ANALYSIS OF FACTORS AFFECTING THE DURATION OF POSTOPERATIVE ATRIAL FIBRILLATION

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ABSTRACT

Purpose: Atrial Fibrillation (AF) is the most common arrythmia seen after coronary artery bypass surgery (CABG). AF significantly increases the risk of all-cause mortality, cardiovascular mortality, and stroke. There are many publications about why POAF develops. However, the duration of patients' stay in POAF has not been adequately investigated. Current study is the first in the literature to investigate the factors affecting the duration of POAF. Methods: 110 patients who developed AF after CABG were divided into groups according to the duration of their stay in AF (Group 1; <24 hours, Group 2 ;24-48 h, Group 3; > 48 h). We compared the factors that could be related with the duration of POAF.Results: Pre op calculated systemic immune-inflammation index (SII) was found to be lower in group 2 (p: 0,007) and in group 3 (p: 0,029). Postoperative bleeding revision was found to be higher in group 2 (p: 0,025) and incidence of postoperative high diastolic blood pressure was found to be higher in group 2 (p:0,011) and group 3 (p: 0,004). Permanent AF was detected in 11 of the patients during long-term follow-up. The incidence of permanent AF was higher in group 3 (p: 0.018) and in patients with high Syntax SCORE 1 (p: 0.026).

Conclusion: Diastolic blood pressure, low preoperative SII levels and postoperative bleeding revision are independent risk factors that affect the duration of POAF. Permanent AF was associated with high Syntax SCORE 1 and prolonged POAF duration.

Keywords

Atrial Fibrillation, Coronary Bypass Surgery, Systemic Inflammatory Index

INTRODUCTİON

Coronary artery disease (CAD) is the most common cardiovascular disease(1) , while atrial fibrillation (AF) is the most common cardiac arrhythmia(2).The definition of newly emerging postoperative atrial fibrillation (POAF) includes patients who had normal sinus rhythm before surgery and no history of atrial fibrillation, but developed AF after cardiac surgery(3). AF significantly increases the risk of all-cause mortality, cardiovascular mortality, and stroke(4).

There are many publications about why POAF develops. However, the duration of patients' stay in POAF has not been adequately investigated. To our knowledge, this study is the first in the literature to investigate the factors affecting the duration of POAF.

MATERİAL AND METHODS

A total of 2322 patients who underwent CABG between March 1, 2017 and January 1, 2023 at Mersin City Training and Research Hospital were retrospectively

reviewed, and 509 patients who had postoperative AF were identified. Patients with no P waves on the surface electrocardiogram and an irregular R-R interval were defined as AF. Patients who developed atrial fibrillation after CABG and returned to normal sinus rhythm with amiodarone treatment were included in the study. Patients who are between 18 and 75 years old were chosen for the study. And the patients who did not have chronic and/or paroxysmal atrial fibrillation and/or other known cardiac arrhythmia or conduction disorder, a pacemaker, moderate-severe valve disease and heart valve prosthesis were included in the study. Also, the patient who did not undergo dialysis, and met all the criteria of GFR≥30 ml/min and euthyroid were included in the study, as well. It is known that advanced age and chronic renal failure increase the frequency of AF. These patients were excluded from the study because it was thought that they would affect the results of our study. 110 patients met all the criteria. The patients' left atrium diameters were normal. Our study was approved by the local ethics committee with the decision numbered 02-37-18/01/2023.

Operations were performed using the conventional cardiopulmonary bypass surgery technique. The operations were performed with cardiopulmonary bypass. Antegrade cold blood cardioplegia was used in all patients. The left internal mammary artery was used as a graft for LAD and the saphenous vein was used as a graft for other coronary arteries. The patients were divided into three groups according to the duration of their stay in atrial fibrillation as less than 24 hours (Group 1), between 24-48 hours (Group 2) and more than 48 hours (Group 3). All patients were treated with amiodarone infusion according to the standard protocol.

Amiodarone infusion was started within the first hour after AF developed. Amiodarone infusion was given as 1200 mg in the first 24 hours, an additional 600 mg in 24-48 hours, and a second additional dose of 600 mg after 48 hours. Electrolyte imbalance was corrected in all patients who developed AF. Beta blockers and acetylsalicylic acid were added to the treatment of patients who did not use them before surgery. All patients used beta-blockers during the postoperative period. All patients were discharged in sinus rhythm. Patients' data were obtained retrospectively from the hospital's electronic system and patient registry files. The medical histories of the patients, the drugs they used, the procedures performed before, during and after the operation, interventions, cross-clamp time, laboratory results, electrocardiography, and transthoracic echocardiography reports were examined.

