ORIGINAL ARTICLE

Frontal plane QRS-T angle may be a predictor for post-coronary artery bypass graft surgery atrial fibrillation

Mevlüt Serdar Kuyumcu[1]
Dinçer Uysal[2]
Mustafa Bilal Özbay[3]
Oğuz Aydın[1]
Erdoğan İbrişim[2]

1. Süleyman Demirel University, Faculty of Medicine, Department of Cardiology, Isparta, Turkey.
2. Süleyman Demirel University, Faculty of Medicine, Department of Cardiovascular Surgery, Isparta, Turkey.
3. Ankara State Hospital, Department of Cardiology, Ankara, Turkey.

http://dx.doi.org/10.1590/1806-9282.66.12.1673

SUMMARY

BACKGROUND: *New-onset postoperative atrial fibrillation (POAF) is the most common arrhythmia following coronary artery bypass graft surgery (CABG) and is associated with prolonged hospitalization, stroke, and mortality. The frontal plane QRS-T [f(QRS-T)] angle, which is defined as the angle between the directions of ventricular depolarization (QRS-axis) and repolarization (T-axis), is a novel marker of ventricular repolarization heterogeneity. The f(QRS-T) angle is associated with adverse cardiac outcomes. In light of these findings, in this study, we aimed to investigate the potential relationship between the f(QRS-T) angle and POAF.*

METHODS: *180 patients who underwent CABG between August 2017 and September 2018 were included in the study retrospectively. Two groups were established as patients who preserved postoperative sinus rhythm (n=130) and those who developed POAF (n=50). The f(QRS-T) angle and all other data were compared between groups.*

RESULTS: *The fF(QRS-T) angle (p<0.001), SYNTAX score (p=0.039), serum high-sensitivity CRP levels (p=0.026), mean age (p<0.001), electrocardiographic left ventricular hypertrophy rate (LVH) (p=0.019), and hypertension rate (p=0.007) were higher, and the mean left ventricular ejection fraction (LVEF) (p<0.001) was lower in the POAF group. Multivariable logistic regression analyses demonstrated that lower LVEF (p=0.004), LVH (p=0.041), and higher age (p=0.008) and f(QRS-T) angle (p<0.001) were independently associated with POAF.*

CONCLUSIONS: *High f(QRS-T) angle level is closely associated with the development of POAF. The f(QRS-T) angle can be a potential indicator of POAF.*

KEYWORDS: *Atrial fibrillation. Coronary artery bypass. Myocardial revascularization. Postoperative complications. Electrocardiography.*

INTRODUCTION

New-onset POAF is the most common arrhythmia following CABG, affecting about one-third of patients in the post-operative period[1]. It typically peaks on the postoperative day 2[2]. POAF is associated with increased risk of stroke, heart failure (HF), prolonged hospitalization, short-term and long-term mortality[3]. Thus, determining significant pre-operative risk factors for the development of POAF will improve risk

DATE OF SUBMISSION: 26-May-2020
DATE OF ACCEPTANCE: 08-Aug-2020
CORRESPONDING AUTHOR: Mevlüt Serdar Kuyumcu
Süleyman Demirel University, Faculty of Medicine, Department of Cardiology, Isparta, Turkey – 32000
Tel: +90 505 221-1458
E-mail: kuyumcuserdar@hotmail.com

stratification and help clinicians execute perioperative prophylactic strategies.

A twelve-lead electrocardiogram (ECG) is a low-cost routine cardiac examination used in daily practice that is noninvasive, rapidly deployable, and available in every hospital. The frontal plane QRS-T [f(QRS-T)] angle, which is defined as the angle between the directions of ventricular depolarization (QRS axis) and repolarization (T axis), is a novel marker of ventricular repolarization heterogeneity[4]. Abnormal f(QRS-T) angle has been shown to have a prognostic value for mortality in the general population, as well as in patients with congestive HF and acute coronary syndrome[5]. Increased f(QRS-T) angle has also been found to be associated with an increased risk of AF in the elderly[6]. But, to our knowledge, there are no studies investigating the risk of new-onset POAF after CABG surgery in patients with increased f(QRS-T) angle.

In this study, we aimed to investigate the predictive value of abnormal ventricular repolarization for new-onset POAF by using the f(QRS-T) angle.

