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Prediction of new-onset atrial fibrillation after off-pump coronary artery bypass surgery using left atrial area and area index

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Abstract

Aim: This study aimed to determine preoperative echocardiographic predictors of postoperative atrial fibrillation (POAF) in patients undergoing beating-heart coronary artery bypass grafting (CABG) surgery.

Materials and Methods: 84 patients undergoing off-pump isolated CABG were prospectively enrolled. The left atrium area (LAA) was measured from the apical four-chamber projection at the end-ventricular systole, and then indexed to BSA for the left atrial area index (LAAI). POAF was detected with continuous telemetry and surface 12 electrocardiograms throughout hospitalization.

Results: We observed postoperative atrial fibrillation (AF) in 32 patients (38%, 64.9±10.2 years); of whom 87.5% (28 patients) were men. Patients with POAF had significantly larger left atrium (LA) area (18.9 ± 3.7 vs. 21.3 ± 4.9 cm^2, p=0.016), higher LAAI (10.4 ± 2.0 vs. 12.0 ± 2.6 cm^2/m^2, p= 0.001), and higher systolic pulmonary artery pressure (30 (2-37) vs. 33 (20-64), p=0.05). In addition, lateral wall Em (9 (3-14) vs. 7 (3-15), p= 0.047), Am (10.8 ± 2.6 vs. 8.3 ± 3.0, p=0.05), and left ventricular ejection fraction (LVEF) (60.5 (23- 78.50) vs. 57.15 (33.10-74.90), p=0.05) were significantly lower in patients with POAF. Based on the backward stepwise model of multivariate analysis, LAAI (p=0.007, 95% CI for OR:1.374 (1.092-1.729)) and LVEF (p=0.039, 95% CI for OR:0.889 (0.796-0.994)) were found to be the strongest independent predictors of POAF.

Conclusion: In this study, LAAI and LVEF were independent predictors of POAF development after off-pump CABG surgery. These predictors may be helpful in risk assessment for the possibility of POAF in patients undergoing off-pump CABG surgery.

Introduction

Atrial fibrillation (AF) is the most common arrhythmic complication in patients undergoing coronary artery bypass surgery (CABG), manifesting as an important cause of mortality and morbidity [1]. It is known to increase the duration of hospital stay in the postoperative period as well as increase the risk of cerebrovascular events, hypotension, and congestive heart failure [2]. Preoperative risk assessment of postoperative AF (POAF), which has an occurrence rate ranging from 20% to 40% after CABG, is crucial for the improvement of the prognosis of such patients [3]. Several studies are available comparing on-pump and off-pump CABG. Although off-pump surgery is associated with less blood transfusion, reoperation due to bleeding, new onset of AF, and shorter duration of ventilation; both forms of surgery do not differ in myocardial infarction (MI), stroke, mortality, and acute renal failure [4-7]. On-pump surgery has been accused of ischemia/reperfusion injury due to aortic cross-clamping, which may associate with the development of POAF [8].

A search of the literature revealed several studies on the predictors of AF in the preoperative period in patients undergoing on-pump and off-pump CABG [9,10], aortic and mitral valve surgery [11,12], and lung cancer surgery [13]. Although the predictive power of left atrial size indices has been studied in CABG patients [14,15], we found a lack of data on left atrial area index (LAAI) in off-pump CABG patients. Our study aimed to evaluate the efficacy of the preoperative left atrium (LA) size indices, other echocardiographic parameters, and clinical characteristics of the

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patients in predicting POAF risk in patients managed by off-pump CABG.

