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The Predictive Role of Small Airway Dysfunction in Postoperative Atrial Fibrillation After Isolated Coronary Artery Bypass Surgery

İzole Koroner Arter Bypass Ameliyatı Sonrası Postoperatif Atriyal Fibrilasyon Gelişiminde Küçük Hava Yolu Disfonksiyonunun Prediktif Rolü

ORIGINAL ARTICLE
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ABSTRACT

Objective: Atrial fibrillation is the most common arrhythmia following coronary artery bypass graft surgery. The relationship between impaired lung function and atrial fibrillation has been described previously. We aimed to evaluate the prognostic influence of small airway function on predicting postoperative atrial fibrillation undergoing isolated coronary artery bypass graft surgery (CABG).

Methods: We retrospectively analyzed 283 patients who underwent isolated CABG at our institution between January 2020 and August 2020. The patients were divided into 2 groups according to the development of postoperative atrial fibrillation. Demographic characteristics of the patients were recorded; spirometry was performed for each patient before surgery. Small airway function was determined by forced mid-expiratory flow (forced expiratory flow 25%-75%) values measured by spirometry. Propensity score matching was applied to ensure a balanced distribution of demographic data between the 2 groups.

Results: The frequency of postoperative atrial fibrillation was 30.7% in our patient population. After propensity matching, forced expiratory volume in 1 second/forced vital capacity % [80.6 (73.8-87.8) vs. 76.3 (66.7-81.6), $P=0.006$] and forced expiratory flow 25%-75% (87.4 ± 14.2 vs. 75.2 ± 15.8, $P=0.001$) were significantly lower in postoperative atrial fibrillation group. In multivariate analysis, white blood cell count, left ventricular ejection fraction, cross-clamp time, and forced expiratory flow 25%-75% were found to be independent predictors of postoperative atrial fibrillation development after isolated CABG. In the receiver operating characteristic curve analysis, forced expiratory flow 25%-75% with an optimal threshold value of 81% could detect the presence of postoperative atrial fibrillation with 63.8% sensitivity and 70.1% specificity.

Conclusion: Our study demonstrated that small airway obstruction, as indicated by forced expiratory flow 25%-75% in spirometry, can be a simple predictive tool for the development of postoperative atrial fibrillation in patients undergoing isolated CABG.

Keywords: Coronary artery bypass graft surgery, postoperative atrial fibrillation, small airway function, spirometry

ÖZET

Amaç: Atriyal fibrilasyon (AF), koroner arter baypas cerrahisi (KABG) sonrası en yaygın aritmidir. Akciğer fonksiyonlarında bozulma ile AF arasındaki ilişki daha önce tarif edilmiştir. Bu çalışmada amacımız, izole KABG geçiren hastalarda küçük hava yolu fonksiyonunun postoperatif AF (PoAF) tahmin etmede prognostik etkisini değerlendirmekti.

Yöntem: Ocak 2020 ile Ağustos 2020 arasında merkezimizde izole KABG uygulanmış olan 283 hasta retrospektif olarak analiz edildi. Hastalar, PoAF varlığına göre 2 gruba ayrıldı. Hastaların demografik özellikleri kaydedildi; ameliyat öncesi yapılmış olan spirometri parametreleri değerlendirildi. Küçük hava yolu fonksiyonu, spirometri ile ölçülen zorlu orta ekspiratuvar akım (FEF25%-75%) değerleri ile belirlendi. Demografik verilerin iki grup arasında dengeli bir şekilde dağılımını sağlamak için propensity skoru eşleştirme yöntemi uygulandı.

Bulgular: Çalışma popülasyonumuzdaki PoAF sıklığı %30,7 idi. Propensity eşleştirmesi sonrasındaki analizde FEV1/FVC% [80,6 (73,8-87,8) vs. 76,3 (66,7-81,6), $P=0{,}006$] ve FEF25%-75% (87,4 ± 14,2 vs. 75,2 ± 15,8, $P=0{,}001$) PoAF grubunda anlamlı derecede daha düşüktü. Çok değişkenli analizde, lökosit sayısı, sol ventriküler ejeksiyon fraksiyonu, kross-klemp süresi

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ve FEF25%-75% izole KABG sonrası PoAF gelişiminin bağımsız prediktörleri olarak bulundu. ROC eğrisi analizinde, 81% optimal eşik değeri ile FEF25%-75% PoAF varlığını %63,8 duyarlılık ve %70,1 özgüllükle tespit edebildi.

Sonuç: Çalışmamız, özellikle küçük hava yolu obstrüksiyonunun bir göstergesi olan FEF25%-75% gibi spirometri parametrelerinin, izole KABG geçiren hastalarda PoAF gelişimi için basit bir öngörü aracı olabileceğini gösterdi.

