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Predictors of postoperative atrial fibrillation after coronary artery bypass grafting: a prospective observational cohort study

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Abstract

Background: This study was conducted to determine the effect of certain predictors on the incidence of postoperative atrial fibrillation (POAF) during ICU stay after coronary artery bypass graft (CABG) surgery.

Results: We enrolled 123 patients in this study. The mean age was 57.4 ± 8.7 years, and the mean left atrial diameter was 4.1 ± 0.52 cm with male preponderance (76.4%). The incidence of POAF following CABG was 33.3%. There was no statistically significant association between POAF and smoking ($P = 0.123$). However, POAF was significantly associated with higher CHA2DS2-VASc score ($P = 0.002$), valve replacement ($P < 0.001$), and inotropic support ($P = 0.005$). Moreover, patients with POAF had significantly higher mean age ($P = 0.031$) and left atrial (LA) diameter ($P < 0.001$). Logistic regression showed that LA diameter ($P < 0.001$), potassium level at 36 h ($P = 0.016$), and female gender ($P = 0.001$) were independent predictors of POAF.

Conclusions: We had several significant epidemiological, clinical, and operative variables that were significantly associated with post-CABG AF, including older age, female gender, large LA diameter, valve replacement, higher CHA2DS2-VASc score, and postoperative inotropic support. However, only LA diameter, female gender, and potassium level at 36 h were independent predictors of POAF. Nevertheless, further large-scale studies are needed to confirm our findings.

Keywords: Atrial fibrillation, Organ dysfunction scores, Coronary artery bypass, Postoperative complications, Intensive care units, Prognosis

Introduction

Postoperative atrial fibrillation (POAF) is one of the most critical and common complications after cardiovascular surgery, precipitating early, and late morbidities. Incidence of POAF after coronary artery bypass graft (CABG) surgery is about 30%, about 40% after valve surgery, and about 50% after combined CABG and valve replacement/repair surgery, with peaks occurring two to 3 days after surgery (Chebbout et al., 2018).

Postoperative atrial fibrillation may lead to hemodynamic instability, thromboembolic manifestation, prolonged hospital stay, readmissions to intensive care unit (ICU), organ failure, healthcare costs, and mortality. So, much attention is focused on the prevention of atrial fibrillation (AF) in high-risk patients (Lahtinen et al., 2004; Maisel et al., 2001).

The pathophysiological mechanism of AF is complex and affected by various factors. A variety of diagnostic modalities are useful in predicting POAF (Lowres et al., 2018). Multiple investigations and studies have tried to identify demographic risk factors and predictors of POAF after CABG with or without valve replacement (Dobrev et al., 2019). The aim of this study was to determine the effect of certain predictors on the incidence of

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POAF during the ICU stay after CABG surgery with or without valve replacement.

Methods

This prospective observational cohort study was conducted after approval of the Institutional Review Board and written informed consent from patients or first kin. It was carried out from March to September 2018. The study was registered at [ClinicalTrial.gov](https://clinicaltrials.gov) (registry number: NCT04193813). We included patients undergoing isolated CABG or CABG with aortic and/or mitral valve replacement with an age of 18 to 70 years old.

All patients were pre-medicated 1 h before surgery with intramuscular morphine (0.1 mg/kg). Hemodynamic monitoring consisted of heart rate using a five-lead ECG, systolic arterial blood pressure, diastolic arterial blood pressure, and mean arterial blood pressure using radial artery catheter, which was inserted before the induction of anesthesia, under local anesthesia and sedation with 0.07 mg/kg midazolam. The central venous pressure, temperature, and urine output were recorded.

Induction of anesthesia was done by fentanyl 5 mg/kg, propofol 0.5 mg/kg, and rocuronium 0.6 mg/kg. After intubation, the lungs were ventilated with air-oxygen mixture and anesthesia was maintained with 0.5–2% sevoflurane, and additional fentanyl and rocuronium were administered as necessary.

