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Predictors of Postoperative Atrial Fibrillation after Isolated On-Pump Coronary Artery Bypass Grafting in Patients ≥60 Years Old

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ABSTRACT

Background: Postoperative atrial fibrillation (POAF) after coronary artery bypass grafting (CABG) is one of the most common complications that can contribute to an increased risk of mortality, particularly in older patients. The identification of predictors of POAF after CABG could impact patient care. This study aims to determine the risk factors of POAF in patients ≥60 years old who underwent isolated on-pump coronary artery bypass grafting (ONCAB) in order to provide a basis for the prevention and treatment of POAF after ONCAB.

Methods: Between October 2011 and November 2015, a total of 304 patients ≥60 years old underwent isolated ONCAB in our department. The patients were divided into 2 groups, the AF group and the non-AF group, according to the occurrence of POAF. A retrospective analysis was performed on the general characteristics and perioperative data of the patients. Logistic regression analysis was used to identify the predictors of POAF after ONCAB in patients ≥60 years old.

Results: The incidence of POAF after ONCAB in patients ≥60 years old was 23.36% (71/304). Statistically significant differences were observed in patients' age, history of hypertension, left atrium diameter, European System for Cardiac Operative Risk Evaluation (EuroSCORE) I and II, and the highest level of serum creatinine after operation (all $P < .05$). Logistic regression analyses showed that a history of hypertension (OR = 2.575, CI 1.208-5.488, $P = .014$), left atrium diameter (OR = 1.105, CI 1.047-1.167, $P = .000$) and EuroSCORE I score (OR = 1.132, CI 1.001-1.279, $P = .048$) were independent risk factors for POAF after ONCAB in patients ≥60 years old.

Conclusion: The occurrence of POAF after isolated ONCAB in patients ≥60 years old was affected by many risk factors; a history of hypertension, the left atrium diameter and the EuroSCORE I score were all predictors of POAF.

INTRODUCTION

Postoperative atrial fibrillation (POAF) is one of the most common complications affecting approximately 10% to 65% of patients undergoing coronary artery bypass grafting (CABG) [Mitchell 2011]. POAF contributed to a four-fold increased risk of stroke compared with patients who remained in sinus rhythm [Barbieri 2013]. It also doubled the overall mortality rate in the postoperative period and is associated with additional postoperative complications [Auer 2005; Fuster 2006]. The underlying mechanisms that lead to onset and persistence of POAF have been poorly elucidated. Clinically useful prediction models for POAF in patients, which could reduce postoperative complications and hospitalization time, particularly in older patients undergoing CABG, are still lacking. The objective of this study was to examine the incidence of POAF in patients ≥60 years old who underwent on-pump coronary artery bypass grafting (ONCAB) and identify risk factors and predictors associated with the development of POAF.

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METHODS

Study Design

A retrospective study was performed on 304 consecutive patients subjected to isolated ONCAB in the Department of Cardiovascular Surgery, Beijing Hospital, National Center of Gerontology, China, between October 2011 and November 2015. This study was approved by the Institutional Review Board of Beijing Hospital. The subjects were divided into the two following groups: patients not presenting with POAF (non-AF group) and patients presenting with POAF (AF-group).

Inclusion criteria: All patients subjected to isolated ONCAB ≥60 years old.

Exclusion criteria: Previously documented AF and/or other cardiac arrhythmias, heart valve disease, emergency surgery, cardiac reoperation, or renal dysfunction.

Outcome Parameters

The relevant preoperative, intraoperative, and postoperative data of the patients were analyzed.

The preoperative variables included the following: age, sex, body mass index (BMI), history of diabetes mellitus (DM), hypertension, dyslipidemia, smoking, cerebrovascular disease, peripheral vascular disease (PVD), symptom of angina, left main disease, three-vessel disease, use of β-blockers, use of angiotensin converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB), use of statins, chronic obstructive pulmonary disease (COPD), serum creatinine, left ventricular ejection fraction (LVEF), left ventricular end-diastolic diameter (LVEDD), left atrium diameter, and

European System for Cardiac Operative Risk Evaluation Score I and II (EuroSCORE I and II).

The intraoperative and postoperative variables included the following: cardiopulmonary bypass (CPB) time; aortic cross-clamping time; minimum of hematocrit (HCT) in cardiopulmonary bypass; number of grafts; use of internal mammary artery; mechanical ventilation time; infective, pulmonary, neurologic, or other complications; acute kidney failure; sterna dehiscence; time of stay in the ICU; and hospital mortality (defined as death in the first 30 days after CABG).