Materials and Methods

Study population

In this single-center study, the population was prospectively selected before off-pump CABG between January 2019 and December 2020. The patients were divided into two groups based on the development of POAF during the postoperative period until discharge and compared according to their baseline clinical characteristics, preoperative baseline echocardiographic characteristics, and perioperative outcomes. POAF was diagnosed as evidence of new-onset AF with any duration detected by continuous monitorization of the cardiac rhythm using five-lead telemetry in the intensive care unit (ICU) or standard 12- lead electrocardiogram (ECG) recordings. Hypertension (HT) was diagnosed as having blood pressure $\geq$140/90 mmHg or a history of using antihypertensive drugs. Diagnosis of diabetes mellitus (DM) necessitated an individual to have the following conditions: any current use of antidiabetic medicines, fasting blood glucose level >126 mg/dl, or HbA1c $\geq$7. Diagnosis of hyperlipidemia (HL) required the following criteria: total cholesterol level $\geq$200 mg/dL, LDL-c level $\geq$130 mg/dL, or use of cholesterol-lowering medication. Smoking was defined as those who currently smoke or have a history of >10 pack-years of smoking.

Off-pump beating-heart CABG technique was performed by the same surgical team. The surgical technique was assigned according to the patient's demographics, clinical features, aortic and coronary vasculature, and the evaluation of coronary anatomy and ascending aorta during the surgery. All patients were operated through median sternotomy under general anesthesia. The left internal mammary artery (LIMA), vena saphena manga, right internal mammary artery (RIMA), and radial artery were used as bypass grafts according to frequency.

In the postoperative period, prophylactic treatment for AF was not used on the patients. Amiodarone infusion was used as an antiarrhythmic option in patients who developed POAF. None of the patients needed electrical cardioversion. Anticoagulation treatments with low molecular weight heparin were applied according to the patient's weight and estimated glomerular filtration rate (eGFR).

Exclusion criteria included any prior cardiac surgery, emergent procedure, significant valvular disease, presence of a permanent pacemaker, implantable cardioverter defibrillator, or cardiac resynchronization therapy, atrial fibrillation or flutter, atrioventricular conduction abnormalities, pregnancy, systemic inflammatory or infectious disease, chronic obstructive pulmonary disease, end-stage renal failure (estimated glomerular filtration rate (eGFR) <15 ml/min/1.73 m^2), and liver failure. Patients with a history of AF available from medical records, Holter monitors, or prior ECGs were also excluded from the study. The study was approved by the local institutional board, and written informed consent was obtained from all patients (Ethic committee approval number: 2019/257; approval date: 07.11.2019).

Standard echocardiography and electrocardiogram

All patients were analyzed by a 12-lead resting ECG (Nihon Kohden, Cardiofax M, Tokyo, Japan) and transthoracic echocardiography (PhilipsEPIQ 7C ultrasound machine, Andover, MA, USA) during the preoperative period. We obtained continuous three-lead ECG during echocardiography recording. Echocardiographic examinations were performed in the left lateral decubitus position. Parasternal and apical views were used for 2-D and conventional Doppler examinations according to the guidelines of the American Society of Echocardiography [16]. We measured left ventricular end-diastolic diameter (LVEDD), 1eft ventricular end-systolic diameter (LVESD), septum wall thickness (IVS), and posterior wall thickness (PW) with M-mode tracings. Mitral inflow filling velocities (early (E) and late (A) diastolic peak velocities) and mitral inflow deceleration time were determined by pulse wave Doppler. Lateral mitral annulus systolic (Sm), peak early (Em), and late diastolic (Am) velocities were measured via tissue Doppler imaging. The E/A ratio and E/Em ratio were calculated. Left ventricular ejection fraction (LVEF) was calculated by Simpson's method using apical four-chamber and apical two-chamber views [16].

The left atrial diameter (LAD) was measured using M-mode tracings from the middle of the mitral annular plane to the posterior wall and indexed to body surface area (BSA) to calculate the left atrial diameter index (LADI). The left atrium area (LAA) evaluated from the apical four-chamber view at the end-ventricular systole, planimetered with the inferior LA border defined as the plane of the mitral annular plane excluding the confluence of the pulmonary veins and the LA appendage, then indexed to BSA for LAAI [17]. The simplified Bernoulli equation (P = 4x[Peak tricuspid regurgitation velocity]2) was used to calculate estimated systolic pulmonary artery pressure (sPAP) [18]. All parameters were measured three times, and average values were calculated for each parameter.