METHODS

A total of 208 patients who underwent isolated on-pump coronary artery bypass grafting at the Suleyman Demirel University Faculty of Medicine Education and Research Hospital were evaluated retrospectively. Patients with risk factors associated with the development of atrial fibrillation (AF) such as chronic obstructive pulmonary disease (n=2) and valvular heart diseases (n=5), as well as patients with existing preoperative AF or flutter (n=8), renal insufficiency (n=3), and patients which required additional surgical intervention (n=4), preoperative inotropic or mechanical support (n=2), redo surgery or emergency coronary surgery (n=4) were excluded from the study.

The diagnosis of hypertension was made when the systolic blood pressure was 140 mmHg or higher, or if the diastolic blood pressure was 90 mmHg or higher in at least three different measurements, or when there was use of anti-hypertensive medication. The diagnosis of diabetes mellitus was established when the fasting blood glucose was 126 mg/dL or higher, or when there was use of anti-diabetic medication. Hyperlipidemia was defined as total cholesterol levels of 200 mg/dL or higher, or a history of statin use except in the previous three months. Patients who were smoking before hospitalization were considered smokers.

The study protocol was approved by the local Ethics Committee. The study was conducted in accordance with the Declaration of Helsinki, Good Clinical Practice, and International Conference on Harmonisation guidelines.

Electrocardiography

The 12-lead ECG was recorded at a paper speed of 50 mm/s in the supine position (Nihon Kohden, Tokyo, Japan). ECGs taken at the first hospitalization of the patients were used. ECG intervals were calculated according to the guidelines[7]. Frontal QRS and T-wave axes were present in the automatic reports of the ECG machine. The calculation of the f(QRS-T) angle was made from these axes as the absolute difference between the frontal plane QRS axis and the frontal plane T axis. In case the angle exceeded 180°, it was calculated by subtracting it from 360°[4]. The subjective component of the individual measurements was ruled out by calculating the f(QRS-T) angle based on an automatic report of the ECG machine.

Echocardiography and surgical procedure

Echocardiography was performed in all patients before surgery. LVEF was calculated by using the modified Simpson method. Standard cardiopulmonary bypass (CPB) was performed with median sternotomy and mild hypothermia (32°C). The CPB was performed with two-stage aortovenous cannulation. An X-clamp was placed to the ascending aorta and cardiac arrest was provided with cold antegrade cardioplegia (10 to 15 mL/kg) with high potassium. Cardiac arrest was maintained with blood cardioplegia, which was given every 15 to 20 min. The CPB was established with a roller pump with a membrane oxygenator and an arterial line filter at pump flow rates of 2 to 2.4 L/min/m2. The left internal thoracic artery and the saphenous vein graft were prepared. The distal anastomoses were constructed during a single period of total X-clamp, and proximal anastomoses were established with partial clamping of the aorta. Hot blood shot cardioplegia was given immediately before the X-clamp was removed. Extubation was performed at the earliest stage possible following the provision of hemodynamic stability.

POAF assessment

The presence of AF documented by ECG for at least 5 minutes was recorded and analyzed as POAF[1]. The development of AF was assessed by continuously monitoring the patients on the first 4 postoperative days and on the following days until discharge by regularly performing 12-lead ECG, 3 times a day. AF was also evaluated using 12-lead ECG when patients complained of palpitations.

Statistical analysis

All statistical analyses were performed using SPSS for Windows version 21.0 (SPSS, Chicago, IL, USA). The minimum number of individuals that should be sampled with 90% power and 0.05 Type I error was at least 46 (R 3.0.1. open-source program). The primary effect variable was determined as the QRS angle. A 1% change in the total f(QRS-T) angle [3.6 degrees on the f(QRS-T) plane] was accepted as clinically relevant. The standard deviation of the primary effect variable was calculated as ± 0.36. For the descriptive statistics of the data, mean, standard deviation, rate, and frequency values were used. The Kolmogorov-Smirnov test was used to evaluate whether the distribution of continuous variables was normal. For the analysis of parametric data, the Student's t-test was used. For the analysis of non-parametric data, the Mann-Whitney U-test was used. The chi-square test was used to compare the categorical variables between groups. Logistic regression analysis was used to determine the impact of variables. The standardized beta coefficients and 95% confidence intervals were calculated. Statistical significance was defined as p-values < 0.05.

RESULTS

The baseline clinical and demographic characteristics of the study population are shown in Table 1. There was no difference between the groups except that the mean age (p<0.001) and hypertension rate (p=0.007) were higher in the POAF group. The echocardiographic measurements and surgery features of the groups are shown in Table 2. The mean SYNTAX score was higher in the POAF group (p=0.039). The mean LVEF was lower in the POAF group (p<0.001). The electrocardiographic features of the groups are shown in Table 3. LVH was higher in the POAF group (p=0.019). The mean f(QRS-T) angle was higher in the POAF group (p<0.001). The laboratory parameters of the study groups are shown in Table 4. There were no differences between the groups, except for the high-sensitivity C-reactive protein (hs-CRP) (p=0.026).

