Fragmented QRS may predict postoperative atrial fibrillation in patients undergoing isolated coronary artery bypass graft surgery

Fragmente QRS izole koroner arter baypass greftleme operasyonu geçiren hastalarda postoperatif atriyal fibrilasyon gelişimini öngörebilir

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ABSTRACT

Objective: Fragmented QRS complexes (fQRS) are defined as various RSR' patterns in 2 contiguous leads corresponding to a major coronary artery territory. Although the reason of association between fQRS and cardiac events was documented as cardiac fibrosis, the predictive role of fQRS was not studied for postoperative atrial fibrillation (POAF) which is a frequent and serious complication in patients undergoing isolated coronary artery bypass graft (CABG) surgery. Therefore, this issue was investigated in the present study.

Methods: The current study has a prospective observational design. Two hundred and seventy two eligible patients who underwent isolated CABG surgery were enrolled consecutively. The patients were divided in two groups with post-op atrial fibrillation (AF) and non-AF. The occurrence of new-onset AF following CABG and the relationship with fQRS were searched. The logistic regression analysis was used to determine independent predictors for POAF. The sensitivity and specificity of study variables in predicting POAF were calculated using a receiver-operating characteristic curve (ROC).

Results: POAF occurred in 62 of 272 patients (22.8%). Patients with POAF were generally older (p<0.001) and female (p=0.006), with preexisting hypertension (p=0.008), lower hemoglobin levels (p=0.011), chronic obstructive lung disease (p=0.003), prolonged QRS time (p=0.004), and higher EUROSCORE (p<0.001) compared to non-AF patients. Patients with POAF had lower left ventricular ejection fraction (p<0.001) and high fQRS rate (p<0.001), but similar left atrial size (LA, p=NS). Interestingly, LA size was significantly enlarged in patients with fQRS (3.8±0.6 vs. 4.1±0.5 cm, p=0.002). In addition, the patients with POAF had prolonged stay in the cardiac surgery intensive-care unit (p<0.001) and extended in-hospital care (p=0.001). New-onset POAF was significantly related to the presence and number of fQRS. In the logistic regression analysis, only age (OR: 1.044, 95% CI: 1.008-1.082, p=0.016), female gender (OR: 2.347, 95% CI: 1.079-5.106, p=0.031), the presence and number of fQRS (OR: 6.020, 95% CI: 3.152-11.5 and OR: 1.522, 95% CI: 1.282-1.807, both of, p<0.001) were independent predictors of POAF. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and the diagnostic accuracy (DA) of presence of fQRS on pre-op electrocardiogram to predict POAF were 66%, 76%, 45%, 88% and 74%, respectively. The area under ROC was found as 0.733 (p<0.001, 95% CI: 0.657-0.810).

Conclusion: In our study, we found that new-onset POAF was independently related to the presence and number of fQRS in patients undergoing CABG surgery. In addition, fQRS on pre-op surface ECG had high predictive values for new-onset POAF. *(Anadolu Kardiyol Derg 2012; 12: 576-83)*

Key words: Fragmented QRS, postoperative atrial fibrillation, coronary artery bypass graft surgery, sensitivity, specificity, predictive value, regression analysis

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ÖZET

Amaç: Fragmente olmuş QRS kompleksleri (fQRS) bir majör koroner arter bölgesine karşılık gelen 2 ardışık derivasyonda çeşitli RSR' paternleri olarak tanımlanılmaktadır. FQRS ve kardiyak olaylar arasında miyokardiyal fibrozisin sebepsel ilişkisi ortaya konulmuş olsa da, izole koroner arter baypass greftleme cerrahisi (KABG) yapılan hastalarda sık ve ciddi bir komplikasyon olan postoperatif atriyal fibrilasyon (POAF) için fQRS'in öngörücü rolü şimdiye kadar araştırılmamıştır. Bundan dolayı bu ilişki çalışmamızda incelendi.

Yöntemler: Çalışma gözlemsel yapılı olarak düzenlendi. İzole KABG cerrahisine giden, çalışma kriterlerine uygun 272 hasta ardışık olarak çalışmaya dahil edildi. Hastalar postoperatif atriyal fibrilasyon (AF)'u olan ve olmayan olmak üzere iki gruba ayrıldı. KABG cerrahisini takiben yeni başlangıçlı AF gelişimi ve fQRS ile ilişkisi araştırıldı. Lojistik regresyon analizi POAF'yi öngören bağımsız değişkenlerin belirlenilmesinde kullanıldı. Çalışma parametrelerinin POAF'yi öngörmedeki duyarlılık ve özgüllükleri ROC eğrisi altında kalan alan ile hesaplandı.