All patients were followed up in the ICU after surgery, and all ICU follow-ups were performed under continuous cardiac rhythm monitoring by five-lead telemetry. Standard 12- lead ECG recordings were performed preoperatively, immediately after the operation, and at least once time per day throughout the hospitalization period in the ICU and the inpatient ward. Additional ECG recordings were obtained in case of any suspected arrhythmia noticed by the patient, a nurse, or a doctor.

Statistical analysis

Analyses were carried out using SPSS 18.0 Statistical Package Program for Windows (SPSS Inc, Chicago, Illinois, USA). Quantitative and qualitative variables were expressed as mean±standard deviation (SD) and as numbers and percentages, respectively. Differences between independent groups were assessed by Student t-test for normally distributed quantitative variables, Mann-Whitney's U-test for variables without normal distribution, and Chi-square test for qualitative variables. Spearman correlation analyses were used to assess the correlations of the LAA, Em, Am, LVEF, and LAAI length of ICU stay with POAF. A multivariate logistic regression model with the backward stepwise method was used to determine the value of significant variables in the univariate analysis as the independent prognostic factors of POAF. The diagnostic ability of LAAI to detect POAF was evaluated using receiver operating characteristic (ROC) curves. All results were considered statistically significant at the level of $p \leq 0.05$.

Results

In this prospective follow-study, a total of 94 patients for whom off-pump CABG was planned between January 2019 and December 2020 were included. All the patients had sinus rhythm during the preoperative period. Surgery was postponed in two patients due to COVID-19; four patients did not accept surgery because of the high surgical risk; one had paroxysmal atrial fibrillation during the preoperative period; one patient required concurrent aortic valve prosthesis; medical follow-up was advised for one patient because of scar dominance on myocardial perfusion scintigraphy; the surgery canceled in one patient after detection of a mass in the lung. Overall 10 patients were excluded from the study, and therefore the final study population decreased to 84 patients (Figure 1).

Postoperative AF was observed in 32 patients (38%, 64.87 ± 10.15 years) whom 28 (87.5%) were men. In 52 patients (62%, 62.54 ± 9.37 years) did not have postoperative AF, and 42 (80.8%) were men. There were no significant differences in any demographic and preoperative variables between AF and non-AF groups (all p values were > 0.05) (Table 1). The mean age was slightly higher in the AF

Table 1. Demographic and preoperative variables.

Variables	Non-AF (n: 52)	AF (n: 32)	P
Age (years)	62.54 ± 9.37	64.87 ± 10.15	0.065
Male/Female n (%)	42/10 (81/19%)	28/4 (88/12%)	0.313
SBP (mmHg)	124.34 ± 12.66	121.63 ± 10.20	0.321
DBP (mmHg)	75.94 ± 8.71	74.60 ± 8.79	0.504
PP (mmHg)	48.20 ± 10.61	46.7 ± 9.68	0.524
BSA (m^2)	1.8 ± 0.33	1.8 ± 0.35	0.939
BMI (kg/m^2)	29 ± 4.3	28 ± 4.7	0.451
Medical history			
Hypertension n (%)	30 (58%)	19 (59%)	0.531
Diabetes Mellitus n (%)	21 (40%)	11 (36%)	0.376
Dyslipidemia n (%)	6 (12%)	5 (16%)	0.411
Family history of CAD n (%)	30 (58%)	14 (44%)	0.154
Smoking n (%)	31 (60%)	19 (59%)	0.581
Medications			
ASA n (%)	17 (33%)	7 (22%)	0.208
Clopidogrel n (%)	1 (2%)	0 (0%)	0.619
Nitrate n (%)	1 (2%)	0 (0%)	0.619
Statin n (%)	4 (8%)	2 (6%)	0.585
Beta-blockers n (%)	15 (29%)	9 (28%)	0.574
ACE inhibitors n (%)	10 (19%)	5 (16%)	0.456

*SBP: systolic blood pressure; DBP: diastolic blood pressure; PP: pulse pressure; BSA: body surface area; BMI: body mass index; CAD: coronary artery disease; ASA: acetylsalicylic acid; ACE: Angiotensin-converting enzyme.

