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Original Article

Incidence, Predictors, and Prognostic Impact of New-onset Atrial Fibrillation After Isolated Primary Coronary Artery Bypass Grafting

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Abstract

Background: New-onset atrial fibrillation (NOAF) after coronary artery bypass grafting (CABG) is associated with considerable morbidity and mortality. The objectives of this study were to estimate the incidence and predictors of NOAF after isolated primary CABG and evaluate its prognostic impact on the hospital outcomes of surgery.

Methods: This study included 154 consecutive patients who underwent isolated primary CABG between October 2021 and February 2022. Patients were divided into two groups; Group 1 included patients with NOAF, and Group 2 had patients without NOAF.

Results: NOAF occurred in 29 patients (18.8%). NOAF patients were significantly older (52.13± 6.30 vs. 55.45± 7.47 years; p =0.028), with more prevalence of diabetes mellitus but did not reach a significant level (62.1% vs. 44.8%; p = 0.094) and had a greater preoperative white blood cells count (WBCs) (8.87± 2.95 vs. 8.0± 2.17 /mm3; p = 0.071). Preoperative creatinine clearance (137.58± 53.94 vs. 114.94± 39.18 ml/min; p = 0.04), postoperative ischemic ECG changes (55.2% vs. 30%; p = 0.004), perioperative myocardial infarction (31% vs. 15.2%; p= 0.046), postoperative CK-MB (84.83± 81.26 vs. 64.76±46.58 units; p= 0.077), hemodynamic instability (72.4% vs. 41.6%; p= 0.003), and postoperative significant ECG changes (34.5% vs. 17.6%; p= 0.044) were greater in patients with NOAF. Age, preoperative creatinine clearance, preoperative WBC, and DM were associated with NOAF in the univariable analysis. None were found to be predictors of NOAF in the multivariable analysis.

Conclusions: NOAF after isolated primary CABG is common. Advanced age, renal function, hemodynamic instability, and perioperative myocardial infarction might be associated with NOAF.

KEYWORDS

Atrial fibrillation; Coronary artery bypass grafting; Cardiac surgery; Postoperative care

Article History

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Introduction

Postoperative atrial fibrillation (POAF) after cardiac surgery is a common complication, with an incidence of 30 - 50% [1]. Furthermore, POAF was associated with a 3.5-fold increase in mortality risk [2]. The European Society of Cardiology (ESC) guidelines defined POAF as atrial fibrillation in the immediate postoperative period with a peak incidence between day two and four [3]. The incidence of POAF varied according to the surgery performed. The pathogenesis of atrial fibrillation is multifactorial and includes atrial fibrosis,

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inflammation, oxidative stress, ischemia, and excessive secretion of catecholamines into the circulation [4]. However, the exact mechanism of new-onset atrial fibrillation (NOAF) is unclear. Dilatation, hypertrophy, and fibrosis of the atrium due to aging-related processes can lead to a heterogeneous myocardium, which can develop inflammation and edema when subjected to surgical stress and trauma. Therefore, the myocardial tissue undergoes different refractory periods with conduction abnormalities [5]. Ischemia is the most likely cause of NOAF that occurs on the day of surgery, while an inflammatory response and oxidative stress after the use of a cardiopulmonary bypass (CPB) appear on the 2nd postoperative day [6]. NOAF episodes after CABG often last 24 hours after surgery since most patients have a normal left atrial diameter and ejection fraction (EF) [7]. Long-standing NOAF may cause electrophysiological remodeling with progression into malignant arrhythmia or death [1]. The impact of NOAF after coronary artery bypass grafting (CABG) is still a subject of ongoing research. Thus, this study estimated the incidence and predictors of NOAF after isolated primary CABG and assessed the prognostic impact of NOAF on the outcome of CABG.

Patients and Methods

Design and patients

This prospective observational single-center study was conducted on 154 consecutive patients who underwent isolated primary CABG. The study was conducted over five months between October 2021 and February 2022. All patients were eligible for surgical revascularization according to the ESC guidelines. The study included patients who were scheduled for isolated primary CABG. Patients with preoperative atrial fibrillation were excluded.

