

# Postoperative Atrial Fibrillation after Minimally Invasive Direct Coronary Artery Bypass: A Single-Center, 5-Year Follow-Up Study

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## ABSTRACT

**Objective:** To evaluate the risk factors and explore the mid-term outcomes of postoperative atrial fibrillation (POAF) after minimally invasive direct coronary artery bypass (MIDCAB).

**Methods:** A total of 165 patients, who underwent isolated MIDCAB from 2012 to 2015, were enrolled in the study and retrospectively reviewed. Patients with preoperative arrhythmia, concomitant surgical procedures were excluded. All patients were continuously monitored for POAF until discharge, and two groups were formed: the non-POAF group (140 patients, 71.4% men, mean age 58.83±10.3 years) and the POAF group (25 patients, 84.0% men, mean age 64.52±9.0 years). Early and mid-term outcomes were evaluated, perioperative factors associated with POAF were analyzed with a binary logistic regression model, and the relationship between POAF and major adverse cardiac event (MACE) was analyzed with Cox regression model.

**Results:** The incidence of POAF in this study was 15.15%. Patients in the POAF group had a significant higher risk of re-entry to ICU (2 cases: 2 cases=8.0%: 1.4%,  $P = 0.049$ ), renal failure (2 cases: 1 case=8.0%: 0.7%,  $P = 0.018$ ), and death (1 case: 0 case=4.0%: 0%,  $P = 0.018$ ). Binary logistic regression showed gender (male), age were independent risk factors of POAF ( $P = 0.038$ , 95% confidence interval 1.082-16.286;  $P = 0.011$ , 95% confidence interval 1.015-1.117, respectively), preoperative ACEI or ARB usage was a protective factor of POAF ( $P = 0.010$ , 95% confidence interval 0.113-0.748). With a 5-year follow up, the overall MACE rate showed no statistical difference between the two groups ( $P = 0.067$ ).

**Conclusions:** POAF after MIDCAB was related to postoperative morbidities, such as re-entry to ICU, renal failure, and death. Gender (male) and age were independent risk factors, while preoperative ACEI or ARB usage was a protective factor. POAF was not associated occurrence of MACE with a mid-term follow up.

## INTRODUCTION

Postoperative atrial fibrillation (POAF) remains the most common arrhythmia after coronary artery bypass grafting (CABG). The incidence of POAF after CABG has been reported between 15%-40% [Mariscalco 2008]. POAF is associated with worse patient mortality, prolonged hospital stays, hemodynamic disorders, thromboembolism, and death [Farouk 2018]. Therefore, it is important to identify patients with high risk of developing POAF, so that targeted prophylactic therapy can be given.

To minimize surgical morbidity in coronary artery bypass grafting, minimally invasive cardiac surgery has gained popularity. Minimally invasive direct coronary artery bypass (MIDCAB) offers unique advantages compared with conventional off-pump coronary artery bypass, involving the surgical revascularization of the left anterior descending (LAD) artery through a left anterior thoracotomy; this has been advocated as an acceptable alternative to standard CABG through full sternotomy [Jaffery 2007]. The minimally invasive nature of the procedure, avoidance of cardiopulmonary bypass, and use of the left internal mammary artery (LIMA) with its well-established long-term patency are some of the widely recognized advantages [Diegeler 2002; Calafiore 1996]. Despite these advantages, POAF still could not be eliminated after MIDCAB. Therefore, this study originally aims to explore the risk factors of POAF after MIDCAB and identify the potential impact of POAF on the outcomes from in-hospital to mid-term follow up.

## METHODS

**Patient characteristics:** A total of 165 patients, who underwent elective and isolated MIDCAB at Peking University People's Hospital from January 1, 2012 to December 30, 2015, were selected for this study. The exclusion criteria included preoperative arrhythmia, concomitant cardiac disease or surgical procedure, and cardiac pacemaker implantation.

**Ethics:** The study was approved by the Institutional Ethics Committee of Peking University People's Hospital (2020PHB127-01). All patients provided the informed consent.

**Data collection:** All data were collected from the Chinese Cardiac Surgery Registry (CCSR). The perioperative variables were collected. In-hospital complications were

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recorded carefully by two researchers to ensure a high consistency.

Follow-up information was obtained from annual outpatient reviews or telephone questionnaire (which was offered to those unable to attend an outpatient review). The major adverse cardiac events (MACE), including death, non-fatal myocardial infarction, stroke and repeat revascularization, were recorded.