Bulgular: POAF 272 hastanın 62'sinde (%22.8) gelişti. POAF'lı hastalar AF'siz hastalar ile karşılaştırıldığında, genellikle daha yaşlı (p<0.001) ve bayandı (p=0.006). Bu grupta hipertansiyon (p=0.008), düşük hemoglobin düzeyi (p=0.011), kronik obstruktif akciğer hastalığı (p=0.003), uzamış QRS süresi (p=0.004) ve yüksek EUROSCORE (p<0.001) daha sık saptandı. POAF'lı hastalar daha düşük sol ventrikül ejeksiyon fraksiyonu ve daha yüksek fQRS oranları sergilerken (p<0.001), benzer sol atriyal çapa sahiptiler (p>0.05). İlgi çekici bir bulgu sol atriyum boyutunun fQRS'li hastalarda artmış olmasıydı (3.8±0.6 vs. 4.1±0.5 cm, p=0.002). Ek olarak, POAF'lı hastalar daha uzun kardiyak cerrahi yoğun bakım ünitesi yatışına (p<0.001) ve uzamış hastane içi bakım sürelerine gereksinim duydular (p=0.001). Yeni başlangıçlı POAF, fQRS varlığı ve sayısı ile istatistiksel olarak anlamlı bir ilişkiye sahipti. Lojistik regresyon analizinde, sadece yaş (OR: 1.044, %95 GA: 1.008-1.082, p=0.016), kadın cinsiyet (OR: 2.347, %95 GA: 1.079-5.106, p=0.031), fQRS'in varlığı ve sayısı bağımsızdır (OR: 6.020, %95 GA: 3.152-11.5 and OR: 1.522, %95 GA: 1.282-1.807, her ikisi için de; p<0.001). POAF gelişimi için bağımsız etkenlerdi. Operasyon öncesi elektrokardiyogram üzerindeki fQRS'in varlığının POAF'ı öngörmedeki duyarlılığı, özgüllüğü, pozitif öngörücü değeri, negatif öngörücü değeri ve tanısal kesinliği sırasıyla %66, %76, %45, %88 ve %74 idi. ROC eğrisi altındaki alan 0.733 (p<0.001, %95 GA: 0.657-0.810) olarak belirlendi.

Sonuç: Bu çalışmada yeni başlangıçlı POAF, KABG cerrahisi yapılan hastalarda fQRS'in varlığı ve sayısı ile bağımsız anlamlı bir ilişkiye sahipti. Ek olarak, operasyon öncesi yüzey EKG'si üzerindeki fQRS olması yeni başlangıçlı POAF gelişimi için yüksek öngörücülük değerlerine sahipti. *(Anadolu Kardiyol Derg 2012; 12: 576-83)*

Anahtar kelimeler: Fragmente QRS, postoperatif atriyal fibrilasyon, koroner arter baypass greftleme, duyarlılık, özgüllük, öngörücü değer, regresyon analiz

Introduction

The QRS complex fragmentations, frequently seen on the surface electrocardiograms (ECGs) with narrow or wide QRS complex, include paced rhythm, bundle branch block or ventricular premature beats (1). These fragmentations on surface ECG were associated with increased adverse cardiovascular events (CVEs) in previous studies (2-5). The reason of documented association between fragmented QRS (fQRS) and increased morbidity and mortality, sudden cardiac death and recurrent CVEs were investigated by several studies (4-10). In these studies, the main causative mechanism of fQRS was cardiac fibrosis (11,12).

Additionally, fQRS may represent altered ventricular depolarization, caused by heterogeneous activation of ischemic ventricles. Sometimes, fQRS might be the only electrocardiographic marker of myocardial damage in patients with non-Q myocardial infarction and in patients with resolved Q wave (6).

Fragmented QRS is related to myocardial scar, heterogeneous depolarization and chronic ischemia. Elevated ventricular filling pressure due to abnormal LV diastolic and systolic functions may be a potential pathophysiological mechanism for left atrial enlargement and POAF. To our knowledge, there is not any report investigating risk of new-onset POAF after CABG surgery in patients with fQRS.

We hypothesized that fragmented QRS complexes (fQRS) may be useful for determining patients at high risk for new-onset postoperative atrial fibrillation (POAF) which is a frequent and serious complication of coronary artery bypass graft (CABG) surgery.

In this study, we investigated the predictive value and the relationship of fQRS with new-onset POAF. The results of this study may have an additional importance in identifying patients, eligible for preventive treatments of POAF, undergoing isolated CABG surgery.

Methods

Study design
The current study has a prospective observational design.

Study population
The study was conducted in the cardiology and cardiovascular surgery departments at the Rize Education and Research Hospital in Rize, Turkey. Two hundred and seventy two eligible patients who underwent isolated CABG surgery at our institution between January 2009 and December 2010 were enrolled consecutively.

Of the 272 patients included in the study, the diagnosis was stable angina pectoris (SAP) in 57% of patients, unstable angina pectoris/non-ST elevation myocardial infarction (USAP/NSTEMI) in 32% of patients, ST segment elevation myocardial infarction (STEMI) in 11% of patients.

Patients with a preoperative history of AF, moderate or significant organic valvular heart disease, left or right incomplete or complete bundle branch block, antiarrhythmic use, duration of QRS≥120 msn and patients with permanent pacemakers were excluded from the study. In addition, we only included patients undergoing electively cardiac surgery after hospitalization; therefore, patients undergoing emergency cardiac surgery were also excluded.

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The study was performed in accordance with the principles stated in the Declaration of Helsinki and approved by the Local Ethics Committee.

Study protocol and definitions

Clinical characteristics, which consisted of multiple descriptors from each patient's history and physical examination, were collected by physicians from the cardiology and cardiovascular surgery clinics of each patient prior to CABG surgery and were stored at our institution. We recorded the baseline characteristics, which include hypertension, diabetes mellitus, smoking history, family history for coronary artery disease (CAD), and lipid parameters.

Previous MI was defined as a myocardial infarction occurred within 90 days.

POAF was defined as any episode of atrial fibrillation within the hospital stay after CABG surgery.

Study variables

In our study, POAF was a predictor variable and the outcome variables were presence and number of fQRS. All demographical, biochemistry and hematological parameters, the echocardiographic measurements, medications as well as of were used as baseline variables. In addition to the patient characteristics, the surgical and follow-up parameters were used as possible confounding variables in the analyses.

