMI (kg/m^2)			28.31±4.24	21.56-39.33			29.13±4.55	18.67-41.52	0.254*
Diabetes mellitus	21	60			54	37.7			0.106†
Hypertension	17	48.5			64	44.7			0.684†
LDL (mg/dL)			150.5±32.85	91-289			144.31±33.47	100-240	0.280*
Triglyceride (mg/dL)			222.19±154.74	43-1279			216.6±106.45	101-707	0.487*
Preoperative LVEF (%)			41.51±10.96	28-60			52.14±8.54	30-68	<0.001*
Postoperative 3rd month LVEF (%)			52.06±10.99	36-70			57.38±6.15	36-70	<0.001*
N/L			2.73±2.32	0.71-20.8			2.81±1.46	1.04-6.98	0.205*
P/L			126.89±124.32	39.19-1481.2			108.03±41.39	45.39-233.65	0.428*
E/L			0.09±0.08	0.002-0.578			0.07±0.06	0.013-0.267	0.335*
hs-CRP (mg/L)			8.8±16.74	0.2-88.12			6.21±8.91	1-40.91	0.577*
Number of coronary artery bypass grafts			4.71±0.99	1-8			4.22±1.18	2-7	0.026*
CPB duration (min)			135.46±27.64	28-192			119.63±30.73	26-187	0.017*
ACT (min)			67.2±17.94	20-109			60.97±16.87	40-126	0.074*
Inotrop need after CPB	5	14.2			9	6.3			0.155¶
POAF	3	8.5			3	2.1			0.091¶
Duration of intubation (h)			9.19±13.46	6-168			16.51±28.61	6-144	0.072*
Duration of ICU (day)			2.46±1.4	2-9			2.15±0.84	2-10	0.020*
Duration of in-hospital stay (day)			5.51±2.65	5-18			5.79±1.48	5-20	0.010*
Mortality	2	5.7			4	2.7			0.336¶
Follow-up (month)			12.31±6.74	7-24			13.54±7.84	8-24	0.425*

fQRS: Fragmented QRS; SD: Standard deviation; IQR: Interquartile range; BMI: Body mass index; LDL: Low-density lipoprotein; LVEF: Left ventricular ejection fraction; N: Neutrophil count; L: Lymphocyte count; P: Platelet count; E: Eosinophil count; hs-CRP: High-sensitivity C-reactive protein; CPB: Cardiopulmonary bypass; ACT: Aortic clamping time; POAF: Postoperative new-onset atrial fibrillation; ICU: Intensive care unit; p value extracted from ‡ Student t-test; † Chi-square test; * Mann-Whitney U test (U); ¶ Fisher exact test.

Table 2
The diagnostic accuracy of the variables in predicting the presence of fQRS

	fQRS +		fQRS –			AUC (95% CI)			Sensitivity (95% CI)		Specificity (95% CI)	
	Mean±SD	IQR	Mean±SD	IQR	Cut-off point	Mean±SD	IQR	*p*	Mean±SD	IQR	Mean±SD	IQR
CPB duration (min)	135.46±27.64	28-192	119.63±30.73	26-187	≥97.5	0.631	0.533-0.729	0.017	1	1-1	0.211	0.144-0.278
Number of coronary artery bypass grafts	4.71±0.99	1-8	4.22±1.18	2-7	≥3.5	0.616	0.522-0.71	0.026	0.971	0.916-1	0.224	0.155-0.292
Preoperative LVEF (%)	41.51±10.96	28-60	52.14±8.54	30-68	≤46.5	0.784	0.688-0.881	<0.001	0.686	0.532-0.84	0.881	0.828-0.934
Postoperative LVEF (%)	52.06±10.99	36-70	57.38±6.15	36-70	≤57.5	0.784	0.698-0.871	<0.001	0.629	0.468-0.789	0.817	0.753-0.881

fQRS: Fragmented QRS; AUC: Area under curve; CI: Confidence interval; CPB: Cardiopulmonary bypass; LVEF: Left ventricular ejection fraction.

after CPB in the fQRS+ group. The mean duration of intubation in the fQRS+ group after CABG was 9.19±13.46 (range, 6 to 168) h. The mean