**Perioperative medication management:** Before the operation, medications such as aspirin,  $\beta$ -blocker and statin were routinely given when there is no contraindication. Aspirin, statin and  $\beta$ -blocker were prescribed on postoperative day 1, clopidogrel was given at existence of venous graft or planned sequential hybrid revascularization. Other drugs were given when necessary, such as blood pressure or glucose control.

**Surgical procedure:** All operations were performed without cardiopulmonary bypass. The MIDCAB was suitable for patients with single or multivessel patients. The incision between the 4th or the 5th rib was approximately 6-8 cm. Under direct vision, the LIMA was obtained to complete the LIMA-LAD anastomosis. For the non-LAD grafts, the proximal anastomosis is sutured to the ascending aorta. Coronary anastomosis was performed by using running 7-0 polypropylene. Tissue stabilizer and an intracoronary shunt were used during grafting. At the end of the procedure, all grafts were measured by The Transit-time flow measurement device.

**Evaluation of POAF:** POAF was defined as any episode of atrial fibrillation (AF) noted by continuous telemetry monitoring, or documented by a physician in the chart, lasting for 30s or more.

All patients were monitored by hardwire monitoring electrocardiogram or continuous telemetry monitoring until discharge. In case of POAF occurrence, 12-lead ECG and blood gas examinations were performed, and oral or intravenous amiodarone would be given. For those patients who suffered AF more than 24 hours, an anticoagulant therapy would be added. All patients were converted into sinus rhythm before discharging. No patients required electrical cardioversion.

Patients were divided into the POAF group and non-POAF group, according to the development of POAF.

**Statistical analysis:** The Kolmogorov-Smirnov test was used to check the normality of continuous variables. If the data were conformed to the normal distribution, they were described by mean  $\pm$  standard deviation. Otherwise, they were described by median (minimum, maximum). Categorical variables were expressed as numbers and percentages. Continuous variables were analyzed by t-test, and categorical variables were compared by Mann-Whitney U test or Chi-square test/Fisher's exact test. Independent predictors of POAF were then determined by a binary logistic regression analysis of those variables found to have a p-value < 0.10 on univariate analysis. A bilateral P value < 0.05 were considered statistically significant. To evaluate the survival rate, study groups were compared with the log-rank test. Statistical analyses were performed using SPSS (version 24.0, SPSS Inc., Chicago, IL, USA).

Table 1. Preoperative characteristics of included patients

	POAF group (N = 25)	non-POAF group (N = 140)	P
Age (years)	64.52 $\pm$ 9.0	58.83 $\pm$ 10.3	0.010
Male	21(84.0%)	100(71.4%)	0.190
Body mass index (kg/m <sup>2</sup> )	25.25 $\pm$ 2.0	25.18 $\pm$ 3.3	0.885
Smoking situation	11(44.0%)	58(41.4%)	0.810
Hypertension	14(56.0%)	76(54.3%)	0.874
Diabetes mellitus	-	-	0.677
Diet control (n, %)	1(4.0%)	15(10.7%)	
Oral medication (n, %)	4(16.0%)	15(10.7%)	
Insulin (n, %)	2(8.0%)	12(8.6%)	
Hyperlipidemia	3(12.0%)	20(14.3%)	0.761
COPD	0(0%)	2(1.4%)	0.548
Peripheral vascular disease	1(4.0%)	6(4.3%)	0.948
Cerebrovascular disease	2(8.0%)	11(7.9%)	0.981
Thyroid disease	-	-	0.046
Hypothyroidism	0(0%)	3(2.1%)	
Hyperthyroidism	1(4.0%)	0(0%)	
History of MI (n, %)	8(32.0%)	43(30.7%)	0.898
Previous PCI (n, %)	3(12.0%)	19(13.6%)	0.831
Coronary heart disease	-	-	0.116
Stable angina (n, %)	12(48.0%)	41(29.3%)	
Unstable angina (n, %)	12(48.0%)	93(66.4%)	
STEMI (n, %)	1(4.0%)	3(2.1%)	
NSTEMI (n, %)	0(0%)	3(2.1%)	
NYHA Class	-	-	0.776
NYHA I (n, %)	5(20.0%)	26(18.6%)	
NYHA II (n, %)	15(60.0%)	74(52.9%)	
NYHA III (n, %)	5(20.0%)	37(26.4%)	
NYHA IV (n, %)	0(0%)	3(2.1%)	
Preoperative medications			
Nitrate (n, %)	7(28.0%)	66(47.1%)	0.076
Catecholamine (n, %)	0(0%)	2(1.4%)	0.548
Beta blockers (n, %)	22(88.0%)	133(95.0%)	0.177
ACEI/ARB (n, %)	12(48.0%)	30(21.4%)	0.005
Statins (n, %)	19(76.0%)	108(77.1%)	0.901
Aspirin (n, %)	24(96.0%)	128(91.4%)	0.435
Clopidogrel (n, %)	0(0%)	9(6.4%)	0.192
LVEF (%)	65.62 $\pm$ 9.5	64.00 $\pm$ 10.7	0.479
LVEDD (cm)	5.19 $\pm$ 0.7	4.99 $\pm$ 0.6	0.139
LA (cm)	3.56 $\pm$ 0.7	3.65 $\pm$ 0.5	0.489