Table 2. Echocardiographic baseline characteristics of groups.

Variables	Non-AF (n: 52)	AF (n: 32)	P
Left atrium diameter (cm)	3.6 ± 0.4	3.6 ± 0.5	0.333
LADI (cm/m^2)	2.0 ± 0.29	2.0 ± 0.45	0.390
LA maximum area (cm^2)	18.9 ± 3.7	21.3 ± 4.9	0.016
LAAI (cm^2/m^2)	10.4 ± 2.0	12.0 ± 2.6	0.001
sPAP(mmHg)	30.0 (2.0 − 37.0)	33.0 (20.0 - 64.0)	0.030
Epicardial fat tissue (cm)	0.71 ± 0.22	0.69 ± 0.17	0.682
Aortic diameter change	0.19 (0- 0.45)	0.13 (0 - 0.46)	0.359
LVEF (%)	60.5 (23.0 - 78.5)	57.15 (33.1 - 74.9)	0.050
Lateral E_m	9 (3 - 14)	7 (3 - 15)	0.047
Lateral A_m	10.8 ± 2.6	8.3 ± 3.0	0.050
Lateral S_m	9 (5 - 15)	7.5 (4 - 12)	0.237
E/E_m ratio	9.5 (6 - 35.1)	12.9 (6.2 - 31.7)	0.072

*LADI: left atrial diameter index; LA: Left atrium; LAAI: left atrial area index; sPAP: systolic pulmonary artery pressure; LVEF: Left ventricular ejection fraction.

Table 3. Intraoperative and postoperative variables in the study population.

Variables	Non-AF (n: 52)	POAF (n: 32)	P
ICU stay (day)	3 (2-5)	3 (2-7)	0.014
Service stay (day)	3 (0-6)	4 (2-19)	0.723
Number of bypass graft	3 (1-5)	3.5 (2-5)	0.077
LIMA use (%)	49 (94%)	31 (97%)	0.507
RIMA use (%)	8 (15%)	5 (16%)	0.604
Saphenous vein use (%)	41 (79%)	24 (75%)	0.440
Radial artery use (%)	6 (12%)	2 (6%)	0.347
Endarterectomy (%)	2 (4%)	2 (6%)	0.493
IABP (%)	0 (0%)	4 (12%)	0.019

*ICU: intensive care unit; LIMA: left internal mammary artery; RIMA: right internal mammary artery; IABP: intra-aortic balloon pump.

Table 4. Multiple logistic regression analysis for the assessment of independent predictors of postoperative atrial fibrillation.

Variables	OR 95% CI	P
LVEF	0.889 (0.796 − 0.994)	0.039
Lateral E_m	0.974 (0.791-1.198)	0.800
Lateral A_m	0.923 (0.771-1.106)	0.385
LA maximum area	1.005 (0.866-1.167)	0.948
LAAI	1.374 (1.092-1.729)	0.007
sPAP	1.055 (0.919 − 1.210)	0.448

*LVEF: Left ventricular ejection fraction; LA: Left atrium; LAAI: Left atrial area index; sPAP: systolic pulmonary artery pressure; CI: Confidence interval, OR: Odds ratio.