Electrocardiography
Definition and determination of fragmented
QRS prior surgery

A 12-lead admission ECG was obtained from all patients. The 12-lead ECG (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 blind to study design and data. The fQRS on a 12-lead resting ECG 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) (≥1 R' or notching of S wave or R wave) without typical bundle branch block in two contiguous leads corresponding to a major lead set for major coronary artery territory (6) (Fig. 1).

Any QRS morphology with QRS duration ≥120 ms, including bundle branch block or intra-ventricular conduction delay were excluded from study. Analysis of the standard 12-lead ECG was performed without using any magnification, and fragmentations were considered to be present if a visually identifiable signal was demonstrated in all complexes of a particular lead. In this wise, for statistical analysis, fQRS was defined to be present if found in ≥2 contiguous anterior leads, lateral leads, or inferior leads. The QRS duration was determined by the longest QRS in any lead.

Documentation of new-onset atrial fibrillation after cardiac surgery

All patients were monitored for the occurrence of POAF with continuous electrocardiographic telemetry until the day of dis-

charge from the hospital. A standard, 12-lead electrocardiogram was recorded on the day of discharge for each patient. POAF was based on documentation of AF episodes with continuous telemetry throughout hospitalization after cardiac surgery.

EuroSCORE

The European System for Cardiac Operative Risk Evaluation (EuroSCORE), which uses several risk factors to predict the mortality of cardiac surgery (13,14), was calculated for all patients.

Statistical analysis

The SPSS statistical software (SPSS 15.0 for windows, Inc., Chicago, IL, USA) was used for all statistical calculations. Continuous variables are given as mean±standard deviation; categorical variables are defined as percentages. Continuous variables were compared by Student t test and the Chi-square test was used for comparison of categorical variables between two groups. Spearman's rank correlation coefficient was used to analyze relationships between study variables. The binary logistic regression analysis with enter method was used for all relevant independent variables predictive of POAF with a p value <0.15 in the univariate analysis including age, gender, hypertension, COPD, hemoglobin level, LMCA involvement, left ventricular EF, QRS time, presence and number of fQRS, clinical diagnosis, perioperative hypotension and drugs. Further the analysis was repeated after a pre-elimination with backward likelihood ratio method for the independent variables. The sensitivity and speci-
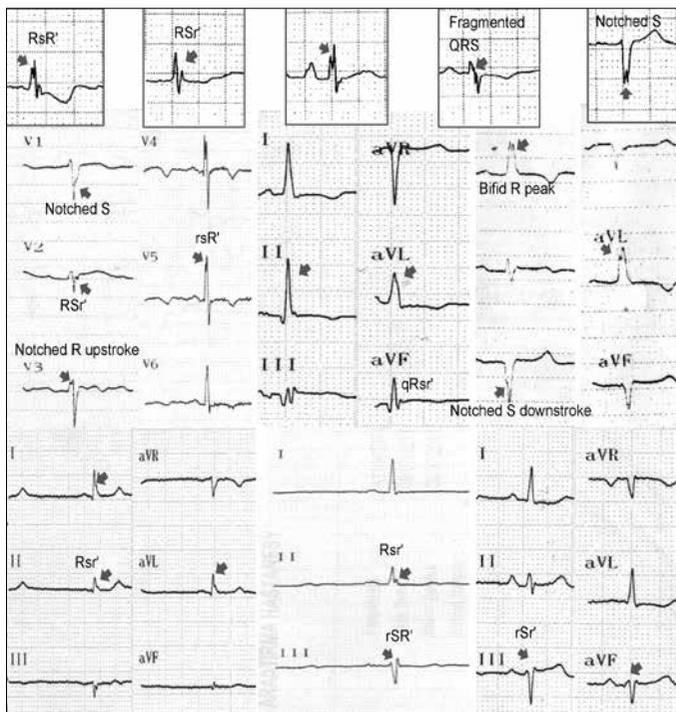

Figure 1. The various types of notched and fragmented QRS complexes used for selecting patients in our study
Different fQRS patterns are shown by arrows including rSr´, rSR´, RSr´, notched R up-stroke, notched S down-stroke, bifid R peak and bifid R nadir

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ficity of study variables in predicting POAF were calculated using a receiver-operating characteristic curve (Fig. 1). In addition, the positive predictive value (PPV), negative predictive value (NPV) and the diagnostic accuracy (DA) of fQRS for prediction of POAF were calculated. All tests of significance were two-tailed. Statistical significance was defined as p< 0.05.

Results

Baseline clinical and perioperative characteristics

POAF occurred in 62 of 272 patients (22.8%). Data are stratified according to new-onset POAF and the baseline characteristics of the patients are detailed in Table 1. Surgical data is presented in Table 2.

Patients with POAF were generally older (p<0.001) and female (p=0.006), with preexisting hypertension (p=0.008), lower hemoglobin levels (p=0.011), chronic obstructive lung disease (COPD, p=0.003), prolonged QRS time (p=0.004) and higher EUROSCORE (p<0.001) compared to non-AF patients (Table 1, 2). Patients with POAF had lower left ventricular EF (p<0.001) and high fQRS rate (p<0.001), but similar left atrial size (p>0.05). Interestingly, left atrium was significantly enlarged in patients with fQRS (3.8±0.6 vs. 4.1±0.5cm, p=0.002).