Anahtar kelimeler: Koroner arter baypas cerrahisi, postoperatif atriyal fibrilasyon, küçük hava yolu fonksiyonu, spirometri

Postoperative atrial fibrillation (PoAF) is an important risk factor affecting short and long-term survival after cardiac surgery. Postoperative atrial fibrillation complicates approximately one-third of cases of cardiac surgery and is associated with major adverse consequences, including prolonged in-hospital length of stay, increased healthcare costs, and increased rehospitalization rates.[1-3] Despite advances in surgical techniques and perioperative care, the incidence of PoAF is still high. Cardiac surgery causes direct and indirect myocardial damage that increases the risk of negative atrial remodeling and arrhythmias.[4] In addition to myocardial damage and atrial remodeling, many factors have been identified that affect the development of PoAF. Rheumatic heart disease, chronic renal failure, diabetes mellitus (DM), hypertension (HT), chronic obstructive pulmonary disease (COPD), peripheral vascular disease left ventricular hypertrophy, preoperative digoxin use, prolonged aortic cross-clamp time, discontinuation of beta-blocker therapy in the preoperative period and increased sympathetic activation in the postoperative period, insufficient atrial protection, advanced age, postoperative fluid, and electrolyte loss play a role in the development of PoAF.[5,6] In addition to all these factors, hypoxia is also associated with the development of AF.[7]

Evaluation of pulmonary function before cardiac surgery is a guiding tool for determining the risk of anesthesia, intraoperative approach, and postoperative care.[8] The respiratory function test (RFT), also known as spirometry, is the most commonly used method to determine pulmonary function.[9] Spirometry assesses the patient's forced expiratory volume in 1 second (FEV-1) and forced vital capacity (FVC), which are used in the diagnosis of obstructive or restrictive ventilation defects. Peak expiratory flow (PEF), which reflects the diameter of the central airways and the activity of the expiratory muscles, and forced expiratory flow (FEF25-75), which indicates obstruction in the small airways, are the other parameters measured by spirometry.[8] Spirometry is closely associated with COPD, asthma, and interstitial lung disease. Previous studies showed that airflow limitation (FEV1/FVC <70% predicted) is an independent risk factor for postoperative complications in thoracic surgery.[10,11] However, data on the relationship between RFT and PoAF after coronary artery bypass graft surgery (CABG) is limited.

In this study, we aimed to investigate the relationship between RFT, especially FEF25-75 values as indicator of small airway function, and development of atrial fibrillation after isolated CABG.

ABBREVIATIONS

CABG	Coronary artery bypass graft surgery
COPD	Chronic obstructive pulmonary disease
DM	Diabetes mellitus
ECG	Electrocardiography
FEF	Forced expiratory flow
FEV-1	Forced expiratory volume in 1 second
FVC	Forced vital capacity
HT	Hypertension
LA	Left atrium
LIMA	Left internal mammarian artery
LVEF	Left ventricular ejection fraction
PEF	Peak expiratory flow
POAF	Postoperative atrial fibrillation
RFT	Respiratory function test
ROC	Receiver operating characteristic

Material and Methods

Study Population

Two hundred eighty-three eligible patients who underwent isolated CABG surgery at our institution between January 2020 and August 2020 were analyzed in this single-center, observational, retrospective study. Patients with a preoperative history of AF, severe COPD or use of inhaler drugs, severe heart failure (left ventricular ejection fraction < 40%), left atrium (LA) size greater than 50 mm, moderate or significant organic valvular heart disease, left or right incomplete or complete bundle branch block, antiarrhythmic use except beta-blockers, 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; therefore, patients undergoing urgent or emergent cardiac surgery were also excluded. Also, patients with a history of acute coronary syndrome in the last 6 months were not included in our study. Preoperative data included age, sex, body mass index, smoking status, and comorbid conditions: DM, HT, hyperlipidemia, left ventricular ejection fraction (LVEF), LA diameter, and presence of diastolic dysfunction. Diastolic dysfunction was determined according to the American Society of Echocardiography guidelines.[12] Biochemical parameters were obtained from samples taken in a maximum of 1-week period before surgery. The investigation conforms to the principles outlined in the Declaration of Helsinki. The University of Health Sciences, Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital Ethics Committee approved this retrospective study (Approval Number: 2019-10, Date: 12.02.2019).

Detection of Postoperative Atrial Fibrillation

After surgery, subjects were followed for at least 48-72 hours by continuous telemetry. A 12-lead electrocardiography (ECG) was obtained from the subjects every 12 or 24 hours at the intensive care and in-patient units, respectively. An additional 12-lead ECG was taken when the subjects complained of dyspnea, palpitation, or angina. Rhythm monitoring was continued until the discharge of the patients from the hospital. Postoperative atrial fibrillation was described as irregular, fast oscillations, or fibrillatory waves instead of regular *P* waves at ECG. An AF episode lasting longer than 30 seconds was accepted as PoAF.[13]

Pulmonary Function Evaluation

All measurements were assessed preoperatively (at most 1 month before the surgery). Measurements were performed according to the recommendations of the American Thoracic Society and European Respiratory Society. Forced vital capacity, FEV1, FEV1/ FVC, PEF, and forced expiratory flow between 25% and 75% of vital capacity (FEF25-75) were assessed by RFT. The patients were examined in a sitting position, and a nose clip was used. Predicted values were related to age, sex, and height.[14]

Statistical Analyses

Statistical analysis of the study was performed with the SPSS Version 26.0 program (SPSS Inc., Chicago, Ill, USA). Whether the variables indicate a normal dispersion; normally numerical dispersion variables as mean ± SD, non-normally dispersion numerical variables as median (interquartile range), and categorical variables were described as a percentage (%). Receiver operating characteristic (ROC) curve and Youden index [maximum (sensitivity + selectivity − 1)] were used to identify the predictive value of the FEF25/75% value that best detects postoperative AF development. Statistical analysis of numerical variables between independent groups was performed with Student's *t*-test or Mann–Whitney *U*-test. Analysis of categorical variables such as the AF and non-AF groups was performed with chi-square or Fisher's exact test. Because the study was nonrandomized, a logistic regression model with propensity scores (exact matching) was created with variables that were shown to be associated with postoperative AF in patients with CABG to balance patient characteristics and to perform propensity-matched analysis of the patients with and without postoperative AF. The variables used in this model were as follows: age, gender, DM, HT, and troponin-T level. The match tolerance was calculated as 0.011 and a total of 150 patients remained, and the analysis was continued on this patient group. In order to evaluate the value of variables in predicting PoAF, we performed logistic regression (stepwise backward elimination) analysis. Receiver working characteristic curve analysis of FEF25/75% was performed to calculate an optimal threshold value to detect the presence of postoperative AF. If the area under the ROC curve was above 0.5 and the *P*-value was <0.05, it was considered statistically significant.