EuroSCORE 2 was calculated by entering the patient's data to http://www.euroscore.org/calc.html. SII calculation was made by the hemogram samples taken from the patients before, on the day of the operation and post operation. SII calculation formula is: SII = P x N/L where (P) is the number of blood platelets, (N) is the number of neutrophils and (L) is the number of lymphocytes per liter(5) .The Syntax SCORE 1 is a scoring system that is used for grading the extent and severity of coronary artery disease angiographically before the operation. Dominance of coronary arteries were determined according to its supply to the posterior diaphragmatic face. SyntaxSCORE 1 was calculated by two experienced interventional cardiologists using the programm in http://www.syntaxscore.com.

The EuroSCORE 2 scoring system was used for evaluating the preoperative risk of the patients(6) .

In our study, we evaluated the factors that can be related with the duration of POAF. We developed a model to adress the independent parameters that affect the POAF time. In this model, group 1 was taken as reference group. And it was compared with group 2 and 3, by means of Euroscore 2, Syntax SCORE 1, LVEF, age, cross clamp time (CCT), diabetes mellitus (DM), sex, preoperative SII, postoperative SII, postoperative bleeding revision (In patients undergoing revision due to bleeding, conventional rules for revision were taken into consideration), diastolic pressure increases when AF occurs, heart rate, hemoglobin, hematocrit, LDL, triglyceride and hypertension. The parameters were evaluated by multivariate logistic regression analyzes.

All analysis were performed using SPSS version 26 for Windows (SPSS Inc. Chicago, IL, USA). Numerical variables are presented as means standard deviations, and nominal variables as percentages. For comparison of continuous variables between groups, ANOVA test was used for those with normal distribution and Kruskal Wallis test for those who were not normally distributed. Chi-square test was used for analyzing categorical variables. To evaluate the effects of various factors on POAF duration, we performed multivariate regression analyses using backward logistic regression method. Coefficients with 95% confidence intervals (CIs) were presented. A p-value <0.05 was considered significant. Independent T test and Mann-Whitney tests were used for parameters affecting permanent AF that

developed during the follow-up of the patients. Independent T test was applied to Syntax SCORE 1 which was normally distributed. Mann-Whitney Test statistics was used for amiodarone dose, which was not normally distributed.

RESULTS

Demographic, preoperative, operative, postoperative, clinical and laboratory characteristics were found to be similar among three groups. There was no statistically significant difference among 3 groups in view of EuroSCORE 2 and Syntax SCORE 1 (Table 1). ROC analysis (Figure 1), proportional changes and SII related results regarding the SII index can be seen in the table 2-3. Preop and postop cut-off values of the SII index are shown in table 4. Parameters evaluated by multivariate logistic regression analyzes according to our model is summorized in Table 5. Among these parameters postoperative bleeding revision was found to be higher in group 2 (p: 0,025) and incidance of post operative high diastolic blood pressure was found to be higher in both group 2 and 3 (p:0,011) and (p: 0,004) respectively. Pre op calculated SII was found to be lower in group 2 (p: 0,007) and in group 3 (p: 0,029) (Table 5). Permanent AF was detected in 11 (10%) of the patients during long-term follow-up. These patients were discharged with sinus rhythm as mentioned above. It was determined that the cases that developed permanent AF were all in group 3 (p: 0.038). Syntax SCORE 1 (p: 0.026) levels were found to be high in patients with permanent AF (Table 6).

It was found that RCA dominancy and which coronary arteries are bypassed had no effect on the duration of POAF (Table 7)

DİSCUSSİON

This is the first study to show the effects of the factors such as EuroSCORE 2, SyntaxSCORE and SII on POAF duration in post operative CABG patients. In our study, it was shown that EuroSCORE 2 and SyntaxSCORE 1 are not associated with POAF duration terminated with standard amiodarone treatment. However, preoperative SII, postoperative bleeding revision and diastolic blood pressure increase were found to be affecting the duration of POAF.