We performed univariate and multiple linear regression analyses for the predictors of POAF, as depicted in Tables 1, 2, 3, and 4 (Table 5). In univariate regression analysis, older age (p<0.001), Hypertension (p=0.010), lower LVEF (p<0.001), higher hs-CRP levels (p=0.032), higher f(QRS-T) angle (p<0.001), and LVH (p=0.029) were associated with POAF. Older age (p=0.008), LVEF (p=0.004), higher f(QRS-T) angle (p<0.001), and LVH (p=0.041) were detected as independent predictors for POAF after multiple linear regression analysis.

DISCUSSION

In our study, we found that an increased f(QRS-T) angle in CABG patients may be predictive, as well as age and other factors, which are the classic risk factors for POAF.

There are many potential pathophysiological mechanisms that lead to POAF. The most common and consistent variable for developing POAF across the studies is aging[8]. Other preoperative risk factors include a previous history of AF, obesity, diabetes mellitus, increased left atrial size, chronic obstructive pulmonary disease, valvular disease, withdrawal from beta-blocker treatment, and electrolyte imbalances like hypokalemia and hypomagnesemia[8]. In our study, increased age, low LVEF, LVH, and larger f(QRS-T) angle were independent predictors for POAF.

Aberrant ventricular repolarization is one of the known mechanisms of arrhythmiogenesis[9]. The development of aberrancy in ventricular repolarization has also been found to be associated with AF. Long QT syndrome patients have increased atrial action potential durations which can result in polymorphic atrial tachyarrhythmias[10]. These polymorphic atrial arrhythmias are also likely to degenerate into AF[11]. Increased activity of late sodium channels currents leading to initiation of atrial ectopic activity may be another explanation for the occurrence of AF[12]. The association of abnormal ventricular repolarization with AF may be due to common comorbid conditions such as diabetes and hypertension. An increased f(QRS-T) is closely related to abnormal ventricular repolarization[5].

Another pathophysiological mechanism involved in the pathophysiology of atrial fibrillation is increased adrenergic hyperactivity[13]. Variations in cardiac autonomic neural tone and elevated sympathetic activity on the ventricular myocardium are related to the total dispersion of repolarization and an increased risk of AF. The total dispersion of repolarization reflects the heterogeneity like the f(QRS-T) angle[4].

TABLE 1. BASELINE CHARACTERISTICS OF THE STUDY GROUPS.

Variables	Postoperative sinus rhythm (n = 130)	Postoperative Atrial fibrillation (n = 50)	p-value
Age, years	59.87 ± 12.45	68.10 ± 8.83	< 0.001
Female, n(%)	41 (31.5%)	10 (20.0%)	0.124
BMI, kg/m^2	29.01 ± 5.35	27.97 ± 4.60	0.227
Diabetes Mellitus, n(%)	54 (41.5%)	26 (52.0%)	0.206
Hypertension, n(%)	92 (70.8%)	45 (90.0%)	0.007
Smoking, n(%)	43 (33.1%)	23 (46.0%)	0.107
Cerebrovascular event history, n(%)	18 (13.8%)	7 (14.0%)	0.979
Peripheral vascular disease, n(%)	13 (10.0%)	5 (10.0%)	0.998

Data are given as mean ± SD, n, or median (interquartile range). HDL: high-density lipoprotein; Hs-CRP: high-sensitivity C-reactive protein; LDL: low-density lipoprotein; WBC: white blood cells; BMI: body mass index.

TABLE 2. ECHOCARDIOGRAPHIC AND SURGICAL CHARACTERISTICS OF THE GROUPS.