Surgical Procedure and Postoperative Management

The patients were placed under general anesthesia and conventional median sternotomy was performed. All patients underwent ONCAB, and cardiopulmonary bypass was established by cannulating the ascending aorta and right atrium. The activated clotting time was maintained at longer than 450 seconds with heparin (4 mg/kg). A roller pump and nonpulsatile flow (2.0-2.5 L/m^2/min) were used. Cooled blood cardioplegia was delivered via intermittent anterograde routes at the root of the ascending aorta. The body was cooled to a core temperature of 30°C to 32°C when distal anastomosis was performed, and was gradually warmed to 36°C at the beginning of the last distal anastomosis, usually via the left internal mammary artery or the saphenous vein to the left anterior descending. Proximal anastomosis was performed after the aorta was unclamped and the heart restarted. At the end of CPB and upon achievement of stable hemodynamic conditions, anticoagulation was reversed by administration of protamine sulfate (1-1.5 mg per 1 mg of heparin administered in the previous hour). No patients required pacing. All patients received a β-blocker, and calcium blockers were used postoperatively if a radial artery graft was chosen. All patients received twice-daily subcutaneous low-molecular-weight heparin postoperatively for a week. All postoperative patients received nitrate, atorvastatin, and aspirin as a routine protocol. ACEI, ARB, or calcium blockers were chosen for hypertensive patients if required. The criteria for extubation included an alert, a hemodynamically stable patient with no excessive bleeding, the ability of the patient to breathe through continuous positive airway pressure with 12 cm H2O pressure support for at least 20 minutes, inspired oxygen less than 0.40, a respiratory rate less than 25 breaths/min, an arterial blood PO2 greater than 70mmHg, and a CO_2 less than 40 mmHg, with no metabolic acidosis. All patients were administered to the ICU unit. Continuous electrocardio-monitoring was used for assessing cardiac rhythm and electrocardiogram changes for at least 48 hours. After discharge from the ICU, the radial pulse rate of each patient was evaluated at least 4 times daily and for symptoms suggestive of arrhythmia at each pulse check by residents and nurses. A 12-lead ECG trace was recorded immediately if a patient showed clinical signs of arrhythmia.

Diagnosis and Treatment of POAF

POAF was diagnosed if the 12-lead ECG demonstrated rapid oscillations or fibrillatory *P* waves that varied in size, shape, and timing, associated with irregular QRS complexes.

Table 1. Preoperative variables of patients subjected to ONCAB

	AF Group	Non-AF Group	t or χ^2	*P*
Age, y	69.51 ± 7.52	66.39 ± 7.96	-2.925	.004
Sex, female	15	57 (176)	0.335	.563
BMI, kg/m^2	25.52 ± 2.86	25.47 ± 2.99	-.153	.878
DM	28	103	0.505	.477
Hypertension	61	158	8.855	.003
Hyperlipidemia	47	151	0.046	.830
History of smoking	18	72	0.804	.370
COPD	5	13	0.029	.865
Symptom of angina	69	227	0.000	1
Blood sugar, mmol/L	5.94 ± 1.39	6.24 ± 2.05	1.383	.168
Serum creatinine, μmol/L	91.87 ± 64.31	79.62 ± 52.44	-1.631	.104
LVEF, %	58.49 ± 11.42	58.92 ± 11.35	0.276	.783
LVEDD, mm	48.57 ± 5.92	47.75 ± 6.13	-0.981	.327
Left atrium diameter, mm	39.61±6.19	36.32 ± 4.76	-4.066	.000
EuroSCORE I	5.32 ± 2.30	4.32 ± 2.30	-3.213	.001
Logistic EuroSCORE	5.36 ± 4.68	3.98 ± 3.77	-2.542	.012
EuroSCORE II	1.84 ± 1.53	1.38 ± 1.12	-2.360	.020
Use of β-blocker	45	156	0.310	.578
Use of ACEI or ARB	35	96	1.454	.228
Use of statins	64	206	0.164	.686
History of myocardial infarction	32	93	0.598	.440
Recent myocardial infarction	13	37	0.234	.629
PVD	12	26	1.641	.20
History of cerebrovascular disease	14	46	0.000	.996
Left main disease	24	97	1.392	.238
Three-vessel disease	58	207	2.488	.115
Cardiac function level 3-4 (NYHA)	18	44	1.402	.236

P values provide comparisons between patients in the AF group and non-AF group.
BMI indicates body mass index; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; LVEF, left ventricle ejection fraction; LVEDD, left ventricular end-diastolic diameter; EuroSCORE, European System for Cardiac Operative Risk Evaluation Score; ACEI, angiotensin converting enzyme inhibitors; ARB, angiotensin receptor blocker; PVD, peripheral vascular disease.