POAF is the most common arrhythmia with an incidence of 10-33% in CABG (7). It usually occurs 2-4 days after surgery. Although it is generally well tolerated, it can be life-threatening in elderly patients as well as patients with poor left ventricular function(8). On the other hand, POAF is also associated with increased thromboembolic events, stroke, and prolonged hospitalizations(9-12) . Postoperative factors, anesthesia, surgery itself, and patient-related multifactorial causes are among the pathophysiological causes of POAF. Changes such as vasoplegia, systemic inflammation, excessive catecholamine release, changes in sympathetic and parasympathetic tone, excessive fluid shifts and neurohormonal activation that develop with cardiac surgery are potential triggers for arrhythmias(12-14). The change in diastolic blood pressure in groups 2 and 3 may be caused by increased neurohormonal activity. We also think that the prolongation of the POAF duration triggered by postoperative bleeding is due to systemic inflammation that leads to fluid shifts.

Surgical trauma causes changes in the whole body organs, profound physiological changes including inflammatory, metabolic and immune reactions occur(15).Surgical stress response occurs through the activation of afferent sympathetic nervous systems and biologically potent inflammatory mediators(16). Elevation in Postoperative SII levels in all patients was expected and no difference among groups was determined. We have found that this elevation itself did not have a significant effect on the duration of POAF. There was no statistically significant difference among the groups in view of proportional change of preoperative and postoperative SII. POAF duration was prolonged in patients with low preoperative SII. This may be related with the stronger acute inflammation in patients with low inflammation index. We think that the duration of POAF does not increase in patients with high preoperative SII because the severity of this acute exacerbation is milder. These patients already have a higher number of neutrophils in their tissues. In contrast, in patients with a low preoperative SII, neutrophil immigration causes a more severe acute inflamation. Therefore, patients with a low preoperative SII index remain in AF for a longer period of time. This causes patients to use amiodarone infusion and anticoagulants for a longer period of time in the postoperative period.

Significant stenosis in the arteries supplying the atrium has been reported as an independent predictor for the development of POAF in CABG(17). Demographic characteristics of the patients are also effective on the development of POAF. The risk of POAF increases with age in patients undergoing CABG (18-21). In addition, there are differences between male and female patients in the

development of POAF in CABG patients (22). In studies including meta-analysis, there is a 12% increased risk of all-cause mortality, a 55% cardiovascular mortality risk, and a 2-fold increase in the risk of stroke in females compared to males (23). Diabetes was associated with AF only in females (24). Heart failure, hypertension, and prolonged aortic cross clamp time are also associated with an increased incidence of POAF (25). It is known that stenosis of the RCA increases the incidence of POAF (12). However, when it comes to the duration of atrial fibrillation, we have found that RCA dominance, DM, gender and which vessel was bypassed had no effect on the duration of POAF.

EuroSCORE is a scoring system developed according to the preoperative information, demographic findings and operations of the patients. The purpose of this scoring system is to provide information about mortality and morbidity. The SYNTAX scoring system is based on the anatomical localization of atherosclerosis in the coronary arteries (26). SYNTAX score has predictive importance for POAF development (27). The relationship between EuroSCORE 2 and SyntaxSCORE 1 and the development of POAF has also been demonstrated (28-29). The scores of the groups in our study had homogeneous values. The factors that affected this homogeneous situation in the study may be associated with low avarage age, not having chronic kidney disease and EF values which is not low. Since Euroscore and SYNTAX scores were similar in all groups, we couldn't evaluate the effect of SYNTAX and EuroSCORE 2 scores on POAF duration. However, SyntaxSCORE 1 was higher in patients whom we found permanent AF in our long-term follow-up. Additionally, permanent AF was seen more frequently in patients with POAF

duration longer than 48 hours. Patients with a higher SyntaxSCORE 1 and a POAF duration longer than 48 hours should be closely monitored for permanent AF. Because even patients who have returned to sinus rhythm may need long-term use of oral anticoagulants to reduce the risk of stroke in POAF.

It is stated in the literature that persistent AF is more common in obese patients due to the large distribution volume of cordoron drug (30). In our study, we observed that obesity had no effect on POAF because there was no significant difference in weight and height between the groups. Although our study is the first to evaluate the factors affecting the POAF termination time, it has a number of limitations. Firstly, left atrium (LA) diameters were evaluated as normal in transthoracic echocardiography, the numerical value of the diameter size was not specified, and the LA volume was not evaluated. The stages of patients with left ventricular diastolic dysfunction are not specified in detail. Secondly, our current study is a single-center, retrospective, non-randomized study that included only CABG patients.