Variables	Postoperative sinus rhythm (n = 130)	Postoperative Atrial fibrillation (n = 50)	p-value
In-hospital mortality, n(%)	4 (3.1%)	2 (4.0%)	0.757
SYNTAX score	29.98 ± 8.45	34.74± 5.27	0.039
Graft number	2.56 ± 0.81	2.74± 0.72	0.174
Cardiopulmonary bypass time, minutes	78.84 ± 27.41	83.76 ± 34.71	0.321
Aortic cross clamp time, minutes	47.61 ± 19.09	46.31 ± 16.86	0.674
Left ventricular ejection fraction, %	56.54 ± 9.46	49.27 ± 11.94	<0.001
Left ventricular diastolic diameter, mm	45.80 ± 5.47	47.29 ± 8.46	0.168
Left ventricular systolic diameter, mm	29.67 ± 6.85	31.42 ± 5.86	0.120
Interventricular septum diameter, mm	11.05 ± 3.24	11.30 ± 3.51	0.652
Posterior wall thickness, mm	10.47 ± 2.28	0.97 ± 2.28	0.590
Left atrial diameter, mm	39.09 ± 6.20	41.26± 7.85	0.056
Systolic pulmonary artery pressure, mmHg	26.65 ± 9.08	28.26 ± 6.68	0.257

Data are given as mean ± SD, n, or median (interquartile range).

TABLE 3. ELECTROCARDIOGRAPHIC FEATURES OF THE GROUPS.

Variables	Postoperative sinus rhythm (n = 130)	Postoperative Atrial fibrillation (n = 50)	p-value
Sinus rhythm	84 (64.6%)	50 (18.2%)	0.072
Left bundle branch block	5 (3.8%)	4 (8.0%)	0.252
Left anterior fascicular block	24 (18.2%)	13 (26.0%)	0.265
Left posterior fascicular block	0	0	
Right bundle branch block	12 (9.2%)	2 (4.0%)	0.241
Right bundle branch block + Left anterior fascicular block	1 (0.8%)	1 (2.0%)	0.480
Left ventricular hypertrophy	4 (3.1%)	6 (12.0%)	0.019
QT, ms	361.3 ± 32.3	368.5 ± 29.9	0.174
QTc, ms	400.2 ± 34.4	404.2 ± 23.4	0.452
Tpe, ms	81.6 ± 12.1	84.8 ± 16.0	0.150
Tpe/QTc	0.20 ± 0.04	0.21 ± 0.04	0.481
f(QRS)-T (°)	57.9 ± 17.5	71.1 ± 13.6	<0.001

Data are given as mean ± SD, n, or median (interquartile range). QTc: corrected QT interval; f(QRS)-T: frontal QRS-T angle

TABLE 4. LABORATORY PARAMETERS OF THE STUDY GROUPS.

Variables	Postoperative sinus rhythm (n = 130)	Postoperative Atrial fibrillation (n = 50)	p-value
Glucose, mg/dL	142.54 ± 67.23	161.46 ± 80.35	0.121
Creatinine, mg/dL	1.09 ± 0.33	1.14 ± 0.29	0.318
Sodium, mmol/l	136.1 ± 2.7	138 ± 3.1	0.696
Potassium, mmol/l	3.91 ± 0.36	3.87 ± 0.41	0.731
Magnesium, mg/dL	1.73 ± 0.24	1.65 ± 0.43	0.534
WBC,$10^3/mm^3$	8.89 ± 4.27	8.46 ± 2.44	0.419
Hemoglobin, g/dL	13.77 ± 1.85	13.74 ± 1.77	0.922
Platelet, $10^3/mm^3$	232.34 ± 63.08	227.64 ± 72.84	0.669
Hs-CRP, mg/L	6.24 ± 4.85	11.24 ± 7.54	0.026
Total cholesterol, mg/dL	196.33 ± 48.11	196.8 ± 45.54	0.798
LDL-C, mg/dL	129.58 ± 51.06	126.26 ± 38.45	0.749
HDL-C, mg/dL	42.14± 10.72	41.22 ± 9.45	0.675
Triglyceride, mg/dL	147.30 ± 59.66	150.50 ± 62.10	0.798

Data are given as mean ± SD, n, or median (interquartile range). HDL, high-density lipoprotein; Hs-CRP, high-sensitivity C-reactive protein; LDL, low-density lipoprotein; WBC, white blood cells.

TABLE 5. MULTIVARIATE LOGISTIC REGRESSION ANALYSIS FOR PREDICTING POAF.

	Univariable OR (95% CI)	P value	Multivariable OR (95% CI)	p-value
Age	1.081 (1.040 - 1.124)	< 0.001	1.068 (1.017 - 1.122)	0.008
Hypertension	3.717 (1.370 - 10.087)	0.010	1.156 (0.970 - 1.376)	0.064
SYNTAX score	1.290 (1.001 - 1.579)	0.066		
Left ventricular ejection fraction	0.939 (0.908 - 0.971)	< 0.001	0.939 (0.900 - 0.981)	0.004
Hs-CRP, mg/L	1.025 (1.002 - 1.049)	0.032	1.016 (0.983 - 1.050)	0.341
f(QRS)-T	1.051 (1.028 - 1.076)	< 0.001	1.079 (1.005 - 1.153)	< 0.001
Left ventricular hypertrophy	4.295 (1.158 - 15.934)	0.029	8.368 (1.657 - 42.255)	0.041

CI: confidence interval; OR: odds ratio; Hs-CRP: high-sensitivity C-reactive protein; f(QRS)-T: frontal QRS-T angle.