Pre-operative use of beta-blockers, angiotensin converting enzyme inhibitors, angiotensin-receptor blockers or oral antidiabetics/insulin was not different significantly between the two groups. While non-AF group had higher statin use, POAF group had higher usage of calcium channel blockers. In addition, the patients with POAF had prolonged stay in the cardiac surgery intensive-care unit (CSICU, p<0.001) and extended in-hospital care (p=0.001). New-onset POAF was significantly related to the presence and the number of fQRS (Table 2).

Correlations of number of fQRS with study parameters

The number of fQRS significantly correlated with left ventricular ejection fraction (r=-0.452, p<0.001), left atrial size (r=0.317, p<0.001), EUROSCORE (r=0.303, p<0.001), QRS time (r=0.479, p<0.001), stay in CSICU (r=0.459, p<0.001) and extended in-hospital care (r=0.385, p<0.001).

The predictive value of fQRS for POAF

In the binary logistic regression analysis, only age (OR: 1.044, 95% CI: 1.008-1.082, p=0.016), female gender (OR: 2.347, 95% CI: 1.079-5.106, p=0.031), the presence and number of fQRS (OR: 6.020, 95% CI: 3.152-11.5 and OR: 1.522, 95% CI: 1.282-1.807, both of, p<0.001) were independent predictors of POAF (Table 3).

The sensitivity and the specificity of FQRS for detecting POAF in the study participants were evaluated by ROC analysis. The area under ROC was found as 0.733 (95% CI: 0.657-0.810, p<0.001) (Fig. 2). Sensitivity, specificity, PPV, NPV and DA of presence of fQRS on pre-op ECG to predict new-onset POAF were 66%, 76%, 45%, 88% and 74%, respectively.

Discussion

In this study, we investigated the predictive value and the relationship of fQRS with new-onset POAF. We revealed a significant association between new-onset POAF and pre-operative, operative and postoperative poor prognostic factors and the presence of fQRS. Additionally, fQRS had high predictive values for POAF. To our knowledge, this is the first report demon-

Table 1. Baseline characteristics of the study population according to the presence or absence of new-onset postoperative atrial fibrillation

Variables	New-onset postoperative atrial fibrillation		
	Non-AF (n=210)	POAF (n=62)	*p
Age, years	61±9	66±9	<0.001
Gender, female, %	14	30	0.006
Height, cm	167±7	166±9	NS
Weight, kg	79±11	82±17	NS
BMI, kg/m^2	29±4	30±6	NS
Hypertension, %	57	75	0.008
Diabetes mellitus, %	44	48	NS
Smoking, %	49	47	NS
Hyperlipidemia, %	56	57	NS
Family history of CAD, %	22	24	NS
Admission blood glucose, mg/dL	130±58	136±54	NS
Na$^+$, mmol/L	140±0.4	137±0.6	NS
K$^+$, mmol/L	4.3±0.06	4.4±0.03	NS
BUN, mg/dL	36±13	41±9	0.011
Creatinine, mg/dL	1.0±0.3	1.0±0.2	NS
eGFR, mL/min	86±26	81±27	NS
Total cholesterol, mg/dL	178±48	172±44	NS
LDL, mg/dL	112±37	111±38	NS
HDL, mg/dL	36±9	38±11	NS
Triglyceride, mg/dL	152±89	136±66	NS
Leukocytes, 10^3/mm^3	8.1±2.1	7.7±2.0	NS
Neutrophils, 10^3/mm^3	5.0±1.7	5.0±1.9	NS
Hemoglobin, mg/dL	13.6±1.4	13.0±1.2	0.011
Medications (pre-operative)			
ACEi / ARB, %	40	44	NS
Beta-blockers, %	72	74	NS
CCB, %	7	18	0.013
Statin, %	55	37	0.012
OAD/Insulin, %	15	18	NS

Data are presented as mean±standard deviation and percentages
*unpaired Student t and Chi-square tests
ACEI - angiotensin converting enzyme inhibitor, AF - atrial fibrillation, ARB - angiotensin II receptor blocker, BMI - body mass index, BUN - blood urea nitrogen, CAD - coronary artery disease, CCB - calcium channel blocker, eGFR - estimated glomerular filtration rate, HDL - high-density lipoprotein, LDL - low-density lipoprotein, NS - not significant, OAD - oral anti-diabetic drugs, POAF - postoperative atrial fibrillation

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Table 2. Fragmented QRS and the prognostic markers in patients with and without new-onset POAF

Variables	New-onset postoperative atrial fibrillation		
	Non-AF (n=210)	POAF (n=62)	*p
Pre-CABG characteristics			
Clinical diagnosis, % (SAP/NSTEMI-USAP/STEMI)	55/ 34/ 11	62/ 28 / 10	NS
History of CVE, %	1	2	NS
History of PAD, %	38	47	NS
COPD, %	17	34	0.003
CRF, %	1	1	NS
LMCA involvement, %	9	20	0.029
EUROSCORE	2.8±1.9	4.4±2.4	<0.001
QRS time, ms	90±10	96±12	0.004
Q wave on ECG, %	18	19	NS
Presence of fQRS, %	24	66	<0.001
Number of fQRSs, n	0.8±1.6	2.1±1.9	<0.001
The location of fQRS, %			
Anterior (V1-V4)	9	30	<0.001
Inferior (II, III, aVF)	21	46	<0.001
Lateral (V5, V6, I, aVL)	6	16	0.014
LVEF, %	54±13	46±11	<0.001
LA diameter, cm	3.8±0.6	3.9±0.7	NS
CABG and in-hospital course			
Number of used grafts	2.9±0.9	3.0±1.1	NS
LIMA use, %	94	89	NS
Number of saphenous grafts	2±1	2±1	NS
Technique of CABG (off-pump), %	4	8	NS
Re-thoracotomy[†], %	4	5	NS
Duration of cross-clamp time, minutes	60±24	65±25	NS
Duration of extracorporeal circulation, minutes	95±31	105±37	0.066
Perioperative hypotension[‡], %	35	63	<0.001
Duration of stay in CSICU, hours	39±11	56±30	<0.001
Duration of in-hospital care, days	7±3	9±3	0.001