Results

Postoperative atrial fibrillation occurred in 87 of 283 patients (30.7%). Data are stratified according to new-onset PoAF, and the baseline characteristics of the patients are detailed in Table 1. The mean age was 60.7 ± 9.3 years and 216 patients were male (76.3%). Patients with PoAF were generally older (65 ± 9.2 vs. 58.8 ± 8.7, *P* < 0.001) and female (39.1% vs. 16.4%, *P* < 0.001). Body mass index (BMI) was also higher in PoAF group (30.8 ± 4.7 vs. 28.9 ± 4.0, *P* < 0.001). Preexisting HT (*P*=0.003) and DM (*P*=0.013) were higher in PoAF group than in non-AF group. In terms of echocardiographic parameters, LVEF was significantly lower (51 ± 10.3 vs. 57.1 ± 8.0, *P* < 0.001), and LA diameter was higher (39.5 ± 4.0 vs. 37.2 ± 3.7, *P* < 0.001) in the PoAF group. In the biochemical evaluation, low hemoglobin levels (13.4 ± 1.4 vs. 14 ± 1.6, *P* < 0.001), high troponin-T [10 (6-16) vs. 7 (4-13), *P*=0.002], and low high-density lipoprotein (HDL) levels (37.3 ± 7.7 vs. 41 ± 7.9, *P* < 0.001) were significant in the PoAF group. Electrolyte parameters determined by potassium, sodium, and calcium values were similar in 2 groups. While beta-blocker use was numerically higher in the non-AF group, there was no statistically significant difference between the 2 groups [154 (78.6) vs. 61 (70.1), *P*=0.124]. Left internal mammarian artery (LIMA) graft use was higher in the non-AF group [189 (96.4) vs. 75 (86.2), *P*=0.002]. Cross-clamp time (51.9 ± 15.8 vs. 43.1 ± 14.7, *P* < 0.001) was significantly longer in the PoAF group. The comparison of spirometry variables according to the presence of PoAF is shown in Table 2. When the spirometry parameters were evaluated, it was found that FEV1/FVC was lower in the PoAF group [80 (73-86.4) vs. 76.3 (66.7-81.6), *P*=0.015]. No significant difference was observed between the 2 groups in terms of PEF (L and L/min). Forced expiratory flow 25-75L (2.4 ± 0.9 vs. 1.6 ± 1.0, *P* < 0.001) and FEF25%-75% (84.9 ± 13.9 vs. 77.9 ± 15.8, *P* < 0.001) values were found to be significantly lower in the PoAF group compared to the non-AF group. In order to tackle the substantial differences observed between the patient cohorts with and without PoAF, as well as to account for potential confounding variables previously shown to be associated with PoAF, we have opted for a technique known as propensity score matching. The variables that were used for propensity matching were the followings: age, gender, DM, HT, and troponin-T level. A total of 63 patients were selected from among the patients without PoAF and matched with 87 patients with PoAF. In the matched population, BMI was significantly higher in the PoAF group (29.1 ± 4.8 kg/m^2 vs. 30.8 ± 4.7 kg/m^2, *P*=0.032). In the group that developed AF after surgery, LVEF was lower (57.8 ± 8 vs. 51.1 ± 10.4, *P* < 0.001) and LA diameter was higher (38.1 ± 4.1 mm vs. 39.5 ± 4.0 mm, *P*=0.027). White blood cell (WBC) values were higher in the PoAF group than in the group without AF (7.7 ± 1.9 vs. 8.7 ± 2.4, *P*=0.010). High-density lipoprotein values were lower in the PoAF group (41.2 ± 8.6 vs. 37.3 ± 7.7, *P*=0.005). Cross-clamp time was significantly longer in the group with PoAF (42.2 ± 12.5 vs. 51.9 ± 15.8, *P* < 0.001). Among the spirometry parameters, FEV1/FVC [80.6 (73.8-87.8) vs. 76.3 (66.7-81.6), *P*=0.006], FEF25-75L (2.8 ± 1.1 vs. 1.6 ± 1.0, *P* < 0.001), and FEF25%-75% (87.4 ± 14.2 vs. 75.2 ± 15.8, *P*=0.001) were found to be significantly lower in the PoAF group. Other demographic, clinical, laboratory, and spirometry parameters were similar between the 2 groups. The demographic, clinical, and laboratory characteristics of the matched group are listed in Table 3.