As determined in our study, common myocardial ischemia associated with a high SYNTAX score is one of the causes of POAF[2]. Zhang et al.[14] detected that an increase in the f(QRS-T) angle was associated with myocardial ischemia and found that the f(QRS-T) angle was normalized after successful revascularization therapy. An increased f(QRS-T) angle may be indicative of total ischemic load in POAF patients.

It is a well-known fact that inflammation is associated with cardiovascular diseases[15]. Indicators of electrocardiographic ventricular repolarization have been found to be correlated with systemic inflammation in a study[16]. Increased inflammatory activity may be responsible for the pathogenesis of arrhythmia either by direct arrhythmogenic effects by locally activating complements or by inducing oxidative stress and apoptosis[17]. POAF has also been linked to increased inflammatory activity and oxidative stress[18]. We have found higher Hs-CRP in patients with POAF compared to patients with sinus rhythm. Thus, an abnormal f(QRS-T) angle caused by systemic inflammation may be an explanation for patients with POAF.

CONCLUSIONS

The measurement of the f(QRS-T) angle, which is a basic and low-cost parameter, may allow physicians to predict POAF after CABG surgery. This novel parameter is more reliable, consistent, and less susceptible to false calculation and definition than other traditional electrocardiographic myocardial repolarization parameters. This may allow physicians to take tighter precautions and modify risk factors in advance by predicting POAF development. However, further studies are needed to determine the relationship between POAF and the f(QRS-T) angle.

Limitations of the study

The present study has a cross-sectional design with a relatively small sample size. We do not have data on major adverse cardiovascular events during follow-up.

Author's Contribution

Mevlüt Serdar Kuyumcu - Methodology, writing of the original draft; Dinçer Uysal - Data curation, investigation; Mustafa Bilal Özbay - Writing of the original draft; Oğuz Aydın, Erdoğan İbrişim - Supervision.

RESUMO

OBJETIVO: *A fibrilação atrial pós-operatória de início recente (Poaf) é a arritmia mais comum após a cirurgia de revascularização do miocárdio (CABG) e associada a hospitalização prolongada, acidente vascular cerebral e mortalidade. O ângulo QRS-T [f(QRS-T)] do plano frontal, que é definido como o ângulo entre as direções da despolarização ventricular (eixo-QRS) e repolarização (eixo-T), é um novo marcador da heterogeneidade da repolarização ventricular. O ângulo f(QRS-T) está associado a desfechos cardíacos adversos. À luz desses achados, neste estudo, objetivamos investigar a relação potencial entre o ângulo f(QRS-T) e a Poaf.*

MÉTODOS: *Cento e oitenta pacientes submetidos a CABG entre agosto de 2017 e setembro de 2018 foram incluídos no estudo retrospectivamente. Dois grupos foram estabelecidos como pacientes com ritmo sinusal pós-operatório (n=130) e com Poaf (n=50). O ângulo f(QRS-T) e todos os dados foram comparados entre os grupos.*

RESULTADOS: *Ângulo f(QRS-T) (p<0,001), escore Syntax (p=0,039), níveis séricos de PCR de alta sensibilidade (p=0,026), idade média (p<0,001), taxa de hipertrofia ventricular esquerda eletrocardiográfica (LVH) (p=0,019) e taxa de hipertensão (p=0,007) foram maiores; a fração de ejeção média do ventrículo esquerdo (LVEF) (p<0,001) foi menor no grupo com Poaf. As análises de regressão logística multivariável demonstraram que menor LVEF (p=0,004), LVH (p=0,041), maior idade (p=0,008) e maior ângulo f(QRS-T) (p<0,001) foram independentemente associados à Poaf.*

CONCLUSÕES: *Níveis de ângulo altos f(QRS-T) estão intimamente associados à Poaf. O ângulo f(QRS-T) pode ser um indicador potencial de Poaf.*

PALAVRAS-CHAVE: *Fibrilação atrial. Ponte de artéria coronária. Revascularização miocárdica. Complicações pós-operatórias. Eletrocardiografia.*

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