Data are presented as mean±standard deviation and percentages
*unpaired Student t and Chi-square tests
AF - atrial fibrillation, CABG - coronary artery bypass graft surgery, COPD - chronic obstructive lung disease, CRF - chronic renal failure, CSICU - cardiac surgery intensive-care unit, LIMA - left internal mammary artery, LMCA - left main coronary artery, LVEF - left ventricular ejection fraction, NSTEMI-USAP-non-ST segment elevated myocardial infarction-unstable angina pectoris, SAP - stable angina pectoris, STEMI-ST segment elevated myocardial infarction, CVE - cerebrovascular event, PAD - peripheral artery disease, POAF - postoperative atrial fibrillation
[†]Revision operation: need of new surgery for surgical infection or bleeding
[‡]reported as the need for inotropic support (dopamine, dobutamine or intraaortic balloon pump)

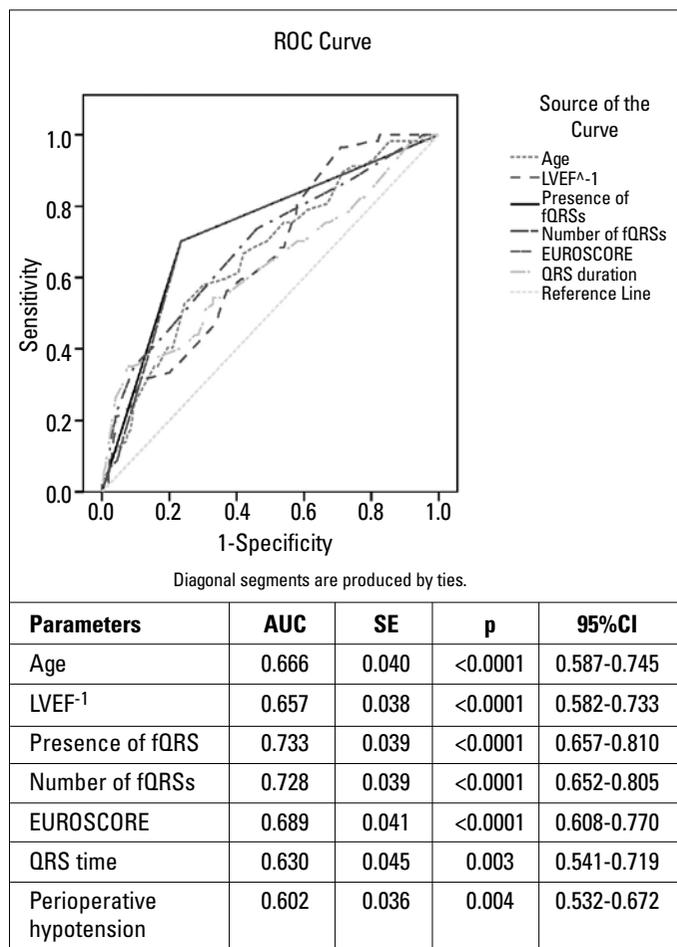| Parameters	AUC	SE	p	95%CI
Age	0.666	0.040	<0.0001	0.587-0.745
LVEF^{-1}	0.657	0.038	<0.0001	0.582-0.733
Presence of fQRS	0.733	0.039	<0.0001	0.657-0.810
Number of fQRSs	0.728	0.039	<0.0001	0.652-0.805
EUROSCORE	0.689	0.041	<0.0001	0.608-0.770
QRS time	0.630	0.045	0.003	0.541-0.719
Perioperative hypotension	0.602	0.036	0.004	0.532-0.672

Figure 2. Receiver-operating characteristic curves for the sensitivity and the specificity of age, left ventricular ejection fraction-1, presence and number of fQRS, EUROSCORE and QRS duration to detect postoperative atrial fibrillation
AUC - area under the curve, CI - confidence interval, LVEF - left ventricular ejection fraction, SE - standard error

strating an increased risk of new-onset POAF after CABG surgery in patients with fQRS.

Atrial fibrillation is a relatively frequent complication of cardiac surgery, occurring in approximately 25%-40% of patients following CABG (15-17). In our study, POAF occurred in 22.8% of patients who had undergone isolated CABG surgery. In a large previous retrospective study, Shen et al. (18) reported a 29% incidence of POAF after isolated CABG. In this study, all patients received continuous 24-hour telemetry with arrhythmia-detection algorithms during their hospital stay. POAF incidence in our study was comparable to this study, which was performed in a similar patient population.

POAF is associated with increased mortality and morbidity following CABG (19, 20). Besides, POAF may lead to longer intensive care and in hospital stay with higher usage of hospital resources, all of which in turn significantly increase cost (21). Although new-onset POAF is usually a transient arrhythmia, cerebral embolism is a well-known complication of AF in the postoperative patient. Separately, POAF may cause severe cardiovascular results including heart failure, ischemia, infarction, induction of ventricular arrhythmias and even death at high-risk patients.