Univariate logistic regression showed that BMI, LVEF, LA diameter, WBC, HDL, cross-clamp time, FEV1/FVC%, and FEF25%-75% were significantly associated with the frequency of PoAF following isolated CABG (Table 4). A multivariate logistic regression analysis was performed to determine the independent predictors of PoAF. Left ventricular ejection fraction [(OR=0.922, 95% CI (0.879-0.968), *P*=0.001], WBC [(OR=1.263, 95% CI (1.015-1.571), *P*=0.036] cross-clamp time [(OR=1.042, 95% CI (1.007-1.078), *P*=0.018], and FEF25%-75% [(OR=0.947, 95% CI (0.917-0.978), *P*=0.001] were independently associated with PoAF after isolated CABG (Table 4).

In the receiver operating characteristic (ROC) curve analysis, FEF25/75% with an optimal threshold value of 81% could detect the presence of postoperative AF with 63.5% sensitivity and 69% specificity (Figure 1).

Table 1. Demographics, Clinical, and Procedural Variables of Patients With and Without Postoperative Atrial Fibrillation

	All Patients (n=283)	Non-AF (n=196)	PoAF (n=87)	*P*
Age, years, mean (SD)	60.7 ± 9.3	58.8 ± 8.7	65 ± 9.2	**<0.001**
Gender (male), n (%)	216 (76.3)	163 (83.2)	53 (60.9)	**<0.001**
BMI (kg/m²), mean ± SD	29.5 ± 4.3	28.9 ± 4.0	30.8 ± 4.7	**<0.001**
DM, n (%)	138 (48.8)	84 (42.9)	54 (62.1)	**0.003**
HT, n (%)	178 (62.9)	114 (58.2)	64 (73.6)	**0.013**
Hyperlipidemia, %	89 (31.4)	65 (33.2)	24 (27.6)	0.351
Smoking status, n (%)	141 (49.8)	104 (53.1)	37 (42.5)	0.102
LVEF (%)	55.2 ± 9.2	57.1 ± 8.0	51 ± 10.3	**<0.001**
LA diameter, cm	37.9 ± 3.9	37.2 ± 3.7	39.5 ± 4.0	**<0.001**
LVDD, n (%)	162 (57.2)	107 (54.6)	55 (63.2)	0.176
Creatinine, mg/dL	0.9 ± 0.3	0.9 ± 0.3	0.9 ± 0.3	0.385
Potassium, mg/dL	4.2 ± 0.5	4.2 ± 0.5	4.1 ± 0.5	0.245
Sodium, mg/dL	138.8 ± 4.1	138.9 ± 3.0	138.6 ± 3.1	0.580
Calcium, mg/dL	9.2 ± 0.6	9.2 ± 0.6	9.3 ± 0.6	0.577
Troponin-T, ng/mL	8 (5-15)	7 (4-13)	10 (6-16)	**0.002**
Hemoglobin, mg/dL	13.8 ± 1.6	14 ± 1.6	13.4 ± 1.4	**<0.001**
WBC, 10³/mm³	8.4 ± 2.2	8.3 ± 2.1	8.7 ± 2.4	0.163
Total cholesterol, mg/dL	181.7 ± 48.1	180.6 ± 49.0	184.2 ± 46.1	0.559
LDL, mg/dL	101 (74-129)	102 (78-129)	99 (71-129)	0.550
HDL, mg/dL	39.9 ± 8	41 ± 7.9	37.3 ± 7.7	**<0.001**
Triglyceride, mg/dL	148 (105-197)	145.5 (107-192)	165 (105-205)	0.052
Beta-blockers, %	215 (76)	154 (78.6)	61 (70.1)	0.124
LIMA graft use, n (%)	264 (93.3)	189 (96.4)	75 (86.2)	**0.002**
Number of grafts, n (%)				0.712
1	13 (4.6)	9 (4.6)	4 (4.6)	
2	96 (33.9)	69 (35.2)	27 (31)	
3	129 (45.6)	90 (45.9)	39 (44.8)	
4	45 (15.9)	28 (14.3)	17 (19.5)	
Cross-clamp time, min	45.8 ± 15.6	43.1 ± 14.7	51.9 ± 15.8	**<0.001**

BMI, body mass index; DM, diabetes mellitus; HDL, high-density lipoprotein; HT, hypertension; LA, left atrium; LDL, low-density lipoprotein; LIMA, left internal mammarian artery; LVDD, left ventricular diastolic dysfunction; LVEF, left ventricular ejection fraction; WBC, white blood cell.

Table 2. Comparison of Spirometry Parameters According to the Presence or Absence of New-Onset Postoperative Atrial Fibrillation

	All Patients (n=283)	Non-AF (n=196)	PoAF (n=87)	*P*
FEV1/FVC%	78.4 (71-85.4)	80 (73-86.4)	76.3 (66.7-81.6)	**0.015**
PEF (L)	5 ± 1.8	5.1 ± 1.7	4.9 ± 2.1	0.331
PEF (L/min)	300.2 ± 109	304.4 ± 100.3	290.8 ± 126.4	0.331
FEF25/75	2.1 ± 1	2.4 ± 0.9	1.6 ± 1.0	**<0.001**
FEF25/75%	82.7 ± 14.8	84.9 ± 13.9	77.9 ± 15.8	**<0.001**

FEF25-75, forced expiratory flow 25–75; FEV-1, forced expiratory volume in the first second; FVC, forced vital capacity; PEF, peak expiratory flow.