Table 2. Intraoperative and postoperative characteristics of included patients

	POAF group (N = 25)	non-POAF group (N = 140)	P
Number of grafts	1.0±0	1.02±0.2	0.578
Planned sequential hybrid revascularization	3(12.0%)	17(12.1%)	0.984
Serum potassium (mmol/L)	4.08±0.3	3.97±0.3	0.122
Preoperative intubation	0(0%)	1(0.7%)	0.672
Preoperative cardiogenic shock	1(4.0%)	0(0%)	0.018
Intraoperative transfusion	0(0%)	5(3.6%)	0.337
ICU time (h)	36.46±29.6	39.18±50.6	0.795
Mechanical ventilation time (h)	12.04±17.1	12.19±21.0	0.974
IABP usage (n, %)	1(4.0%)	0(0%)	0.018
Postoperative maximum TNI (ng/mL)	3.27±13.6	1.32±6.2	0.488
Total drainage (mL)	915.20±450.3	765.61±473.4	0.145
Reoperation	-	-	0.255
For grafting	1(4.0%)	1(0.7%)	
For bleeding	1(4.0%)	2(1.4%)	
Re-entry into ICU (n, %)	2(8.0%)	2(1.4%)	0.049
Renal failure (n, %)	2(8.0%)	1(0.7%)	0.012
Re-intubation (n, %)	1(4.0%)	1(0.7%)	0.167
Death	1(4.0%)	0(0%)	0.018

## RESULTS

**Baseline characters:** There was a total of 165 patients, who underwent elective and isolated MIDCAB. Twenty-five patients (15.15%) developed POAF. The average age of these patients was 59.69±8.1 years, and most of the patients are male (72.8%). The age of the patients in the POAF group was older (64.52±9.0 years: 58.83±10.3 years,  $P = 0.010$ ). Preoperative complications, such as hypertension, diabetes, hyperlipidemia, peripheral or cerebral vascular diseases and COPD, showed no differences between the two groups. There was a significant difference in the thyroid disease ( $P = 0.046$ ) and preoperative ACEI/ARB usage ( $P = 0.005$ ). The parameters from echocardiography showed no statistical differences. (Table 1)

**Clinical outcomes:** Most patients received single vessel revascularization (LIMA-LAD grafting), two patients in the non-POAF group received multiple vessel revascularization, and the number of grafts showed no difference between the two groups ( $P = 0.578$ ). Moreover, 20 patients were implemented with a planned sequential hybrid revascularization.

Patients in the POAF group had more proportion of cardiogenic shock and IABP usage ( $P = 0.018$  and  $P = 0.018$ , respectively). Of the postoperative characteristics, patients with POAF had a high risk of re-entry into the ICU (8.0%: 1.4%,  $P = 0.049$ ) and renal failure (8.0%: 0.7%,  $P = 0.012$ ). There was no difference in the intraoperative transfusion, postoperative maximum TNI level, total drainage, reoperation

(whether for grafting or bleeding), and re-intubation between the two groups. One patient in the POAF group died from postoperative heart failure, and the death rate showed a statistical difference between the two groups ( $P = 0.018$ ). (Table 2)

**Risk factors of POAF:** In a binary logistic regression analysis, gender (male) ( $P = 0.038$ , OR 4.198, 95%CI 1.082-16.286) and age ( $P = 0.011$ , OR 1.064, 95%CI 1.015-1.117) were defined as independent risk factors of POAF after MIDCAB. Preoperative ACEI/ARB usage, however, showed a protective effect on POAF ( $P = 0.010$ , OR 0.291, 95%CI 0.113-0.748). (Table 3)

**Mid-term follow up:** All patients were followed up for 5 years. At the end of the follow up, MACE was recorded in 43 patients, 10 cases in the POAF group (40%) and 33 cases in the non-POAF group (23.6%). Cox regression analysis of freedom from MACE revealed no significant difference between both groups ( $P = 0.067$ , OR 9.517, 95% CI 0.255-1.048). (Figure 1)