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Table 3. The binary logistic regression analysis of independent predictors for development of POAF

Independent variables	Odds Ratio (95% CI)	*p	Odds Ratio (95% CI)	**p
Age, years	1.049 (1.004-1.096)	0.034	1.044 (1.008-1.082)	0.016
Gender, female	2.718 (1.065-6.935)	0.036	2.347 (1.079-5.106)	0.031
Hypertension,+	1.638 (0.728-3.687)	0.233		
COPD,+	1.174 (0.504-2.733)	0.710		
Hemoglobin, mg/dL	1.076 (0.794-1.459)	0.637		
LMCA involvement,+	1.400 (0.396-4.950)	0.601		
LV EF%	0.977 (0.945-1.011)	0.180		
QRS time, ms	1.012 (0.976-1.050)	0.517		
fQRS,+	4.371 (1.796-10.64)	0.001	6.020 (3.152-11.50)	<0.001
[†]Number of fQRSs	1.359 (1.079-1.705)	0.009	1.522 (1.282-1.807)	<0.001
Clinical diagnosis, ACS, +	0.716 (0.340-1.510)	0.380		
Perioperative hypotension, +	1.423 (0.636-3.184)	0.390		
Drugs				
Statin usage, +	0.689 (0.317-1.499)	0.348		
CCB usage, +	1.929 (0.627-5.935)	0.252		

*Logistic regression with enter method was used for multivariate analysis of relevant all independent variables with p value <0.15 in univariate analysis. **After pre-elimination of the variables with backward: LR method
ACS - acute coronary syndrome, BMI - body mass index, CCB - calcium channel blocker, COPD - chronic obstructive lung disease, LMCA - left main coronary artery, LVEF - left ventricular ejection fraction, POAF - postoperative atrial fibrillation
[†]when included in the analysis.

POAF is 'multi-factorial' pathophysiologically. Surgical interventions, structural heart disease and the ageing of the heart might facilitate AF. In our study, age, female gender and the presence of fQRS on pre-op ECG were independent predictors of POAF. Fragmented QRS, which might be derived from the effects of inflammatory and structural factors on myocardial electricity at the cellular level, may represent cardiac status and possibly increased POAF risk by different causative mechanisms in patients undergoing surgery. The exact pathophysiological mechanisms, responsible for the onset and maintenance of POAF, are not totally understood. The mechanisms of POAF are beyond the scope of this study and in the present study, we focused mainly on the role of fQRS for the prediction of POAF. In our opinion, fQRS may have an additional importance in identifying patients, eligible for preventive treatments of POAF, undergoing isolated CABG surgery.

Although fQRS is defined as unexpected deviations in the QRS morphology, what exactly causes QRS complex fractionations on surface ECG is not totally known yet? FQRS predicts cardiac events in variable populations. In addition to previous studies, in a recent study Erdoğan et al. (22) had also searched the relationship of fQRS with prognostic markers and in-hospital MACE in patients undergoing CABG and the predictive value of fQRS on in-hospital MACE was demonstrated.

Pathophysiologically, fQRS is generally due to regional myocardial fibrosis/scar and data suggest that ischemia might cause fQRS via nonhomogeneous myocardial electrical activation (23-27).

In patients with ischemic or non-ischemic left ventricular dysfunction, fQRS correlated with myocardial fibrosis (28). In previous studies using Gadolinium delayed enhancement on cardiac magnetic resonance imaging to determine myocardial structure, fQRS related to extensive myocardial scar (11, 12). Prior studies demonstrated fQRS to be a marker of a prior MI, defined by regional perfusion abnormalities, which has a substantially higher sensitivity and negative predictive value compared to the Q wave (6, 29). Regional fQRS patterns denote the presence of a greater corresponding focal regional myocardial scar on stress myocardial perfusion imaging (30). Additionally, chronic ischemia may cause myocardial patchy fibrosis without prior MI (31). In previous studies were also found that fQRS is independently related to inadequate coronary collaterals in patients with chronic total occlusion (32, 33).

Myocardial ischemia is a well-known cause of heart failure and ventricular arrhythmias due to the development of scar tissue, which is related to increased mortality and morbidity (6, 23, 30, 34). In patients with an acute coronary syndrome, heterogeneous depolarization of myocardium caused by ischemia and infarction may be the main determinant for increased arrhythmic events during the hospital care.

Prolonged QRS time at admission was associated with increased long-term mortality, heart failure, arrhythmia and ischemia in patients presenting with acute coronary syndrome (35, 36). In our study, prolonged QRS time was related to fQRS even in a relatively normal range of QRS (<120 ms). This relation-

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ship may have two possible explanations. Either fragmentation on QRS complex is induced by prolongation of QRS duration or prolongation of QRS is due to QRS complex fragmentation. However, by our study design, we can only speculate which one is the cause and which one is result or response for fragmentation. This interaction should be investigated to clarify the cause-result relationship in an electrophysiology-based study. Moreover, QRS time was not a predictor for POAF independent of fQRS in our study.

FQRS may be helpful in identifying patients at high risk for POAF, which is important for preventive strategies in selected high-risk individuals. POAF is a clinically important and common postoperative complication, and previous studies have shown that prophylaxis may be possible with treatments such as beta-blockers, sotalol, amiodarone and possibly magnesium (37, 38). The preventive measures may be considered when a patient with fQRS is referred to CABG surgery. Additional large-scale clinical studies are needed to determine what types of mentioned agents are more beneficial before they can be considered for routine use.