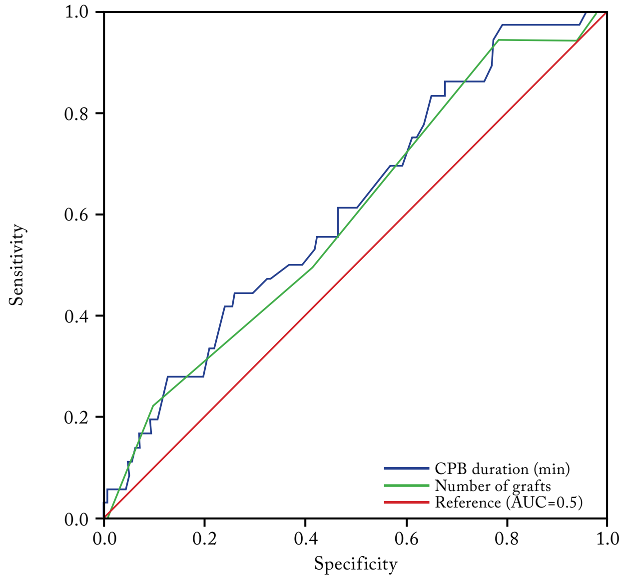

Figure 1. Diagnostic accuracy of values in predicting the presence of fQRS-ROC curve. High values predict the presence of QRS fragmentation.

CPB: Cardiopulmonary bypass; AUC: Area under curve; ROC: Receiver operating characteristics.

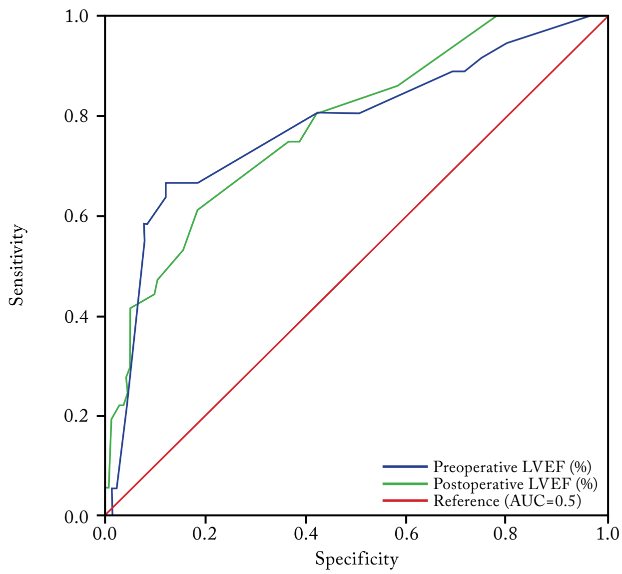

Figure 2. Diagnostic accuracy of values in predicting the presence of fQRS - ROC curve. Low values predict the presence of QRS fragmentations.

LVEF: Left ventricular ejection fraction; AUC: Area under curve; ROC: Receiver operating characteristics.

length of ICU stay and hospital stay was 2.46±1.4 (range, 2 to 9) days (p=0.020) and 5.51±2.65 (range, 5 to 18) days (p=0.010), respectively. Three (8.5%) patients developed in the fQRS+ group. Overall, the postoperative mortality rate was 3.3% (n=6). Mortality was observed within the first 30 days postoperatively. Three (1.7%) patients died from cerebrovascular diseases (CVD), two (1.1%) from pneumoniae, and one (0.55%) from pulmonary embolism. There were two mortality cases in the fQRS+ group, and both patients died from CVD.

Overall, the mean follow-up was 12.31±6.74 (range, 7 to 24) months. The mean LVEF values of the patients in the fQRS+ group at three months were 52.06±10.99% (range, 36 to 70%) (p<0.001).

DISCUSSION

In the present study, we investigated whether the detection of fQRS complexes on ECG in preoperative evaluations of patients undergoing elective CABG was a predictor to determine postoperative cardiac status, short-term prognosis, and mortality. Our study results showed that the duration of CPB (p=0.017), the number of CABG (p=0.026), length of ICU stay (p=0.020), and length of hospital stay (p=0.010) in the fQRS+ group were statistically significantly higher, while preoperative LVEF values were statistically significantly lower (p<0.001). The increase at the postoperative third month in the LVEF values in these patients was statistically significant (p<0.001). However, there was no statistically significant difference between the neutrophil/lymphocyte and hs-CRP values in the fQRS+ group. Hypertriglyceridemia, diabetes mellitus, and hypertension were not statistically significantly different between the groups. Additionally, no statistically significant difference was observed in the rate of POAF, the most common arrhythmia after CABG. The prevalence of fQRS was more common in male patients in our study, whereas increasing age and BMI did not affect the prevalence of fQRS.