## DISCUSSION

MIDCAB, compared with conventional coronary artery bypass, can avoid heart ischemia-reperfusion injury caused by cardiopulmonary bypass and has the advantages of less trauma, less bleeding, fast recovery, and avoiding deep sternal wound infection [Jaffery 2007]. Despite the improvement of surgery techniques and increasing quality of perioperative

Table 3. Binary logistic regression analysis

	B value	P	OR	95% CI
Gender (male)	1.435	0.038	4.198	1.082-16.286
Age	0.062	0.011	1.064	1.015-1.117
Preoperative ACEI/ARB	-1.233	0.010	0.291	0.113-0.748

care, the incidence of POAF has not decreased in recent years. The present study indicated that POAF was still a common arrhythmia after MIDCAB, with an incidence of 15.15%. This ratio is evidently at a lower level compared with the data reported in previous literature [Filardo 2018; Thoren 2016].

In our analysis, preoperative status of patients showed no significant differences in the two groups except thyroid diseases. To our knowledge, higher thyroid hormone level is associated with increased risk for AF and a prolonged total atrial conduction time (TACT). Additionally, thyroid hormone enhanced the effect of angiotensin II in the atrial myocytes, which can induce atrial hypertrophy and cause atrial remodeling, which is an important reason for POAF [Dietrich 2015; Vidotti 2019]. Although the binary logistic regression analysis did not show an independent risk factor of POAF, we still need to pay attention to this situation in the preoperative management of patients.

Previous studies confirmed that age is a risk factor of POAF, which may be related to the retrogressive changes of heart, especially the atrial structure and function [Clement 2019; Kievisas 2017; Amar 2002]. In our study, this result is verified by the binary logistic regression analysis. Additionally, we found that gender (male) also is a risk factor of POAF, which is consistent with previous literature reports, but the underlying mechanism still is not clear [Lee 2017].

For the preventive treatment of POAF, our results of binary logistic regression analysis showed preoperative ACEI/ARB usage may reduce the occurrence of POAF. As an "upstream treatment," by improving atrial structural remodeling, ACEI or ARB was recommended to use to prevent new atrial fibrillation in patients with heart failure and hypertension with

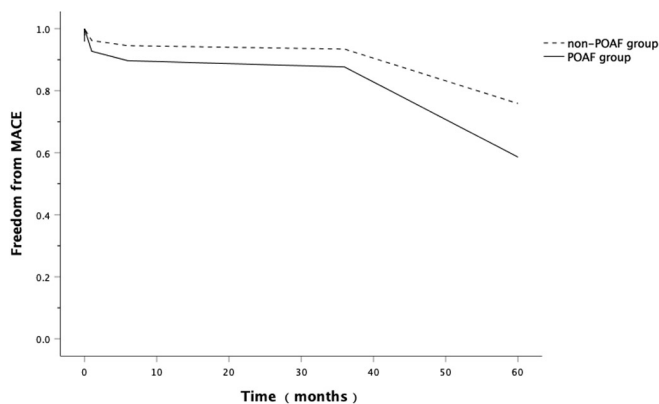


Figure 1. Cox regression curve estimates in the two groups.

decreased left ventricular ejection fraction (level IIa, level B) [January 2019].

Unlike previous studies, the preoperative status of smoking, diabetes, hypertension, COPD, and serum potassium level showed no influence on POAF in our analysis, which may be related to the typical perioperative management of our center. We strongly believe that optimized respiratory management, blood pressure and glucose control, and serum electrolyte maintenance could help to reduce the occurrence of POAF. POAF affects the prognosis of patients undergoing MIDCAB, however, there still are no specific medications that effectively can prevent it [Piccini 2013; Zheng 2016]. Hence, it is important to identify the high-risk clinical variables that correlate with POAF among patients undergoing MIDCAB.

### LIMITATIONS

As a single center retrospective study, our results are limited by the lack of volume for MIDCAB procedure. In addition, single graft of LIMA–LAD coronary surgery or with planned sequential hybrid revascularization mainly was performed in the initial stage of the technique development. However, the manner of single graft may be deviated from the minimally invasive multi-vessel coronary artery bypass grafting at present. Furthermore, as this paper presents the mid-term outcomes with POAF after MIDCAB, long-term follow up and evaluation is awaited.

### CONCLUSION

POAF after MIDCAB is closely related to a variety of postoperative complications, even increasing the mortality of patients. Preoperative evaluation is helpful with identifying high-risk patients of POAF. Old age and gender (male) were the independent risk factors of POAF. The potential benefits of preoperative ACEI or ARB usage should be considered in the typical operation and patients. Cox regression analysis showed that the occurrence of POAF had no significant influence on MACE events with a mid-term follow up.

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