Discussion

In this study, we investigated the relationship between spirometry parameters, especially small airway obstruction parameters and postoperative AF in patients undergoing isolated CABG. We revealed a significant association between new-onset PoAF and respiratory function. Forced expiratory volume in 1 second/FVC%, and FEF25%-75% were determined as independent predictors of PoAF in multivariate analysis. In addition, low LVEF, high WBC, and cross-clamp duration were other factors predicting the development of PoAF. It was determined that FEF25%-75% predicted the development of PoAF at values below 81%. To the best of our knowledge, this is the first study reporting that the small airway obstruction is associated with PoAF in isolated CABG patients.

Atrial fibrillation is the most common type of arrhythmia after cardiac surgery. Despite advanced surgery, myocardial protection,

Table 3. Demographics, Clinical, and Procedural Variables of Patients with Non-AF and AF (*P*-Value in Matched Group)

	All Patients (n = 150)	Non-AF (n = 63)	PoAF (n = 87)	*P*
Age, years	63.8 ± 9.2	62.1 ± 9	65 ± 9.2	0.053
Gender (male), n (%)	98 (65.3)	45 (71.4)	53 (60.9)	0.182
BMI, kg/m^2	30.1 ± 4.8	29.1 ± 4.8	30.8 ± 4.7	**0.032**
DM, n (%)	93 (62)	39 (61.9)	54 (62.1)	0.984
HT, n (%)	103 (68.7)	39 (61.9)	64 (73.6)	0.129
Hyperlipidemia, n (%)	42 (28)	18 (28.6)	24 (27.6)	0.894
Smoking status, n (%)	62 (41.3)	25 (39.7)	24 (27.6)	0.727
LVEF, %	53.9 ± 10	57.8 ± 8	51.1 ± 10.4	**<0.001**
LA diameter, mm	38.9 ± 4.0	38.1 ± 4.1	39.5 ± 4.0	**0.027**
LVDD, n (%)	91 (60.7)	36 (57.1)	55 (63.2)	0.452
Creatinine, mg/dL	0.9 ± 0.3	0.8 ± 0.2	0.9 ± 0.3	0.056
Potassium, mg/dL	4.2 ± 0.5	4.2 ± 0.5	4.1 ± 0.5	0.467
Sodium, mg/dL	138.7 ± 4.1	138.7 ± 3.0	138.6 ± 3.1	0.880
Calcium, mg/dL	9.3 ± 0.6	9.3 ± 0.5	9.3 ± 0.6	0.867
Troponin, ng/mL	10 (6–16)	9 (4–14)	10 (6–16)	0.162
Hemoglobin, mg/dL	13.5 ± 1.5	13.6 ± 1.6	13.4 ± 1.4	0.311
WBC, 10^3/mm^3	8.3 ± 2.3	7.7 ± 1.9	8.7 ± 2.4	**0.010**
Total cholesterol, mg/dL	178.8 ± 45	171.2 ± 42.5	184.2 ± 46.1	0.080
LDL, mg/dL	97.5 (66–123)	94 (63–118)	99 (71–129)	0.181
HDL, mg/dL	38.9 ± 8.3	41.2 ± 8.6	37.3 ± 7.7	**0.005**
Triglyceride, mg/dL	150 (105–199)	145 (105–197)	165 (105–205)	0.256
Beta-blocker use, n (%)	108 (72)	47 (74.6)	61 (70.1)	0.546
LIMA use, n (%)	135 (90)	60 (95.2)	75 (86.2)	0.069
Number of grafts, n (%)				0.784
1	5 (3.3)	1 (1.6)	4 (4.6)	
2	48 (32)	21 (33.3)	27 (31)	
3	68 (45.3)	29 (46)	39 (44.8)	
4	29 (19.3)	12 (19)	17 (19.5)	
Cross-clamp time, min	47.9 ± 15.3	42.2 ± 12.5	51.9 ± 15.8	**<0.001**
FEV1/FVC, %	77.8 (70.4–86.1)	80.6 (73.8–87.8)	76.3 (66.7–81.6)	**0.006**
PEF, L	5 ± 2	5.2 ± 1.7	4.9 ± 2.1	0.262
PEF, L/min	300 ± 117.8	312.7 ± 104.5	290.8 ± 126.4	0.262
FEF25-75, L	2.1 ± 1.2	2.8 ± 1.1	1.6 ± 1.0	**<0.001**
FEF25-75, %	80.3 ± 16.2	87.4 ± 14.2	75.2 ± 15.8	**0.001**

BMI, body mass index; DM, diabetes mellitus; FEF25–75, forced expiratory flow 25–75; FEV-1, forced expiratory volume in the first second; FVC, forced vital capacity; HDL, high-density lipoprotein; HT, hypertension; LA, left atrium; LDL, low-density lipoprotein; LIMA, left internal mammarian artery; LVDD, left ventricular diastolic dysfunction; LVEF, left ventricular ejection fraction; PEF, peak expiratory flow; WBC, white blood cell.

and anesthetic techniques, postoperative AF is still frequently observed in patients undergoing cardiac surgery.[15] The incidence of PoAF following CABG surgery occurs in 25%–40% of cases. However, the incidence increases after combined coronary artery bypass grafting and valve surgery, also in elderly patients as in our study.[16] Due to PoAF, there is an increase in mortality, as well as morbidities such as embolic events, leading to prolonged hospital stays.[17] It has been reported that the risk of PoAF in valvular and combined surgery, including coronary and valve, is higher than in coronary surgery alone. Mariscalco et al[18] found the rates of PoAF for isolated CABG, valve surgery, and combined surgery to be 22.9, 39.8, and 45.2%, respectively. In our study, the incidence of PoAF was 30.7% in isolated CABG, consistent with previous reports.