CONCLUSİON

It is known that many factors affect the development of POAF. However, Predictors affecting the time to return to normal sinus rhythm in atrial fibrillation following coronary artery bypass surgery have not been investigated. In our study we have found that diastolic blood pressure, low preoperative SII levels and postoperative bleeding revision are independent risk factors affecting the duration of POAF. The

development of permanent AF during long-term follow-up was associated with prolonged SyntaxSCORE 1 and POAF duration.

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ETHİCS APPROVAL AND CONSENT TO PARTİCİPATE:

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This manuscript has been approved by the local ethics committee with the decision numbered 02-37-18/01/2023.All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Declaration of Helsinki (as revised in 2013).

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CONFLİCT OF İNTEREST:

The authors declare that there is no conflict of interest**.**

DATA AVAİLABİLİTY:

All available data were included in this orgınal artıcle published.

AUTHORS' CONTRİBUTİONS:

Oya İmadoğlu made the collection of data, editing of the article, discussion and resource editing. Mehmet Erin Tüysüz edited the idea of the article, editing of the article, collection of data and discussion sections.

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Table 1: Patients demography and peroperatif status

Patients Demography	Group-1 (n=18)	Group-2 (n=66)	Group-3 (n=26)	P
Age(years)	62,7±10,17	63,5±10,38	60,11±7,66	0,330
Sex, (female), n(%)	3(%16,7)	17(%25,8)	7(%26,9)	0,692
Height (cm)	166,05±5,7	167,66±9,01	168,15±8,48	0,703
Weight (kg)	75,16±10,54	79,33±12,62	82,84±15,44	0,162
Diabetes Mellitus,n(%)	6(%33)	29(%43,9)	9 (%34,6)	0,584
Hypertension, n (%)	11(%61,1	46(%69,7)	17(%65,4)	0,768
Hyperlipidemia, n/%)	7(%38,9)	36(%54,5)	13(%50)	0,497
Euro SCORE2	2,15±1,47	2,21±2,02	2,63±4,8	0,274
Syntax SCORE	23,47±7,29	25,4±9,16	27,67±10,31	0.535
PVD (n/%)	5(%27,8)	7(%10,6)	3(%11,5)	0,160
Stable angina	10(%55,6)	35(%53)	15(%57,7)	0,917
ACS, n/%)	8(%44,4)	31(%47)	11(%42,3)	0,865
LVEF%	51,11±8,16	50,78±6,68	50±8,71	0,660
Heart rate	81,22±8,86	79,09±8,52	79,15±10,13	0,273
SBP (mmHg)	127,55±16,06	126,83±14,80	132,42±14,87	0,314
DBP (mmHg)	70,94±8,31	73,87±9,82	75,46±10,09	0,429
Peroperatif Status				
Cross clamp time (min)	39,22±9,55	41,63±12,41	43,88±14,42	0,476
Lovest hematocrit (%)	24,38±3,98	24,10±4,31	25,30±3,46	0,447
Number of grafting	3,05±0,80	2,93±0,72	2,88±1,1	0,799
Positive inotrop	24,38 ±3,98	24,10±4,31	25,30±3,46	0,447
Bleeding revision	1(%5,6)	2(% 3)	-	0,523
PO-IABP	13(%72,2)	39(%59,1)	15(%57,7)	0,146

ACS: Acute Coronary Syndrome, LEVF: Left Ventricular Ejection Fraction, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, GFR: Glomerular Fitration Rate, PVD: Peripheral Vascular Disease, CABG: Coronary Artery Bypass Grafting, PO-IABP: Peroperative Intra aortic Pump.