The main studied outcome was new onset POAF following CABG. Patients diagnosed preoperatively with AF or have history of AF, patients with history of existing preoperative rhythm other than normal sinus rhythm, patients with impaired systolic function (ejection fraction < 30%), patients with end-stage renal disease on hemodialysis and patients who refused to participate in the study were excluded from the study.

Using PASS program, alpha error was set at 5% and power at 80%. Results from previous study Ducceschi et al. (Ducceschi et al., 1999) showed that left atrial (LA) diameter was an independent factor affecting AF post CABG. Based on this, the needed sample was 123 cases undergoing CABG, including at least 24 patients with dilated LA.

In the ICU, patients were mechanically ventilated for at least 6 h postoperatively and monitored for heart rate, invasive blood pressure, central venous pressure, temperature, Glasgow coma scale, drains output, complete blood count, coagulation profile, random blood sugar, serum electrolytes, liver profile, renal profile, arterial blood gases, and urine output. All patients received the standard protocol for postoperative sedation and pain management after CABG/valve replacement surgery, which includes propofol infusion 0.3 to 3 mg/kg/h, fentanyl infusion 0.7 to 10 mcg/kg/h, and paracetamol with maximum dose of 4 g daily.

All individuals were monitored for AF during the post-operative ICU stay for 72 h with continuous ECG (5-leads) monitor, daily 12-lead ECG recording to confirm an episode of AF. AF was considered if *P* wave was absent before the QRS complex together with irregular ventricular rhythm on the rhythm strips.

Only AF episodes lasting > 5 min were counted. In the present study, the following data, as potential predictors of POAF, were collected from every eligible participant: age, gender, smoking, and LA diameter based on formal preoperative transthoracic echocardiography. Serum potassium (K) level was routinely measured postoperatively on ICU admission, every 2 h, and on demand (if arrhythmia occurs or suspected abnormal potassium level). It was recorded for statistical analysis on admission, every 12 h, and on demand until the patient was discharged.

Serum magnesium (Mg) level was measured routinely measured postoperatively on ICU admission, every 24 h, and on demand (if arrhythmia occurs or suspected abnormal magnesium level). It was recorded for statistical study on admission, every 24 h, and on demand until the patient was discharged.

Other parameters such as valve replacement (aortic and/or mitral) during the same operative setting, CHA2DS2-VASc score (congestive heart failure, hypertension [blood pressure > 140/90 mmHg or treated hypertension on medication], age \geq 75 years, diabetes mellitus, prior stroke, transient ischemic attack, or thromboembolism, vascular disease, age 65 to 74 years, gender category [female gender]), and postoperative inotropic support usage were recorded.

An Excel spreadsheet was established for the entry of data. We used validation checks on numerical variables and option-based data entry method for categorical variables to reduce potential errors. The analyses were carried with SPSS software (Statistical Package for Social Sciences, version 24, SSPS Inc, Chicago, IL, USA). The normality of the data was assessed using Shapiro-Wilk Test. All numerical data followed normal distribution and were described as mean \pm standard deviation. Frequency tables with percentages were used for categorical variables. Independent Student *t* test was used to compare quantitative variables. Pearson's chi-squared test was used to analyze categorical variables. Multivariable binomial logistic regression analysis with backward elimination was undertaken to assess the predictors of POAF.

Results

This prospective cohort study was carried out from March 2018 to September 2018 on 123 patients who underwent CABG (isolated or with valve replacement). Incidence of POAF was 33.3%; 76.4% were males (94/