Table 4. Univariate and Multiple Logistic Regression Analyses to Identify Predictors of Postoperative AF Development in Matched Group

	Univariate Analysis			Multivariate Analysis		
	Odds Ratio	**95% CI (Lower–Upper)**	***P***	**Odds Ratio**	**95% CI (Lower–Upper)**	***P***
Age	1.037	0.999-1.076	0.057			
Gender	0.624	0.311-1.250	0.183			
BMI	1.081	1.006-1.162	**0.035**	1.096	0.997-1.205	0.057
DM	1.007	0.516-1.964	0.984			
HT	1.712	0.853-3.437	0.130			
LVEF (%)	0.926	0.890-0.963	**<0.001**	0.923	0.879-0.969	**0.001**
LA diameter	1.112	1.009-1.202	**0.030**	1.058	0.937-1.195	0.365
Troponin	1.023	0.998-1.049	0.070			
WBC	1.223	1.044-1.433	**0.013**	1.385	1.119-1.714	**0.003**
HDL	0.942	0.902-0.984	**0.007**	0.953	0.905-1.004	0.071
LIMA use	0.313	0.084-1.158	0.082			
Cross-clamp time	1.052	1.024-1.081	**<0.001**	1.042	1.007-1.078	**0.018**
FEV1/FVC %	0.967	0.941-0.994	**0.017**	0.969	0.932-1.007	0.109
FEF25/75 %	0.947	0.923-0.971	**< .001**	0.950	0.921-0.980	**0.001**

BMI, body mass index; DM, diabetes mellitus; HDL, high-density lipoprotein; HT, hypertension; FEF25-75, forced expiratory flow 25-75; FEV-1, forced expiratory volume in the first second; FVC, forced vital capacity; LA, left atrium; LIMA, left internal mammarian artery; LVEF, left ventricular ejection fraction; WBC, white blood cell.

Previous studies have demonstrated a significant correlation between impaired lung function and the development of AF.[19,20] In general population, it was found that the risk of developing AF was 1.4 times higher in patients with impaired lung function.[21] However, the underlying mechanisms in the relationship between impaired lung function and the development of AF are not yet well understood. However, it is suggested that hypoxia, systemic inflammation, and sympathetic nervous system activation are the most reliable factors in this process. In particular, the presence of hypoxia triggers pulmonary vasoconstriction that causes pulmonary HT and increased afterload in right heart chambers and contributes to the development of AF.[19] Also, recent studies have suggested that ectopic beats initiating AF often originate from the walls of the pulmonary veins, possibly caused by changes in gas composition or pulmonary HT.[22] However, as a result of hypoxia-inducible factor 1 and 2 expressions, reactive oxygen products, and vascular inflammation occur, and AF development is accelerated by the effect of atrial remodeling.[19] Indeed, some studies have revealed the presence of increased inflammatory markers in COPD patients with impaired lung function and suggested that these markers are also associated with the development of AF.

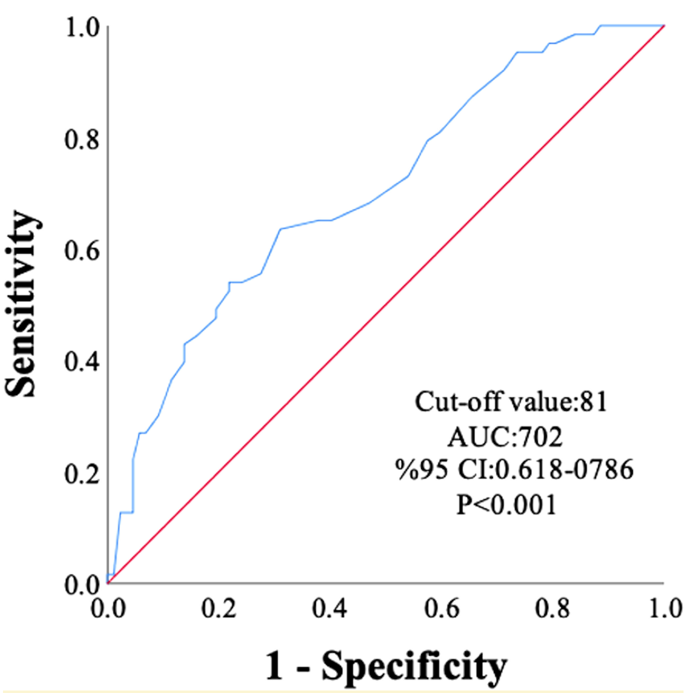

Figure 1. ROC curve analyses of FEF25%-75% in predicting postoperative atrial fibrillation in isolated CABG patients.

Forced expiratory volume in 1 second is the volume of air that can forcibly be blown out in first 1 second, after full inspiration. Decreased FEV-1 suggests large airway obstruction. Forced vital capacity is the maximum volume of air that can be removed from the lungs by exhaling forcefully, deeply, and rapidly after taking a deep breath. Forced vital capacity value indicates restricted lung capacity. The coexistence of COPD and AF is high in patients over 65 years old, and the severity of COPD is associated with an increase in the frequency of AF.[23] Also, the frequency of AF is between 5 and 15% in stable COPD patients, and this frequency reaches 30% in the presence of severe disease.[24] These results also confirm the bidirectional relationship between chronic airway obstruction, a cause of hypoxia, and AF.