Coronary artery bypass grafting is frequently utilized in the treatment of CAD.[8] Although long-term survival is satisfactory after CABG, arrhythmia, need for recurrent myocardial revascularization, cerebrovascular events, sudden death and heart failure may be encountered in approximately one-third of patients in the postoperative follow-up.[9-11] The presence of preoperative fQRS is frequently associated with decreased myocardial contractility and multiple coronary artery occlusions, as evidenced by a decrease in LVEF.[12] It has been shown that patients with preoperative fQRS have significantly lower LVEF values.[13-15] In addition, unlike previous studies, the increase in LVEF at three months after CABG in patients with fQRS+ was statistically significant in our study. Neutrophil/lymphocyte, platelet/lymphocyte, and eosinophil/lymphocyte ratios, and hs-CRP in patients with fQRS+ provided valuable data, particularly following acute coronary syndrome.[16,17] In our study, there was no statistically significant difference in the rate of activated neutrophils, which are the first and most commonly detected white blood cell subtype in damaged myocardial tissue in patients with fQRS, and furthermore lymphocyte count were not also quantifying a diagnostic accuracy, either. Furthermore, there were no significant changes in hs-CRP values, platelet/lymphocyte and eosinophil/lymphocyte ratios in our study.

Postoperative new-onset atrial fibrillation, the most common arrhythmia after CABG, is observed in nearly 10 to 40% of cases.[18] Early and late postoperative POAF increases morbidity.[19] The first study in the literature on the presence of preoperative fQRS to be a significant risk factor for new-onset POAF after CABG was published by Çetin et al.[20] Also, Keskin and Kurtul[21] showed that POAF rate and in-hospital mortality rate were higher in patients with fQRS. However, our study indicates that the presence of preoperative fQRS does not have a statistically significant effect on the development of new-onset POAF.

The QRS fragmentation may be an indicator of early myocardial injury preceding the appearance of fibrosis and scar, and may be used for risk stratification in patients with CAD.[22] Considering the link between multiple critical CAD and fQRS, the increase in the number of CABG and the consequently prolonged CPB durations have gained importance. We consider that revascularization of patients with fibrosis secondary to myocardial ischemia and detection of fQRS in which scar formation is etiologically prominent should be treated with CABG. Preoperative 12-lead ECG is an important diagnostic method in determining morbidity and mortality after CABG. The effects of rhythm disturbances such as long QT interval, T wave alternance, P wave dispersion and atrial fibrillation, which can be detected by 12-lead ECG, on mortality and morbidity after CABG have been investigated in the literature.[23-25] However, short- and long-term effects of fQRS on morbidity and mortality after CABG have not been examined thoroughly, paving the way for us to conduct the current study. Based on these results, the presence of fQRS is an important marker of morbidity and mortality in post-CABG due to inter- and intraventricular conduction abnormalities secondary to myocardial fibrosis.

The single-center, retrospective design of this study is the main limitation. Although our results showed that fQRS could be a predictor for short-term outcomes, further long-term studies are needed to elucidate the effects of the presence of preoperative fQRS on postoperative course following CABG.

In conclusion, the QRS fragmentation on a 12-lead surface ECG has recently gained increasing attention as a simplified non-invasive ECG marker with diagnostic and prognostic value in CAD. It is a very simple method to evaluate patients who are scheduled for elective CABG with a significant predictor in terms of morbidity and mortality that may be encountered in the early postoperative period. Detection of QRS fragmentations is also a cost-effective method to identify patients who would need close follow-up and treatment in the postoperative period. With the detection of fQRS in patients to be treated with elective CABG, patient groups at a higher risk category can be identified. Patients with fQRS regarding fibrosis secondary to myocardial ischemia should be treated with CABG. The QRS complex fragmentations detected on ECG at the time of initial admission may be useful to identify patients at high cardiovascular risk who would need closer follow-up and treatment after CABG.

Ethics Committee Approval: This was a retrospective and single-center study which was approved by the Medicana International Istanbul Hospital Ethics Committee (date: 12.08.2022, no: 2022/041) and was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Idea/concept, design, data collection and/or processing, analysis and/or interpretation, literature review, writing the article: B.Ş.; Analysis and/or interpretation, critical review: G.G.; Literature review, critical review: A.Ö.

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