123 patients), the mean age of studied patients was 57.4 ± 8.7 years, and the mean LA diameter was 4.1 ± 0.5 cm. Patients in POAF group had higher mean age (59.7 ± 7.9 vs 56.3 ± 8.8; *P* = 0.031) and larger mean LA diameters (4.6 ± 0.5 vs 3.9 ± 0.4 cm; *P* < 0.001). The percentage of female patients was significantly higher in the POAF group (43.9% vs 13.4%; *P* < 0.001). A significantly higher percentage of POAF patients underwent both CABG and valve replacement (41.5% vs 12.2%; *P* < 0.001) and received inotropic support postoperatively (73.2% vs 46.3%; *P* = 0.005). There was no statistically significant association between POAF and smoking (*P* = 0.123; Table 1). Regarding cardiopulmonary bypass time, aortic cross clamp time, and type of cardioplegia, there were no significant differences among the studied patients (*P* > 0.05). Twenty-eight patients (23%) were on beta blockers. Seven (6%) patients received milrinone, 20 (16%) received levosimendan, and 41 (33%) received adrenaline.

Patients with POAF had significantly higher mean CHA₂DS₂-VASc score than those who did not suffer POAF (4 ± 1 vs 3 ± 1; *P* < 0.001; Table 1). When the score was dichotomized into two categories: score below 4 and score ≥ 4, the POAF group showed a significantly higher percentage of patients with the high score (score ≥ 4 = 53.7% vs 25.6%; *P* = 0.002; Fig. 1).

Comparison of serum K and Mg levels at different time points between patients who had POAF and those who had not showed the lack of statistically significant differences (*P* > 0.05; Table 2).

Logistic regression analysis was carried out to identify predictors of POAF. The results of logistic regression showed that LA diameter (*P* < 0.001), K level at 36 h (*P* = 0.016), and gender (*P* = 0.001) were independent predictors of POAF. Increase in LA diameter by one cm, elevated serum K at 36 h by 1 mmol/L, and female gender

were significantly associated with increased likelihood of having POAF by approximately 55.8 (95% CI: 11.7–265.3; *P* < 0.001), 3.4 (95% CI: 1.3–9.4; *P* = 0.016), and 8.3 (95% CI: 2.4–28.7; *P* < 0.001) times, respectively (Table 3).

Table 4 shows the diagnostic performance of LA diameter and CHAD₂DS₂-VAS score. The LA diameter had a higher overall accuracy than CHAD₂DS₂-VAS score (79.7% and 69.9%, respectively). Moreover, LA diameter had much higher sensitivity than CHAD₂DS₂-VAS score (70.7% vs 14.6%, respectively), though the specificity of LA diameter was slightly lower than CHAD₂DS₂-VAS score (84.1% vs 97.6%, respectively).

Discussion

Postoperative atrial fibrillation within the first 2 to 3 days after CABG is relatively common with recorded incidence of 20 to 50% and is associated with increased morbidity, higher risk of embolic stroke postoperatively, and increased mortality (Dobrev et al., 2019).

Therefore, we conducted this prospective cohort study to determine the effect of certain predictors on the incidence of POAF after CABG. The present study included 123 patients with coronary artery disease undergoing CABG with or without aortic and/or mitral valve replacement.