Study data:

Data collected for this study included age, gender, body mass index (BMI), chronic obstructive lung disease (COPD), smoking, dyslipidemia, hypertension, chronic heart failure, diabetes mellitus, chronic kidney disease (CKD), peripheral arterial disease (PAD), myocardial infarction (MI), stroke, left ventricular EF, left atrial diameter, multivessel disease and left main (LM) disease. Laboratory data included total leucocytic count, hemoglobin, and HbA1C. Preoperative risk stratification was performed using EuroSCORE. Operative data included operative urgency, cardiopulmonary bypass, ischemic and operative times, and incomplete revascularization. Hospital outcomes included the duration of mechanical ventilation, ECG changes, perioperative MI, stroke, CK-MB, and hospital mortality.

Surgical approach

All procedures were performed under complete aseptic conditions with invasive and noninvasive monitoring exclusively through conventional median sternotomy, mainly with extracorporeal circulation rather than off-pump (91.6% on-pump, 8.4% off-pump). Myocardial protection was achieved mostly (91.5%) by infusion of warm, intermittent, antegrade blood cardioplegia solution every 15-20 minutes. Arterial and venous conduits were used for grafting target coronaries with significant lesions. The left internal mammary artery (LIMA) was the main conduit (n= 149, 96.8%). The right internal mammary artery was used in 10 patients (6.5%) and radial artery in 8 patients (5.2%). Venous conduits were used in all patients. Complete revascularization was achieved in 80 patients (51.9%). Only 18 patients (11.7%) had total arterial revascularization. Most patients had LIMA to left anterior descending artery (LAD) grafting (96.8%) and right coronary artery (RCA) bypass (61.0%). Three patients (1.9%) underwent LAD endarterectomy. Monofilament polypropylene sutures (7/0 or 8/0) were used for distal anastomosis, and (6/0) were used for all proximal anastomosis in a continuous suture manner using different techniques. Finally, the grafts were de-aired, the cardiopulmonary bypass was weaned off, and hemostasis and chest closure were performed. One patient (0.6%) needed to be connected temporarily to the pacemaker. Intraoperative complications included cardiac arrest (n= 2, 1.3%), neck hematoma (n= 2, 1.3%), and protamine sulfate reaction (n= 1, 0.6%).

Statistical analysis

Values are presented as the mean ± standard deviation (SD) or as numbers and proportions, as appropriate. As indicated, the chi-squared test or

Table 1: Comparison of demographic and baseline preoperative data in relation to the incidence of post-CABG new-onset atrial fibrillation (AF). Continuous variables are presented as mean ± standard deviation, and qualitative variables are presented as frequency (percentage)

Variables	Total (n=154)	Study groups		
		AF Group (n=29)	Non-AF Group (n=125)	p-value
Age (years)	54.83±7.36	55.45 ± 7.47	52.13 ± 6.30	0.028
Female	35 (22.7)	9 (31.0)	26 (20.8)	0.236
Body Mass Index, kg/m2	30.56 ± 3.17	31.25 ± 2.55	30.40 ± 3.28	0.193
COPD	35 (22.7)	8 (27.6)	27 (21.6)	0.488
Smoking	99 (64.3)	15 (51.7)	84 (67.2)	0.117
Dyslipidemia	92 (59.7)	21 (72.4)	71 (56.8)	0.122
Hypertension	83 (53.9)	17 (58.6)	66 (52.8)	0.571
CHF	5 (3.2)	1 (3.4)	4 (3.2)	>0.99
Diabetes mellitus	74 (48)	18 (62.1)	56 (44.8)	0.094
CKD	8 (5.2)	0	8 (6.4)	0.353
Peripheral arterial disease	20 (13)	4 (13.8)	16 (12.8)	>0.99
Previous MI	71(46.1)	17 (58.6)	54 (43.2)	0.133
Previous PCI	24 (15.5)	4 (13.8)	20 (16.0)	1.00
Previous Stroke or TIA	8 (5.2)	2 (6.9)	6 (4.8)	0.645
Preoperative LVEF %	57.47 ± 10.34	56.90 ± 12.35	57.61 ± 9.87	0.774
Preoperative LVEF < 40%	9 (5.8)	3 (10.3)	6 (4.8)	0.372
Preoperative LA diameter	38.73 ± 5.36	37.46 ± 6.56	39.02 ± 5.04	0.168
Multivessel disease	117 (75.97)	24 (82.75)	93 (74.4%)	0.343
LM disease	47(30.5)	11 (37.9)	36 (28.8)	0.336
Preoperative TLC /m3	8.16 ± 2.35	8.87 ± 2.95	8.00 ± 2.17	0.071
Preoperative Hgb, g/dl	13.43 ± 1.63	13.67 ± 1.87	13.38 ± 1.58	0.389
Preoperative C. Cl (ml/min)	119.2 ± 43.08	137.58 ± 53.90	114.94± 39.18	0.040
Preoperative ALT unit	32.72 ± 26.61	40.77 ± 45.80	30.85 ± 19.48	0.263
Preoperative HBA1C %	6.12 ± 1.07	6.38 ± 1.07	6.10 ± 1.05	0.209
Euro Score additive	1.32 ± 1.19	1.38 ± 1.05	1.31 ± 1.23	0.765