Some studies suggest that small airway obstruction is a significant factor in early prediction of the development of COPD.[25] In fact, it is stated that the decreased FEF25%-75% values in patients with normal lung function should be taken into account and that these patients are at risk for the development of COPD. As a result of these evidences, it can be claimed that the hypoxic process starts before COPD and affects the development of arrhythmia with its systemic effect.[26,27] In addition, there are publications showing the association of decreased FEF25-75 values with atrial fibrillation.[28] In line with the literature, all of the FEV-1/FVC% and FEF25%-75% values were lower in the PoAF group, and also they were independent predictors of PoAF development after isolated CABG. However, FEF25%-75% seems to be a more valuable parameter than FEV-1/FVC% in predicting PoAF. Although there is no precise explanation for the mechanism in this relationship, the focus is on the connection mediated by inflammation.

In our study, there are other parameters associated with the development of PoAF. Advanced age, which has been shown in many studies to be associated with PoAF after cardiac surgery, was higher in the PoAF group in the present study before the propensity score matching. Similarly, cross-clamp time, low LVEF, and high LA diameter are also important factors in the development of PoAF, consistent with the literature. However, while LVEF was found to be an independent predictor of PoAF, LA diameter did not show statistical significance in the regression analysis. It has been previously known that prolonged cross-clamp time contributes to the development of AF by increasing myocardial damage. In our study, longer cross-clamp times were noted in patients who developed PoAF. There are conflicting reports that beta-blocker use in the preoperative period reduces PoAF rates,[29,30] and in our study, no difference was observed between the 2 groups in this regard. However, numerically beta-blocker use was higher in the group that did not develop PoAF. Finally, WBC level, an important infection biomarker, was also determined as an important independent predictor of PoAF development.

Study Limitations

The most important limitation of our study is that it was single-centered and retrospective. Other outcomes after CABG surgery were not evaluated in our study, although our hypothesis is only related to the prediction of postoperative AF, considering the possibility of other postoperative complications triggering AF, the presence of these data could make our study stronger. In the in-patients unit, electrocardiograms were recorded daily, which could have resulted in missing some of the paroxysmal AF episodes. Some inflammatory and biochemical markers that have been shown to be associated with PoAF in previous studies were not evaluated in our study. Our study's power is limited by the inability to achieve preoperative oxygenation level values as measured by blood gas analysis. In addition, data on the use of angiotensin-converting enzyme inhibitor drugs, which were reported to be associated with PoAF in some previous studies, were not evaluated in our study. Also, all CABG surgeries were not performed by a single operator or surgical team, and this may also be a confounding factor. Finally, propensity score matching could not be performed on all variables due to the limitation in the patient population.

Conclusion

Spirometry, which is one of the most important methods in the evaluation of pulmonary function and applied to almost every patient undergoing cardiac surgery, can be a simple predictive tool for the development of PoAF in patients undergoing isolated CABG. Especially FEF25%-75%, which is an indicator of small airway disease, has a significant predictive value in this regard. Identifying patients who may develop PoAF may be valuable in improving both the preoperative approach and the postoperative care conditions.

Ethics Committee Approval: The University of Health Sciences, Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital Ethics Committee approved this retrospective study (Approval Number: 2019-10, Date: 12.02.2019).

Informed Consent: Verbal informed consent was obtained from the patients who agreed to take part in the study.

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References

1. Hogue CW, Creswell LL, Gutterman DD, Fleisher LA, American College of Chest Physicians. Epidemiology, mechanisms, and risks: American College of Chest Physicians guidelines for the prevention and management of postoperative atrial fibrillation after cardiac surgery. *Chest*. 2005;128(2):9S-16S. [CrossRef]
2. Mitchell LB, CCS Atrial Fibrillation Guidelines Committee. Canadian Cardiovascular Society atrial fibrillation guidelines 2010: prevention and treatment of atrial fibrillation following cardiac surgery. *Can J Cardiol*. 2011;27(1):91-97. [CrossRef]
3. Taha A, Nielsen SJ, Bergfeldt L, et al. New-onset atrial fibrillation after coronary artery bypass grafting and long-term outcome: a population-based nationwide study from the SWEDEHEART registry. *J Am Heart Assoc*. 2021;10(1):e017966. [CrossRef]
4. Goldberger JJ, Arora R, Green D, et al. Evaluating the atrial myopathy underlying atrial fibrillation: identifying the arrhythmogenic and thrombogenic substrate. *Circulation*. 2015;132(4):278-291. [CrossRef]
5. Akintoye E, Sellke F, Marchioli R, Tavazzi L, Mozaffarian D. Factors associated with postoperative atrial fibrillation and other adverse events after cardiac surgery. *J Thorac Cardiovasc Surg*. 2018;155(1):242-251. [CrossRef]
6. Geçmen Ç, Babür Güler G, Erdoğan E, et al. SYNTAX score predicts postoperative atrial fibrillation in patients undergoing on-pump isolated coronary artery bypass grafting surgery. *Anatol J Cardiol*. 2016;16(9):655-661. [CrossRef]
7. Gami AS, Hodge DO, Herges RM, et al. Obstructive sleep apnea, obesity, and the risk of incident atrial fibrillation. *J Am Coll Cardiol*. 2007;49(5):565-571. [CrossRef]
8. Park HJ, Kim SM, Kim HR, Ji W, Choi CM. The value of preoperative spirometry testing for predicting postoperative risk in upper abdominal and thoracic surgery assessed using big-data analysis. *J Thorac Dis*. 2020;12(8):4157-4167. [CrossRef]
9. Kent BD, Mitchell PD, McNicholas WT. Hypoxemia in patients with COPD: cause, effects, and disease progression. *Int J Chron Obstruct Pulmon Dis*. 2011;6:199-208. [CrossRef]