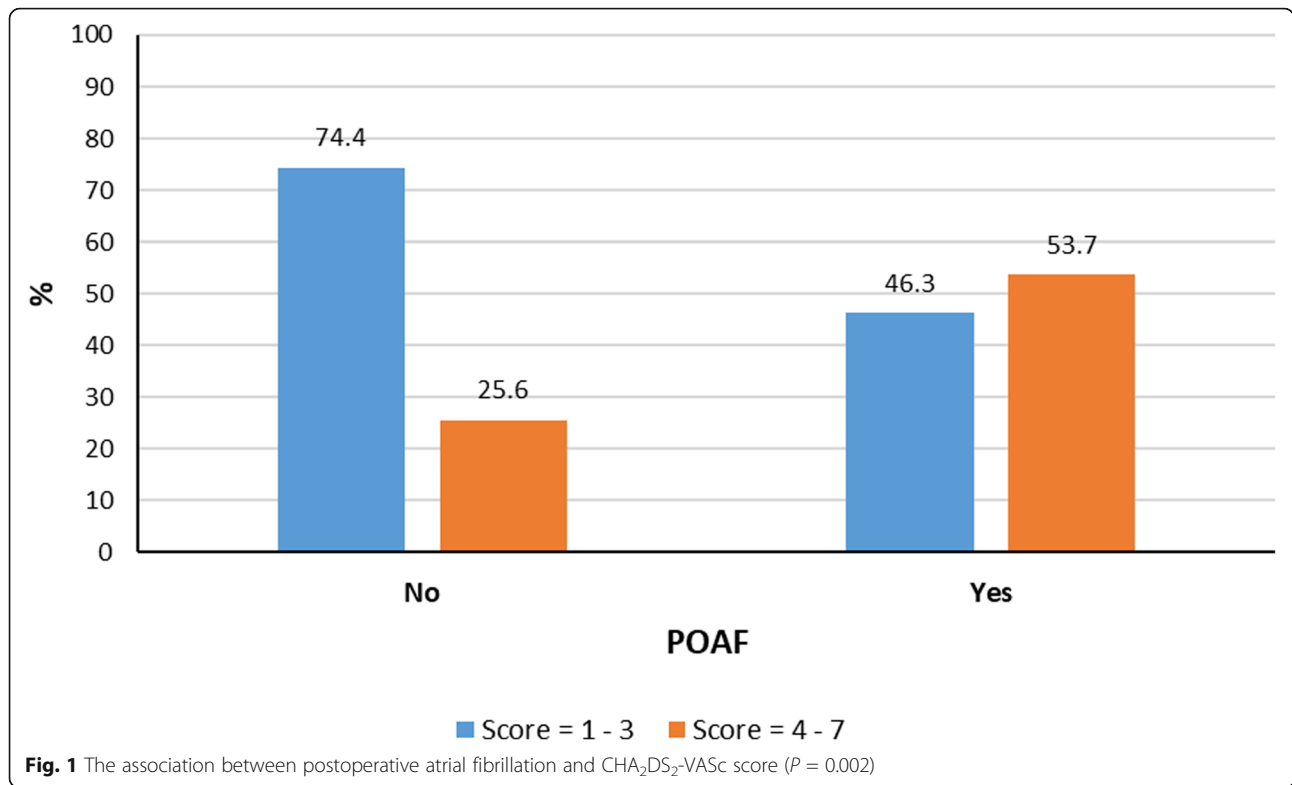
Regarding the incidence of POAF, it was reported in 41 (33.3%) patients in the current study. This incidence is comparable to a prospective study conducted on 170 patients scheduled for isolated CABG, which revealed that 53 patients developed POAF (31%) (Haghjoo et al., 2008). However, a much lower incidence of postoperative atrial tachyarrhythmias (POAT) (22%) was reported in a retrospective study, which was done on 124 patients who undergone off-pump CABG surgery. This might be the reason for lower incidence of POAT than that reported in

Table 1 The association between postoperative atrial fibrillation and patients’ characteristics

Variables		Negative (N = 82)	Positive (N = 41)	t/χ ²	P
Age (years), mean ± SD		56.3 ± 8.8	59.7 ± 7.9	− 2.187	0.031*
Gender, n (%)	Female	11 (13.4%)	18 (43.9%)	14.100	< 0.001*
	Male	71 (86.6%)	23 (56.1%)		
Smoking, n (%)	Yes	50 (61.0%)	19 (46.3%)	2.377	0.123
	No	32 (39.0%)	22 (53.7%)		
Valve replacement, n (%)	Yes	10 (12.2%)	17 (41.5%)	13.667	< 0.001*
	No	72 (87.8%)	24 (58.5%)		
Postoperative inotropic support, n (%)	Yes	38 (46.3%)	30 (73.2%)	7.959	0.005*
	No	44 (53.7%)	11 (26.8%)		
LA diameter (cm), mean ± SD		3.9 ± 0.4	4.6 ± 0.5	− 7.914	< 0.001*
CHA ₂ DS ₂ -VASc score, mean ± SD		3 ± 1	4 ± 1	4.663	< 0.001*