ALT: alanine transaminase; CHF: chronic heart failure; C. Cl: creatinine clearance; CHF: congestive heart failure; CKD: chronic kidney disease; HBA1C: glycated hemoglobin; Hgb: Hemoglobin; LA: left atrium; LM: left main; LVEF: left ventricular ejection fraction; MI: myocardial infarction; PCI: percutaneous coronary intervention; TIA: transient ischemic attack; TLC: total leucocyte count

Fisher's exact test evaluated the relationships between qualitative variables. Continuous variables were checked for normality by using the Shapiro–Wilk test. As the data were normally distributed, an unpaired t-test was used. A logistic regression model included variables with p-values < 0.1 in univariable analysis to detect independent predictors of NOAF. All tests were bilateral, and a p-value of 5% was the limit of statistical significance. The analysis was performed with the statistical package software IBM-SPSS version 21 (IBM Corp- Chicago- IL- USA).

Results

The study included 154 patients with a mean age of 54.83±7 years. The participants were predominantly males (77.3%), chronic smokers (64.28%), and dyslipidemic (59.7%). Patients mainly presented with multivessel disease (76%). The mean EuroSCORE was 1.32 ± 1.19. Most patients underwent on-pump (91%) elective (96%) CABG. The overall mortality rate was 2.6% (n= 4).

NOAF occurred in 29 out of 154 patients (18.8%). Patients were divided into two groups: Group 1 included patients with NOAF, and Group 2 had patients without NOAF. The two groups were compared in terms of demographic and

Table 2: Comparison of procedural characteristics according to the development of post-CABG New-Onset atrial fibrillation (AF). Continuous variables are presented as mean ± standard deviation, and qualitative variables are presented as frequency (percentage)

Variables	Total (n=154)	Study groups		
		AF Group (n = 29)	Non-AF Group (n = 125)	p-value
Emergency CABG	6 (3.9)	2 (6.9)	4 (3.2)	**0.315**
Off-pump	13 (8.4)	3 (10.3)	10 (8.0)	**0.712**
Aortic cross-clamp time (min)	66.15 ± 38.00	71.17 ± 39.73	64.98 ± 37.81	**0.433**
CPB time (min)	107.21 ± 61.67	115.38 ± 59.27	105.31 ± 62.29	**0.430**
Operative time (min)	296.62 ± 92.29	308.28 ± 96.06	293.92 ± 91.58	**0.452**
Incomplete revascularization	74 (48.1)	13 (44.8)	61 (84.4)	**0.700**

CABG: coronary artery bypass grafting; CPB: cardiopulmonary bypass

baseline preoperative data (Table 1), procedural characteristics (Table 2), and postoperative outcomes (Table 3).

NOAF patients were older than non-AF patients, with significantly lower creatinine clearance. There was no significant difference in the preoperative variables between groups. Patients with NOAF had no significant difference in procedural data. Regarding postoperative outcomes, patients with NOAF had significantly higher postoperative ECG changes, perioperative MI, and hemodynamic instability, with no difference in postoperative mortality between groups. Age, preoperative creatinine clearance, preoperative WBC, and DM were associated with NOAF in the univariable analysis. None were found to be predictors of NOAF in the multivariable analysis.