Table 2: POAF Duration Accoring to SII , Proportional Change in SII, Cut-off values to determine 24 hours before for Preop SII and Postop SII

POAF duration		N	Minimum	Maximum	Mean±Std. Deviation
<24h	PreopSII	18	263,25	3235,11	1115,51±882,13
	PostopSII	18	449,78	5791,94	2162,53±453,82
	SIIProportional change	18	-31,12	1122,07	181,82±283,17
24h-48h	PreopSII	66	164,17	2529,26	821,67±465,73
	PostopSII	66	71,68	11173,06	1883,96±1695,28
	SIIProportional change	66	-93,17	1351,05	187,08±261,37
>48h	PreopSII	26	123,90	1997,92	773,02±418,20
	PostopSII	26	234,90	3223,26	1483,84±790,48
	SIIProportional change	26	-50,74	701,47	123,68±161,85

Table-3: Proportional Change in SII

	POAF duration	P
PreopSII	1,27	0.528
PostopSII	1,78	0.409
SIIProportional change	1,27	0.529

Table-4: Cut-off values to determine 24 hours before for Preop SII and Postop SII

Risc Factor	AUC(%95 CI)	CUT off	Sensitivity	Spesifity	P
PreopSII	0,58(0,42-0,745)	790,65	0,55	0,56	0,268
PostopSII	0,57(0,406-0,749)	1587,68	0,55	0,57	0,301

Table 5: Multivariate logistic regression analysis results

Parameters	OR (95% CI)	P
Postoperative Atrial Fibrillation duration <24 h		
	1,00(Ref.)	-
Postoperative Atrial Fibrillation duration 24-48 h		
Diabetes Mellitus	2,81(0,378-20,894)	0,313
Hypertension,	0,97(0,164-5,843)	0,981
Hyperlipidemia	12,94(0,973-172,18)	0,053
Previus stent	0,29(0,025-3,410)	0,326
Coronary artery disease	2,65(0,324-21,684)	0,363
Postoperative bleeding revision	0,01(0,0002-0,575)	**0,025**
Diastolic blood pressure	1,19(1,042-1,374)	**0,011**
Heart rate	0,97(0,875-1,091)	0,677
Hemoglobin	1,49(0,161-13,791)	0,725
Hematocrit	0,68(0,302-1,543)	0,358
LDL cholesterol	0,98(0,970-1,01)	0,331
Triglyceride	0,994(0,984-1,005)	0,304
EUROSCORE 2	0,93(0,695-1,252)	0,644
SyntaxSCORE 1	1,05(0,941-1,186)	0,351
Preoperative SII	0,99(0,996-0,999)	**0,007**
Postoperative SII	0,99(0,999-1)	0,625
Postoperative Atrial Fibrillation duration >48h		
Diabetes Mellitus	1,22(0,119-12,639)	0,863
Hypertension,	0,37(0,045-3,020)	0,353
Hyperlipidemia	18,78(1,135-310,970	0,041
Previus stent	0,22(0,015-3,374)	0,281
Coronary artery disease	8,78(0,816-94,672	0,073
Postoperative bleeding revision	3,978E-11(3,978E-11-3,978E-11	-
Diastolic blood pressure	1,24(1,071-1,442)	**0,004**
Heart rate	0,97(0,870-1,101)	0,723
Hemoglobin	1,57(0,129-19,226)	0,721
Hematocrit	0,65(0,256-1,687)	0,383
LDL cholesterol	0,97(0,955-1,002)	0,069
Triglyceride	0,99(0,981-1,005)	0,244
EUROSCORE 2	1,005(0,741-1,364)	0,974
SyntaxSCORE 1	1,101(0,971-1,251)	0,133
Preoperative SII	0,99(0,996-1)	**0,029**
Postoperative SII	0,99(0,999-1)	0,171

CI, confidence interval; OR, odds ratio; p ≤ 0.05 significance; Sİİ, Systemic Immune-Inflammation Index

Table 6: Permanent AF

	Permenant AF	N	Mean+standart Deviation	P
Amiodarone dosage	+	11	2345,45± 1454,72	0,038
	-	99	1656,06 ±821,84	
Syntax SCORE	+	11	31,45±12,05	0,026
	-	99	24,97±8,66	

Table 7: Bypassed vessels and RCA dominance

POAF duration		<24h	24-48h	>48h	P
RCA dominant	+ - Co-dominant	8 3 4	41 11 11	13 5 7	0,755
Sequential	+ -	5 12	5 58	3 23	0,056
RCA greft	+ -	8 9	42 21	18 8	0,269
CXA greft	+ -	15 2	53 10	18 8	0,189
LAD greft		17	63	26	-

RCA: Right Coronary Artery, CXA: Circumflex Artery, LAD**:** Left Anterior Descending Artery

Graphic 1 . Roc analysis: not significant(p>0.05)