LA left atrium, SD standard deviation, t statistic of independent samples t test, χ² statistic of Pearson’s chi-squared test

*Significant at *P* ≤ 0.05



the current study as all patients undergone CABG with cardiopulmonary bypass (Maslow et al., 2000). Contrary to our findings, a retrospective study conducted on 2511 CABG surgeries performed in a tertiary center, between 2004 and 2011 reported that only 18% of patients developed POAF. The difference from our study might be attributed to different sample size and those patient undergone an isolated CABG surgery without valve replacement as in our study (Haghjoo et al., 2008).

In the present study, univariate analysis was first performed to find potential predictors of POAF. Our results showed that there were statistically significant associations between POAF and older age, higher LA diameter, and female gender. In addition, a significantly higher proportion of patients with POAF had valve replacement, received postoperative inotropic support, and had significantly higher CHA₂DS₂-VASc score compared to those who did not develop POAF.

Table 2 Comparison of serum potassium and magnesium levels between patients with postoperative atrial fibrillation and those without

Variables		Negative (N = 82)	Positive (N = 41)	t	P
K Adm (mmol/L)	Mean ± SD	4.113 ± 0.6597	4.183 ± 0.7064	- 0.526	0.601
K 12 h (mmol/L)	Mean ± SD	4.137 ± 0.5172	4.185 ± 0.6417	- 0.423	0.674
K 24 h (mmol/L)	Mean ± SD	4.089 ± 0.4766	4.115 ± 0.6684	- 0.219	0.827
K 36 h (mmol/L)	Mean ± SD	4.196 ± 0.4235	4.354 ± 0.7218	- 1.289	0.203
K 48 h (mmol/L)	Mean ± SD	4.168 ± 0.4477	4.259 ± 0.7593	- 0.702	0.485
K 60 h (mmol/L)	Mean ± SD	4.201 ± 0.4126	4.051 ± 0.6353	1.374	0.175
K 72 h (mmol/L)	Mean ± SD	4.306 ± 0.2966	4.268 ± 0.6762	0.342	0.734
Mg Adm (mg/dL)	Mean ± SD	2.3652 ± 0.5771	2.2737 ± 0.68948	0.732	0.467
Mg 24 h (mg/dL)	Mean ± SD	2.3735 ± 0.54769	2.34 ± 0.59269	0.303	0.763
Mg 48 h (mg/dL)	Mean ± SD	2.4832 ± 0.5218	2.3522 ± 0.53306	1.294	0.2
Mg 72 h (mg/dL)	Mean ± SD	2.5156 ± 0.50198	2.4241 ± 0.4926	0.964	0.338

K potassium, Mg magnesium, LA left atrium, Adm admission, SD standard deviation

Table 3 Backward, stepwise, multivariable binomial logistic regression analysis for predictors of postoperative atrial fibrillation

Item	Wald	P	OR	95% CI
Gender (female)	11.252	0.001*	8.3	2.4–28.7
LA diameter (cm)	25.533	0.000*	55.8	11.7–265.3
K 36 h (mmol/L)	5.833	0.016*	3.4	1.3–9.4
Constant	25.571	0.000*		

Variables entered on first step: age (years), gender, smoking, LA diameter (cm), K 36 h (mmol/L), K 60 h (mmol/L), Mg 48 h (mg/dL), valve replacement, inotropic support postoperative, CHA2DS2-VASc score
 CI confidence interval, K potassium, Mg magnesium, LA left atrium, OR odds ratio

*Significant at $P \leq 0.05$

In agreement with the present work, a previous study performed on 791 patients who underwent CABG in the Clinical Department of Cardiology in the years 2009–2011, where multivariate analysis revealed that the age ≥ 70 years is a potential predictor of POAF (Haghjoo et al., 2008).