Table 3: Comparison of postoperative outcomes in relation to the incidence of post-CABG new-onset atrial fibrillation (AF). Continuous variables are presented as mean ± standard deviation, and qualitative variables are presented as frequency (percentage)

Variables	Total (n=154)	Study groups		
		AF Group (n = 29)	Non-AF Group (n = 125)	p-value
Mechanical Ventilation Time (hrs)	13.98 ± 19.2	21.31 ± (30.80)	12.28 ± 15.00	**0.134**
Postoperative Ischemic ECG Changes	2 (1.3)	2 (6.9)	2 (1.3)	**0.044**
Postoperative CK-MB	68.54 ± 55.03	84.83 ± 81.26	64.76 ± (46.58)	**0.077**
Postoperative TLC	16.13 ± 5.22	16.29 ± 4.65	16.10 ± (5.36)	**0.857**
Perioperative MI	28 (18.1)	9 (31.0)	19 (15.2)	**0.046**
Postoperative ALT	48.27± 37.98	57.10 ± 44.31	46.21 ± 36.70	**0.226**
Postoperative ECG Changes	32 (20.8)	10 (34.5)	22 (17.6)	**0.044**
Postoperative stroke	3 (1.9)	1 (3.4)	2 (1.6)	**0.468**
Postoperative EF	55.25 ± 8.48	55.55 ± 8.61	55.19 ± 8.49	**0.835**
ICU Stay (Days)	3.32 ± 2.04	3.67 ± 2.07	3.24 ± 2.04	**0.307**
In-Hospital mortality	4 (2.6)	1 (3.4)	3 (2.4)	**0.570**
Hospital Stay (days)	10.34 ± 5.73	11.34 ± 5.63	10.13 ± 3.56	**0.145**
Perioperative Hemodynamic Instability	73 (47.4)	21 (72.4)	52 (41.6)	**0.003**
Perioperative Inotropic Support	97 (63)	19 (65.5)	78 (62.4)	**0.754**
Perioperative use of IABP	9 (5.8)	2 (6.9)	7 (5.6)	**0.678**
Bleeding (ml/24 hrs)	548 ± 328.76	594.83 ± 372.8	537.60 ± 318.36	**0.400**
Exploration For Bleeding	12 (7.79)	3 (10.3)	9 (7.2)	**0.700**

ALT: alanine transaminase; CK-MB; creatine kinase –MB; ECG; electrocardiography; EF: Ejection fraction; ICU: intensive care unit; MI: myocardial infarction; IABP: Intra-aortic balloon pump

Discussion

Postoperative AF is a serious complication following CABG with poor outcomes. Several guidelines have recommended prophylaxis for POAF. However, these suggestions reveal unnecessary exposure to medications; therefore, many physicians do not regularly apply them. This proposition may expose up to 70% of patients undergoing CABG to antiarrhythmic medications and their subsequent side effects [8], so it is essential to predict which patients may develop NOAF.

The incidence of postoperative NOAF varied between studies (20 to 40%), likely reflecting differences in patient populations (e.g., operative urgency, critical state, and hemodynamic stability), the use of preoperative prophylactic therapies (e.g., beta-blockers and amiodarone), and variability in the rigor and duration of detection. In this prospective study, we found that patients with NOAF after CABG were significantly older than those without AF. Dilatation, hypertrophy, and fibrosis of the left atrium due to aging-related processes are the underlying mechanisms. Similar observations were made by Uysal and colleagues [8]. Moreover, Anatolevna and coworkers [9] reported that the left atrial dimension and increased postoperative concentrations of IL-6, IL-8, and superoxide dismutase were independent predictors of POAF after CABG in elderly patients. Uysal and colleagues [8] found that the preoperative LVEF was significantly lower in patients with AF than in those without POAF (50.3 ± 11 vs. 56.6 ± 8.4, respectively, $p < 0.001$). This finding contrasts our study, which found the difference to be nonsignificant.