POAF was defined as AF of any duration during the postoperative period, with the AF diagnosis based on physician

Table 2. Intraoperative and Postoperative Variables of Patients Undergoing ONCAB

	AF Group	Non-AF Group	t or χ^2	*P*
CPB time, min	120 ± 43.90	115.50 ± 34.56	-.897	.370
Cross-clamp time, min	54.29 ± 18.50	55.38 ± 18.40	0.433	.665
Number of grafts	3.59 ± 0.77	3.70 ± 0.67	1.099	.273
Amount of red blood, u	3.37 ± 3.68	3.00 ± 3.15	-.814	.416
Amount of plasma, mL	717.46 ± 773.93	622.75 ± 575.09	-1.115	.266
Mechanic ventilation time, hours	48.55 ± 162.25	21.64 ± 33.84	-1.388	.169
Length of stay in ICU, hours	152.61 ± 254.48	93.28 ± 50.41	-1.953	.055
Amount of drainage, mL	1430.49 ± 1148.33	1353.59 ± 1239.65	-.465	.642
Highest level of creatinine after operation, mmol/L	147.23 ± 118.95	108.15 ± 74.63	-2.615	.011
Stroke	4	2		.028
Acute kidney failure	2	6		1.000
Sternal dehiscence	0	2		1.000
Wound infection	1	2		.551
Death	3	4		.360

P values provide comparisons between patients in the AF group and non-AF group. CPB indicates cardiopulmonary bypass.

assessment and 12-lead ECG findings. Patients who developed POAF were treated initially with a standard protocol of amiodarone before other inducement factors such as hypoxemia, electrolytic imbalance, volume overload, or hypovolemia were eliminated. Excluding 3 deceased patients, all POAF patients were converted to sinus rhythm before being discharged home.

Statistical Analysis

The data were analyzed using SPSS version 22.0 (SPSS, Chicago, IL, USA). The differences among preoperative, intraoperative, and postoperative factors between the AF group and non-AF group were analyzed using different methods: the independent samples t test for normally distributed continuous variables (expressed as the mean ± SD), and Pearson chi-square or Fisher exact test for categorical variables. Each variable that yielded a result of $P \leq .05$ in univariate analysis was further analyzed in a logistic regression equation. The results were assessed within a 95% reliance and at a level of $P < .05$ being significant.

RESULTS

This study included 233 patients (57 females, 176 males) without POAF and 71 patients (15 females, 56 males) with POAF. The incidence of POAF was 23.28% (71/304). The baseline characteristics of the AF group and non-AF group are presented in Tables 1 and 2. The patients in the AF group (mean age, 69.51 ± 7.52 years) were significantly older than those in the non-AF group (mean age, 66.39 ± 7.96 years) ($P = .004$). A significantly larger proportion of the AF group had a history of hypertension (85.92% versus 67.81%, $P = .003$). The atrium diameter in the AF group was significantly larger than that in the non-AF group (mean anterior-posterior diameter, 39.61 ± 6.19 mm versus 36.32 ± 4.76 mm, $P = .000$). The patients who developed AF also exhibited a significantly higher mean EuroSCORE I (5.32 ± 2.30 versus 4.32 ± 2.30, $P = .001$), Logistic EuroSCORE (5.36 ± 4.68 versus 3.98 ± 3.77, $P = .012$), and EuroSCORE II (1.84 ± 1.53 versus 1.38 ± 1.12, $P = .020$) than the non-AF group. There were no significant differences between groups with respect to sex, BMI, hyperlipidemia, history of smoking, COPD, blood sugar, serum creatinine, use of β-blocker, use of ACEI or ARB, PVD, left ventricle ejection fraction, history of myocardial infarction, CPB time, or cross-clamping time (all $P > .05$). Logistic regression analyses identified a history of hypertension (OR, 95% CI, $P = .014$), left atrium diameter (OR, 95% CI, $P = .000$) and EuroSCORE I value (OR, 95% CI, $P = .048$) as independent clinical predictors of POAF after ONCAB in patients ≥60 years old. The ORs and *P* values for each of these factors are shown in Table 3.

DISCUSSION

Owing to complete revascularization and increased patency rate, ONCAB remains the standard procedure to treat coronary heart disease. Incidence of POAF in our study was 23.36%, which is similar to the frequency of POAF after ONCAB or off-pump coronary artery bypass grafting (OPCAB) in the literature [Almassi 2012]. Many defined clinical risk factors for POAF following CABG have been described. In our study, we found significant differences between the AF group and the non-AF group in age, the history of hypertension, left atrium diameter, the EuroSCORE, and the highest level of serum creatinine after operation. Logistic regression analysis revealed that hypertension, left atrial diameter, and EuroSCORE I values were predicting factors of POAF after ONCAB in patients ≥60 years old.