Moreover, a prospective study conducted on 304 patients who underwent isolated on-pump coronary artery bypass grafting reported that patients who developed POAF were significantly older (≥ 60 years) and have larger LA diameter (OR = 1.105, CI 1.047–1.167, $P = .000$) (Haghjoo et al., 2008).

A prospective cohort study was done to identify the preoperative, intraoperative, and postoperative predictors of AF in 302 patients with coronary artery disease who underwent CABG surgery. By univariate analysis, older age, larger LA diameter, and adrenergic use in ICU were significantly associated with occurrence of post-CABG AF ($P < 0.05$) (Haghjoo et al., 2008).

Similar to our findings, Najafi et al. evaluated the relationship blood magnesium level and the incidence of perioperative arrhythmias after CABG surgery reported that differences in serum Mg level on different postoperative occasions between patients did not significantly affect the incidence of POAF (Najafi et al., 2007).

A retrospective cohort study was done on 252 consecutive adult patients who underwent CABG, in the King Faisal Specialist Hospital and Research Center in Jeddah, Saudi Arabia. Patients who developed POAF had

lower ejection fraction ($44.8 \pm 5.7\%$), diastolic dysfunction, and larger LA volume (Perrier et al., 2017).

Another study was conducted on 1481 patients who underwent isolated CABG with cardiopulmonary bypass. A multivariate analysis using informative data-based priors showed that a high CHA2DS2-VASc score was independently associated with POAF risk after isolated CABG (Perrier et al., 2017).

The reported increased likelihood of POAF with increased LA diameter is in line with controlled clinical trials that found prophylactic amiodarone before cardiac surgeries to significantly reduce the risk of POAF (Osmanovic et al., 2019; Pong et al., 2020).

We acknowledge that the present study has some limitations. The sample size of our cohort was relatively small, which may impair generalizability of our findings. Moreover, long-term patient outcomes were not included in our study.

Conclusions

The incidence of POAF following CABG surgery is approximately 33%. There are a wide range of significant epidemiological, clinical, and operative variables that were significantly associated with post-CABG AF, including older age, female gender, large LA diameter, valve replacement, higher CHA2DS2-VASc score, and postoperative inotropic support. However, only LA diameter, female gender and K at 36 h were independent predictors of POAF. Nevertheless, further large-scale studies are still needed to confirm our findings.

Abbreviations

CABG: Coronary artery bypass graft; K: Potassium; LA: Left atrial; Mg: Magnesium; POAF: Postoperative atrial fibrillation; POAT: Postoperative atrial tachyarrhythmias

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Authors' contributions

HE, MD, GE, and AA have full access to all the data in the study and take responsibility for the integrity of the data. Study concept and design: HE and GE; Acquisition of data: MD; Analysis of data and Critical revision of the manuscript: H E and GE. The authors have read and approved the manuscript.

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Availability of data and materials

We intend to share the study protocol as well as the individual de-identified participants' data. Data will be accessible through direct contact with the corresponding author, beginning 12 months and ending 36 months following article publication.

Ethics approval and consent to participate

The study obtained approval from the Institutional Review Board of Al Agouza Police Hospital and El-Manial Specialized Hospital. The study was registered at [ClinicalTrials.gov](https://clinicaltrials.gov) (registry number: NCT04193813). Written informed consent from patients or first kin was obtained.

Table 4 The diagnostic performance of postoperative atrial fibrillation predictors

Variable	Cutoff	TN	FP	TP	FN	%Sp	%Sn	%PN	%PP	%Eff
LA diameter	4.2	69	13	29	12	84.1	70.7	85.2	69.0	79.7
CHA2DS2-VASc score	4	80	2	6	35	97.6	14.6	69.6	75.0	69.9

TN true negative, FP false positive, TP true positive, FN false negative, Sp specificity, Sn sensitivity, PN negative predictive value, PP positive predictive value, Eff diagnostic value

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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