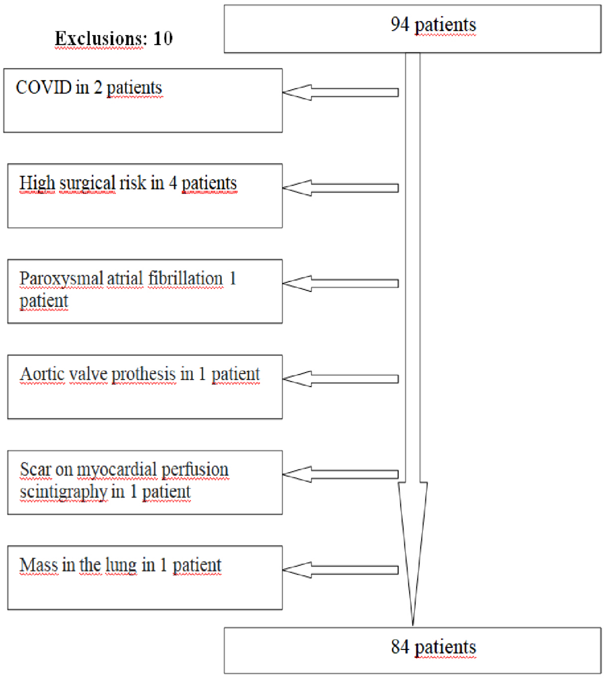
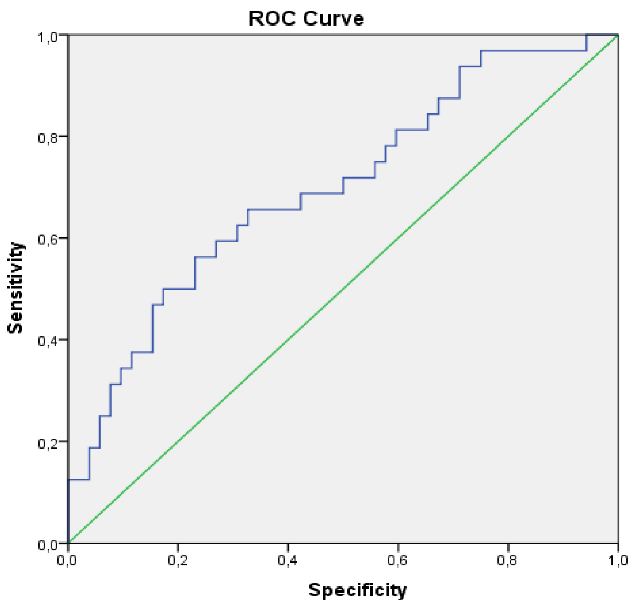


Figure 1. Study population selection flow diagram.



AUC: Area under curve, *CI:* Confidence interval.

Figure 2. Receiver operating curve (ROC) analysis revealed that a LAAI value of >11.25 cm^2/m^2 predicted the presence of POAF with a sensitivity of 66% and specificity of 67% (AUC=0.698, 95% CI, 0.582-0.815).

group, but it did not reach statistical significance (p = 0.065).

Table 2 shows preoperative echocardiographic parameters. Patients with POAF had significantly larger maximum LA area (18.9 ± 3.7 vs. 21.3 ± 4.9 cm^2, p = 0.016), higher LAAI (10.4 ± 2.0 vs. 12.0 ± 2.6 cm^2/m^2, p=0.001) and sPAP (30 (2-37) vs. 33 (20-64), p = 0.030). Also lateral wall Em (9 (3-14) vs. 7 (3-15), p = 0.047 and Am (10.8 ± 2.6 vs. 8.3 ± 3.0, p = 0.05)) , and LVEF (60.5 (23.0-78.5) vs. 57.15 (33.1-74.9), p = 0.050) were significantly lower in patients with POAF.

The patients with POAF had significantly higher use of intra-aortic balloon pumps (IABP) (p = 0.019) and a higher length of ICU stay (p = 0.014) than patients who remained in sinus rhythm. There were no statistically significant differences between the AF and non-AF groups among other perioperative variables (Table 3).