10. Viceconte M, Rocco IS, Pauletti HO, et al. Chronic obstructive pulmonary disease severity influences outcomes after off-pump coronary artery bypass. *J Thorac Cardiovasc Surg*. 2018;156(4): 1554-1561. [CrossRef]
11. Szylińska A, Kotfis K, Listewnik M, Brykczyński M, Marra A, Rotter I. The burden of chronic obstructive pulmonary disease in open heart surgery–a retrospective cohort analysis of postoperative complications: STROBE compliant. *Med (Baltim)*. 2020;99(13):e19675. [CrossRef]
12. Nagueh SF, Smiseth OA, Appleton CP, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr*. 2016;29(4):277-314. [CrossRef]
13. Abdelmoneim SS, Rosenberg E, Meykler M, et al. The incidence and natural progression of new-onset postoperative atrial fibrillation. *JACC Clin Electrophysiol*. 2021;7(9):1134-1144. [CrossRef]
14. Quanjer PH, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R, Yernault JC. Lung volumes and forced ventilatory flows. Report working party standardization of lung function tests, European Community for steel and coal. Official statement of the European Respiratory Society. *Eur Respir J Suppl*. 1993;16:5-40. [CrossRef]
15. Sanjuán R, Blasco M, Carbonell N, et al. Preoperative use of sotalol versus atenolol for atrial fibrillation after cardiac surgery. *Ann Thorac Surg*. 2004;77(3):838-843. [CrossRef]
16. Maisel WH, Rawn JD, Stevenson WG. Atrial fibrillation after cardiac surgery. *Ann Intern Med*. 2001;135(12):1061-1073. [CrossRef]
17. Mariscalco G, Klersy C, Zanobini M, et al. Atrial fibrillation after isolated coronary surgery affects late survival. *Circulation*. 2008; 118(16):1612-1618. [CrossRef]
18. Mariscalco G, Biancari F, Zanobini M, et al. Bedside tool for predicting the risk of postoperative atrial fibrillation after cardiac surgery: the POAF score. *J Am Heart Assoc*. 2014;3(2):e000752. [CrossRef]
19. Simons SO, Elliott A, Sastry M, et al. Chronic obstructive pulmonary disease and atrial fibrillation: an interdisciplinary perspective. *Eur Heart J*. 2021;42(5):532-540. [CrossRef]
20. Goudis CA. Chronic obstructive pulmonary disease and atrial fibrillation: an unknown relationship. *J Cardiol*. 2017;69(5):699-705. [CrossRef]
21. Lee SN, Ko SH, Her SH, et al. Association between lung function and the risk of atrial fibrillation in a nationwide population cohort study. *Sci Rep*. 2022;12(1):4007. [CrossRef]
22. Buch P, Friberg J, Scharling H, Lange P, Prescott E. Reduced lung function and risk of atrial fibrillation in the Copenhagen City Heart Study. *Eur Respir J*. 2003;21(6):1012-1016. [CrossRef]
23. Proietti M, Laroche C, Drozd M, et al. Impact of chronic obstructive pulmonary disease on prognosis in atrial fibrillation: a report from the EURObservational Research Programme Pilot Survey on atrial fibrillation (EORP-AF) General Registry. *Am Heart J*. 2016;181:83-91. [CrossRef]
24. Şahan E, Bulut S. Relationship between disease severity and atrial fibrillation in chronic obstructive pulmonary disease. *Turk Kardiyol Dern Ars*. 2021;49(7):517-521. [CrossRef]
25. Kwon DS, Choi YJ, Kim TH, et al. FEF25-75% values in patients with normal lung function can predict the development of chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis*. 2020;15:2913-2921. [CrossRef]
26. Vlahou A, Diplaris K, Ampatzidou F, Karagounnis L, Drossos G. The role of blood transfusion in the development of atrial fibrillation after coronary artery bypass grafting. *Thorac Cardiovasc Surg*. 2016; 64(8):688-692. [CrossRef]
27. Ho CH, Chen YC, Chu CC, Wang JJ, Liao KM. Postoperative complications after coronary artery bypass grafting in patients with chronic obstructive pulmonary disease. *Med (Baltim)*. 2016;95(8):e2926. [CrossRef]
28. Chahal H, Heckbert SR, Barr RG, et al. Ability of reduced lung function to predict development of atrial fibrillation in persons aged 45 to 84 Years (from the multi-ethnic study of atherosclerosis-lung study). *Am J Cardiol*. 2015;115(12):1700-1704. [CrossRef]
29. Norhayati MN, Shaiful Bahari I, Zaharah S, Nik Hazlina NH, Mohammad Aimanazrul Z, Irfan M. Metoprolol for prophylaxis of postoperative atrial fibrillation in cardiac surgery patients: systematic review and meta-analysis. *BMJ Open*. 2020;10(10):e038364. [CrossRef]
30. Kim SH, Hwang HY, Choi JW, Jang MJ, Kim KH, Kim KB. The impact of beta-blocker use on postoperative atrial fibrillation after aortic valve replacement. *J Thorac Dis*. 2020;12(5):2545-2552. [CrossRef]