Remarkably, we found that LM disease was more common in the NOAF group, but the difference was insignificant. Anatolevna and colleagues [9] also reported the same result. In our study, we also revealed no significant sex difference. At the same time, Lee and associates [10] reported that the percentage of females who survived long-term AF related to POAF decreased, and a significant correlation with long-term mortality after CABG was observed among female patients with POAF. This difference suggests more strict surveillance for AF among female patients. Although the difference was not statistically significant, the current study revealed a greater body mass index in the AF group. Avdagic and colleagues [11] reported similar results. Nonetheless, we found that DM was significantly greater in the AF group. Our study revealed that the left atrial diameter was greater in the NOAF group, but the difference was not statistically significant. Sihombing and colleagues [12] concluded that patients with NOAF had a significantly greater preoperative LA diameter and volume and total pulmonary vein diameter as an independent predictor of postoperative AF. This can be explained by the fact that the ganglionic plexus in the pulmonary vein plays a significant role in the triggering and continuation of AF [13]. Excessive excitement due to sympathetic activity or temporary dysfunction of the central nervous system during surgery may result in dysfunction of the cardiac plexus ganglia [12]. Avdagic and colleagues [11] concluded that the atrial natriuretic peptide (ANP) genotype did not predispose patients to NOAF after CABG. However, the ANP has been reported to be a marker for predicting the occurrence of POAF.

This study found that higher preoperative leucocytic count (TLC) and lower preoperative creatinine clearance were significantly associated with NOAF. In contrast, Aksoy and collaborators [14] reported no significant difference in TLC but a significantly greater C-reactive protein (CRP) level in the POAF group. Similarly, Kosmidou et al. [15] reported greater preoperative ALT in patients with NOAF, although the difference was not statistically significant. We found no significant difference between the AF and non-AF groups regarding EuroSCORE. The same result was reported in a previous study by Anatolevna and colleagues [9]. Our study revealed that emergency surgery was significantly greater but did not reach a significant level in POAF patients than in those who remained in sinus rhythm. Our study showed that the incidence of POAF was lower in patients who underwent off-pump CABG. A recent systemic review and meta-analysis [16] comprising 16261 participants from 54 clinical trials comparing the safety and effectiveness of on-pump and off-pump CABG reported that the incidence of POAF was significantly lower in the off-pump CABG group. Kosmidou and colleagues [15] revealed that retrograde cardioplegia independently predicts NOAF. The present study revealed that postoperative ischemic ECG changes and postoperative CK-MB levels were significantly greater in those who developed POAF. The perioperative MI was significantly greater in those who developed POAF. In contrast, Velioglu and coworkers [17] revealed no significant difference in perioperative MI between patients with and without AF. AF worsens the patient's hemodynamic status compared to sinus rhythm due to low cardiac output. Tachycardia and a lack of coordinated atrial contraction are possible mechanisms. This finding can explain our finding of a significantly greater incidence of hemodynamic instability in the POAF group.

Our study did not find that POAF was associated with postoperative stroke; however, Avdagic et al. [11] reported a greater periprocedural stroke rate in the POAF group. Future studies are warranted to determine the extent to which recurrent AF during long-term follow-up contributes to stroke risk. Our study concluded that POAF was associated with a longer duration of hospitalization but did not reach a significant level. This may be explained by hemodynamic instability due to AF, possible complications, and treatment procedures for AF, which are major reasons for prolonged hospital and ICU stays. Hospital mortality was greater in patients who developed NOAF AF but did not reach a significant level. Velioglu and associates [17] reported no statistically significant difference between patients with and without POAF regarding in-hospital mortality (3.4% vs. 2.4%, respectively, p= 0.57). Sihombing and associates [12] concluded that NOAF independently decreases three-year survival after CABG. This can be explained by the fact that NOAF, like paroxysmal AF in the general population, can cause electrophysiological remodeling over time, which can ultimately progress to death. Ahlsson and colleagues [18] reported a twofold increase in the risk of cardiovascular mortality in patients with postoperative AF.

Further studies are needed to identify patients at high risk for NOAF after CABG to guide prophylactic measures, examine the potential role of implantable monitors for detecting AF recurrence in patients with NOAF who convert to sinus rhythm before hospital discharge, and determine whether the routine use of long-term oral anticoagulation in patients with in-hospital NOAF improves long-term prognosis after CABG. Prospective multicenter studies, including large sample sizes, will help consider future local Egyptian guidelines.

Study Limitation:

The small number of patients was the primary limitation. The small sample size limited the statistical analysis and might have affected the non-significance of the multivariable analysis. Other limitations include the single-center nature of the study and the late presentation of complex coronary lesions.

Conclusion

NOAF after isolated primary CABG is common. Advanced age, renal function, hemodynamic instability, and perioperative myocardial infarction might be associated with NOAF.

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