FQRS is related to myocardial scar, heterogeneous depolarization and chronic ischemia. If we speculate, the potential common pathophysiological mechanisms for POAF may be elevated ventricular filling pressure due to abnormal LV diastolic and systolic functions as well as ischemia; all of which have been related to the presence of fQRS in previous studies. This hypothesis may be supported by our study finding that LA was significantly enlarged in patients with fQRS.

Study limitations

We only included patients with QRS duration <120 ms in our study. We excluded patients with complete bundle branch block, intra-ventricular conduction delay, and patients with permanent pacemakers in our study. Therefore, our results do not apply to patients with wide QRS complexes.

Conclusion

Twelve-lead surface ECG, which is a cheap, non-invasive, and easily apprehensible method, is presently a gold standard in differential diagnosis, determining treatment methods, and performing risk stratification. Fragmentations on preoperative ECG may be useful in identifying patients at higher POAF risk whom will need additional support after their operations. FQRS have an obvious predictive value for POAF in patients undergoing CABG surgery. Therefore, fQRS may be valuable tool for stratification in patients undergoing CABG surgery.

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S.A.K.; Literature search - A.Ç.; Writing - S.A.K.; Critical review-A.T., M.E.D.; Other - S.D.

References

1. Das MK, Suradi H, Maskoun W, Michael MA, Shen C, Peng J, et al. Fragmented wide QRS on a 12-lead ECG: a sign of myocardial scar and poor prognosis. Circ Arrhythm Electrophysiol 2008;1:258-68. **[CrossRef]**
2. Das MK, Michael MA, Suradi H, Peng J, Sinha A, Shen C, et al. Usefulness of fragmented QRS on a 12-lead electrocardiogram in acute coronary syndrome for predicting mortality. Am J Cardiol 2009;104:1631-7. **[CrossRef]**
3. Korhonen P, Husa T, Konttila T, Tierala I, Mäkijärvi M, Väänänen H, et al. Fragmented QRS in prediction of cardiac deaths and heart failure hospitalizations after myocardial infarction. Ann Noninvasive Electrocardiol 2010;15:130-7. **[CrossRef]**
4. Das MK, Saha C, El Masry H, Peng J, Dandamudi G, Mahenthiran J, et al. Fragmented QRS on a 12-lead ECG: a predictor of mortality and cardiac events in patients with coronary artery disease. Heart Rhythm 2007;4:1385-92. **[CrossRef]**
5. Pietrasik G, Goldenberg I, Zdzienicka J, Moss AJ, Zareba W. Prognostic significance of fragmented QRS complex for predicting the risk of recurrent cardiac events in patients with Q-wave myocardial infarction. Am J Cardiol 2007;100:583-6. **[CrossRef]**
6. Das MK, Khan B, Jacob S, Kumar A, Mahenthiran J. Significance of a fragmented QRS complex versus a Q wave in patients with coronary artery disease. Circulation 2006;113:2495-501. **[CrossRef]**
7. Das MK, Zipes DP. Fragmented QRS: a predictor of mortality and sudden cardiac death. Heart Rhythm 2009;6(3 Suppl):S8-14. **[CrossRef]**
8. Cheema A, Khalid A, Wimmer A, Bartone C, Chow T, Spertus JA, et al. Fragmented QRS and mortality risk in patients with left ventricular dysfunction. Circ Arrhythm Electrophysiol 2010;3:339-44. **[CrossRef]**
9. Das MK, El Masry H. Fragmented QRS and other depolarization abnormalities as a predictor of mortality and sudden cardiac death. Curr Opin Cardiol 2010;25:59-64. **[CrossRef]**
10. Das MK, Maskoun W, Shen C, Michael MA, Suradi H, Desai M, et al. Fragmented QRS on twelve-lead electrocardiogram predicts arrhythmic events in patients with ischemic and nonischemic cardiomyopathy. Heart Rhythm 2010;7:74-80. **[CrossRef]**
11. Gardner PI, Ursell PC, Fenoglio JJ Jr, Wit AL. Electrophysiologic and anatomic basis for fractionated electrograms recorded from healed myocardial infarcts. Circulation 1985;72:596-611. **[CrossRef]**
12. Chatterjee S, Changawala N. Fraqmented QRS complex: a novel marker of cardiovascular disease. Clin Cardiol 2010; 33:68-71. **[CrossRef]**
13. Nashef SA, Roques F, Michel P Gauducheau E, Lemeshow S, Salamon R. European system for cardiac operative risk evaluation (EuroSCORE). Eur J Cardiothorac Surg 1999;16:9-13. **[CrossRef]**
14. Roques F, Michel P, Goldstone AR, Nashef SA. The logistic EuroSCORE. Eur Heart J 2003;24:881-2. **[CrossRef]**
15. Ommen SR, Odell JA, Stanton MS. Atrial arrhythmia after cardiothoracic surgery. N Engl J Med 1997; 336:1429-34. **[CrossRef]**
16. Siebert J, Anisimowicz L, Lango R, Rogowski J, Pawlaczyk R, Brzezinski M, et al. Atrial fibrillation after coronary artery bypass grafting: does the type of procedure influence the early postoperative incidence? Eur J Cardiothorac Surg 2001;19:455-9. **[CrossRef]**
17. Leitch JW, Thomson D, Baird DK, Harris PJ. The importance of age as a predictor of atrial fibrillation and flutter after coronary artery bypass grafting. J Thorac Cardiovasc Surg 1990;100:338-42.