Hemodynamic overload in patients with hypertension causes atrial dilatation, collagen deposition, and the development of cardiac fibrosis, which can lead to atrial structural and electrical remodeling with changes in ions and cell junctions. Renin-angiotensin-aldosterone may play a key role in inducing cardiac inflammation and fibrosis [Seccia 2016]. These

Table 3. Logistic Regression Analysis for Prediction of Independent Risk Factors

Covariates	OR	P	95% CI Lower	95% CI Upper
Age		.576		
Hypertension	2.575	.014	1.208	5.488
Left atrial diameter	1.105	.000	1.047	1.167
Postoperative maximum of serum creatinine		.096		
EuroSCORE I	1.132	.048	1.001	1.279
Logistic EuroSCORE		.446		
EuroSCORE II		.775		

mechanisms increase the probability of generating multiple atrial wavelets by enabling rapid atrial activation and dispersion of refractoriness.

The left atrium diameter was a predicting factor of POAF in our study. The enlargement of the left atrium can lead to atrial structural and electrical remodeling, which can attenuate action potential duration and refractory periods [Xu 2013]. Federico demonstrated that the left atrial volume estimated using 2-D echocardiograms was independently associated with the occurrence of POAF in patients subjected to isolated and elective CABG [Nardi 2012].

Advanced age has been proven to be the most robust risk factor for POAF after CABG [Hogue 2000; Nisanoglu 2007; Zaman 2000], primarily due to degenerating ultrastructural changes in cardiac muscle during aging. The loss of atrial myocytes and the increase in areas of age-related, fibrotic infiltrates may create multiple pathways for reentry that induce atrial arrhythmias such as AF [Schauerte 2001]. In our study, we found that patients in the AF group were significantly older than in the non-AF group ($P = .004$). However, logistic regression analysis did not identify older age as a predictor of POAF in this group. This result could be due to the distribution of age and the relatively small sample size.

EuroSCORE is a risk stratification system created to predict hospital mortality and assess quality of care. It takes into account general patient information, general preoperative and cardiac risk factors, and operation information [Roques 1999]. Research has shown that this model can be used to predict numerous outcomes, including the following: mortality in the first 3 months after cardiac surgery, prolonged hospital stay, and specific postoperative complications such as renal insufficiency, respiratory failure sepsis, and endocarditis [Hashemzadeh 2013]. Our study revealed that patients in the AF group had a significantly higher mean EuroSCORE I value, Logistic EuroSCORE I, and EuroSCORE II score than patients in the non-AF group ($P = .004$). Additionally, EuroSCORE I value was a predictive factor for POAF (OR = 1.132, $P = .048$). Applying this risk-scoring model might enable predictions of the incidence of POAF, and guide the administration of appropriate prophylaxis measures before and after CABG [Nisonoglu 2007].

Metabolic disorders can lead to structural remodeling in the atria due to the presence of microvascular lesions on the myocardium and metabolic stresses in diabetic patients. However, research findings on diabetes as a predictor of POAF after CABG have been inconsistent [Almassi 2012; Kalus 2004]. We found no significant difference between the AF group and non-AF group.

The incidence of stroke in the AF group was significantly higher than the non-AF group (5.63% versus 0.858%, $P = .028$) in our study. Similar results were reported in other studies [Burgess 2006; Shen 2011]. Due to a small sample size, the data were inadequate to determine the relationship between stroke and POAF after CABG.

We found no significant difference in hospital mortality in the AF group versus the non-AF group (4.21% versus 1.72%, $P = .360$). However, POAF is a predictor of late mortality in patients undergoing CABG [Bramer 2010]. The cause of increased mortality is still uncertain, but older age may be one factor.

Several other factors have been reported to predict POAF after CABG. These include COPD, PVD, poor left ventricular function, characteristic of coronary artery lesion, CPB time, aortic cross-clamping time, blood transfusion, mechanical ventilation time, length of stay in ICU, and preoperative use of a β-blocker [Hashemzadeh 2013; Erdil 2014; Oliveria 2007; Sood 2009]. However, research findings are still debated. Our study did not support findings in previous reports.

Study Limitations

The potential limitations of this study include the observational and retrospective nature and a relatively small sample size. Preoperative diagnosis of AF is based on clinical documentation with ECG confirmation, and likely underestimates the actual number of asymptomatic or paroxysmal AF incidents. Such misclassification would bias findings in favor of the null hypothesis and result in an underestimation of the difference between patients with POAF and those without. Another limitation is that continuous electrocardiogram-monitoring was not continued after ICU discharge. Twelve-lead ECG was performed 4 times daily and when a patient exhibited clinical signs of arrhythmia. It is possible that short episodes of asymptomatic AF may have been overlooked.

Conclusion

The results of this study confirm that the incidence of POAF after isolated ONCAB in patients ≥60 years old is high. Our data suggest that a history of hypertension, left atrium diameter, and EuroSCORE I value are predictors of POAF after ONCAB in patients ≥60 years old. The identification of risk factors for POAF is essential in order to prevent and reduce the occurrence of this complication.

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