Multivariate linear regression analysis was performed to identify echocardiographic independent predictors of the development of POAF after off-pump CABG operation. Based on the backward stepwise model of multivariate analysis, LAAI (p=0.007, 95% CI for OR:1.374 (1.092-1.729)) and LVEF (p=0.039, 95% CI for OR:0.889 (0.796-0.994)) found to be the strongest independent predictors of POAF. In the present study, neither Em and Am nor sPAP and LA maximum area reached a significant difference in multiple logistic regression analysis (Table 4). Spearman's correlation test revealed that LAAI (r=0.33, p=0.002), length of ICU stay (r=0.27, p=0.01 and LAA (r=0.25, p=0.02) had significant positive correlations, whereas Lateral Am (r=-0.26, p=0.02) and LVEF (r=-0.22, p=0.04) had negative correlation with the presence of POAF.

The area under the ROC curve (AUC) analyses for LAAI value was 0.698; the LAAI value higher than 11.25 cm^2/m^2 was found to be predictive for POAF with 66% sensitivity and 67% specificity in the ROC curve analyses (Figure 2).

Discussion

In this study, we enlightened the importance of preoperative left atrial area index in the prediction of new-onset AF after off-pump coronary artery bypass grafting surgery. It is the first report to show that LAAI is an independent predictor of POAF in this patient group.

Although reported as benign in most cases, POAF was found to cause embolic events, heart failure, prolonged hospitalization, and poor prognosis in some cases [2]. A two-fold increased cardiovascular mortality risk was found in POAF patients after the CABG operation [19]. The strongest known risk factor for developing AF is increased age [20]. The other identified risk factors are male sex, obesity, systemic arterial hypertension, diabetes mellitus, low ejection fraction, history of MI, chronic obstructive pulmonary disease, chronic renal dysfunction, and paroxysmal AF [21,22].

In addition, increased LA size, principally maximal also minimal size, was associated with increased risk of AF development, stroke, heart failure, and mortality [23]. Although the American Society of Echocardiography suggests measuring the left atrial volume as the gold standard for LA measurement [16], in our daily practice, the calculation of the LAAI is both easy and superior to the LAD. In the postoperative period, although the causes of AF development are not fully understood, substrates for atrial fibrillation may include inflammation, oxidative stress, ischemia, catecholamines, atrial fibrosis, imbalance of autonomic tonus, use of vasoactive amines, changes in the expression of connexins [24].

Postoperative AF was reported in published meta-analyses to be less common in off-pump CABG patients compared to on-pump patients [25-27]. Factors leading to cardiopulmonary bypass-associated AF may be due to ischemia during cardioplegic arrest and atrial cannulation [28,29]. Other possible mechanisms are the immunological response induced by the aortic cross-clamp and aortic damage, the resulting inflammation, and complement activation [30]. In another meta-analysis, on-pump CABG surgery was associated with higher POAF and stroke, longer ventilation duration, hospital and ICU stay [7].

Systolic dysfunction of the left ventricle is usually associated with high left ventricular filling pressures. Despite the similar LA size, systolic dysfunction and high filling pressure of the left ventricle can interfere with LA reverse remodeling [31]. Accordingly, we have found that lower LVEF was an independent predictor of POAF.

Similar to the literature, POAF patients had long ICU requirements in our study. The cause of underlying prolonged ICU stay may include hemodynamic changes associated with AF and known complications caused by POAF [2].

It is a single-centered study conducted on a relatively small number of patients. Another limitation is that the results are limited to POAF detection only for the in-hospital period: the absence of post-discharge period records limits the interpretation of the results for this period. The results can not represent all CABG patients since we have selected patients strictly depending on the exclusion criteria. In this study, we excluded patients requiring emergency surgery, but LAA and LAAI can also be used in this patient group through their practical measurement.

Conclusion

LAA and LAAI were found to be independent predictors of POAF in patients who underwent off-pump beating-heart CABG surgery in the present study. Detection of high-risk patients in the preoperative period can enable us to apply early diagnosis and treatment strategies for the prophylaxis of POAF in this patient group. Patients at high risk for POAF can be identified with measurements taken by echocardiography in the preoperative period, which provides practical, repeatable, inexpensive, and easy-to-evaluate solutions.

Ethics approval

The research was approved by the ethical board of the Abant Izzet Baysal University Hospital, number 2019/257, on November 11nd 2019.

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