18. Shen J, Lall S, Zheng V, Buckley P, Damiano RJ Jr, Schuessler RB. The persistent problem of new-onset postoperative atrial fibrillation: a single-institution experience over two decades. J Thorac Cardiovasc Surg 2011;141:559-70. **[CrossRef]**

19. Wolf PA, Kannel WB, McGee DL, Meeks SL, Bharucha NE, McNamara PM. Duration of atrial fibrillation and imminence of stroke:the Framingham study. Stroke 1983;14:664-7. **[CrossRef]**

20. Creswell LL, Schuessler RB, Rosenbloom M, Cox JL. Hazards of postoperative atrial arrhythmia. Ann Thorac Surg 1993;56:539-49. **[CrossRef]**

21. Humphries JO. Unexpected instant death following successful coronary artery bypass graft surgery (and other clinical settings): atrial fibrillation, quinidine, procainamide, et cetera, and instant death. Clin Cardiol 1998;21:711-8. **[CrossRef]**

22. Erdoğan T, Çetin M, Kocaman SA, Çanga A, Durakoğlugil ME, Ciçek Y, et al. Relationship of fragmented QRS with prognostic markers and in-hospital MACE in patients undergoing CABG. Scand Cardiovasc J 2012;46:107-13. **[CrossRef]**

23. Flowers NC, Horan LG, Thomas JR, Tolleson WJ. The anatomic basis for high-frequency components in the electrocardiogram. Circulation 1969;39:531-9. **[CrossRef]**

24. Lesh MD, Spear JF, Simson MB. A computer model of the electrogram: what causes fractionation? J Electrocardiol 1988;21 Suppl:S69-73. **[CrossRef]**

25. Friedman PL, Fenoglio JJ, Wit AL. Time course for reversal of electrophysiological and ultrastructural abnormalities in subendocardial Purkinje fibers surviving extensive myocardial infarction in dogs. Circ Res 1975; 36:127-44. **[CrossRef]**

26. Wiener I, Mindich B, Pitchon R. Fragmented endocardial electrical activity in patients with ventricular tachycardia: a new guide to surgical therapy. Am Heart J 1984; 107:86-90. **[CrossRef]**

27. Başaran Y, Tigen K, Karaahmet T, Işıklar I, Çevik C, Gürel E, et al. Fragmented QRS complexes are associated with cardiac fibrosis and significant intraventricular systolic dyssynchrony in nonischemic dilated cardiomyopathy patients with a narrow QRS interval. Echocardiography 2011;28:62-8. **[CrossRef]**

28. Calore C, Cacciavillani L, Boffa GM, Silva C, Tiso E, Marra MP, et al. Contrast-enhanced cardiovascular magnetic resonance in primary and ischemic dilated cardiomyopathy. J Cardiovasc Med (Hagerstown) 2007;8:821-9. **[CrossRef]**

29. Reddy CV, Cheriparambill K, Saul B, Makan M, Kassotis J, Kumar A, et al. Fragmented left sided QRS in absence of bundle branch block: sign of left ventricular aneurysm. Ann Noninvasive Electrocardiol 2006; 11:132-8. **[CrossRef]**

30. Mahenthiran J, Khan BR, Sawada SG, Das MK. Fragmented QRS complexes not typical of a bundle branch block: a marker of greater myocardial perfusion tomography abnormalities in coronary artery disease. J Nucl Cardiol 2007;14:347-53. **[CrossRef]**

31. Weinberg SL, Reynolds RW, Rosenman RH, Katz LN. Electrocardiographic changes associated with patchy myocardial fibrosis in the absence of confluent myocardial infarction; an anatomic correlative study. Am Heart J 1950;40:745-59. **[CrossRef]**

32. Kadı H, Ceyhan K, Koç F, Çelik A, Önalan O. Relation between fragmented QRS and collateral circulation in patients with chronic total occlusion without prior myocardial infarction. Anadolu Kardiyol Derg 2011;11:300-4.

33. Erdoğan T, Kocaman SA, Çetin M, Canga A, Durakoğlugil ME, Ciçek Y, et al. Relationship of fragmented QRS complexes with inadequate coronary collaterals in patients with chronic total occlusion. J Cardiovasc Med (Hagerstown) 2012 Apr 11. [Epub ahead of print]

34. Varriale P, Chryssos BE. The RSR' complex not related to right bundle branch block: diagnostic value as a sign of myocardial infarction scar. Am Heart J 1992;123:369-76. **[CrossRef]**

35. Rocha S, Torres M, Nabais S, Gaspar A, Rebelo A, Magalheas S, et al. Non-ST elevation acute coronary syndrome: QRS duration and long-term prognosis. Rev Port Cardiol 2009; 28: 697-706.

36. Brenyo A, Zareba W. Prognostic significance of QRS duration and morphology. Cardiol J 2011; 18: 8-17.

37. Davis EM, Packard KA, Hilleman DE. Pharmacologic prophylaxis of postoperative atrial fibrillation in patients undergoing cardiac surgery: beyond beta-blockers. Pharmacotherapy 2010;30:749, 274e-318e.

38. Mitchell LB, Exner DV, Wyse DG, Connolly CJ, Prystai GD, Bayes AJ, et al. Prophylactic Oral Amiodarone for the Prevention of Arrhythmias that Begin Early After Revascularization, Valve Replacement, or Repair: PAPABEAR: a randomized controlled trial. JAMA 2005;294:3093-100. **[CrossRef]**