New-onset postoperative atrial fibrillation is associated with worse long-term outcome in critically ill patients after non-cardiac surgery: 3-year follow-up of a case-control study

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Research article

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Abstract

Background The impact of new-onset postoperative atrial fibrillation (POAF) on long-term outcomes of patients after non-cardiac surgery remains controversial. Here we report the 3-year follow-up of a previous case-control study to determine the relationship between new-onset POAF and long-term outcomes in patients after non-cardiac surgery. Methods In a previous case-control study, 213 patients who were admitted to the intensive care unit (ICU) after non-cardiac surgery were included; of them 71 were in the POAF group and 142 the control group. A telephone interview was performed with patients or their family members at 3 years after surgery. The primary endpoint was the incidence of major adverse cardiovascular events (MACEs) within 3 years, including cardiovascular death, non-fatal cardiac arrest, acute myocardial infarction, congestive heart failure, and ischemic stroke. A logistic regression model was established to assess the association between the occurrence of new-onset POAF and the development of 3-year MACEs. Results 202 patients completed the 3-year follow-up and were included in the analysis; of them 68 were in the POAF group and 134 were in the control group. The incidence of 3-year MACEs was higher in the POAF group than in the control group (64.7% [44/68] vs. 23.1% [31/134], p<0.001). After correction for confounding factors, new-onset POAF was independently associated with an increased risk of 3-year MACEs (odds ratio 5.448, 95% confidence interval 2.202-13.481, p<0.001). Conclusions For adult patients admitted to the ICU after non-cardiac surgery, new-onset POAF was an independent risk factor for the development of MACEs within 3 years.

Introduction

New-onset postoperative atrial fibrillation (POAF) is the most commonly occurred arrhythmia in patients after surgery [1]. The reported incidence varies widely, from 0.39% to 29%, according to the patient populations and the types of surgeries [1-14]. In our previous study, 2.7% of patients admitted to the intensive care unit (ICU) after non-cardiac surgery developed new-onset POAF. Of them, 77.5% occurred within the first 3 days after surgery, 87.3% had rapid ventricular rate (>110 beats per minute), 39.4% had a significant drop in blood pressure (>30% from baseline), and 33.8% complained discomfort (including palpitation, chest distress, and precordial pain or discomfort). Sepsis, hypokalemia, congestive heart failure and other new-onset arrhythmias were risk factors of new-onset POAF [15].

The occurrence of POAF is associated with worse outcomes. In patients after cardiac surgery, new-onset POAF is associated with increased hospital readmission, late atrial fibrillation (AF) and thromboembolic disease, as well as long-term mortality [16-21]. In patients after major non-cardiac surgery, new-onset POAF is reported to be associated with higher in-hospital mortality, longer hospital stays, higher health care costs [9], and increased long-term cardiovascular events (including acute myocardial infarction and stroke) [10, 12, 13]. In a recent prospective cohort study of ICU patients (including surgical patients), new-onset AF is associated with increased 1-year mortality [22]. On the other hand, negative results were also reported regarding the relationship between new-onset POAF and long-term survival [11, 18, 23].

The purpose of this 3-year follow-up study was to investigate the association between new-onset POAF and long-term outcomes in critically ill patients after non-cardiac surgery.

Methods

Study design

This was a 3-year follow-up of patients enrolled in a previous case-control study [15]. The study protocol was approved by the Clinical Research Ethics Committee of Peking University First Hospital (2016[1110]). Since the study was pure observational, the Ethics Committee agreed to waive the written informed consent for this subsequent telephone contact. But all participants or their family members were informed of the purpose and contents of the current study, and provide oral consents via telephone before data collection.

Patient recruitment

In the previous study, 71 adult patients who were admitted to the ICU after non-cardiac surgery from January 1, 2011 to December 31, 2013 and developed new-onset POAF during ICU stay were enrolled. One hundred and forty-two control patients (without new-onset POAF) were enrolled in a ratio of 1:2. The matching conditions included the following: same gender, same type of surgery, age gap within 4 years, and the closest date of surgery. The exclusion criteria were the same for both cases and control subjects, i.e., a previous history of atrial fibrillation, atrial fibrillation revealed by preoperative examination, or missing data.

Collection of baseline and perioperative data

Baseline data included demographic variables (age, sex, body mass index), surgical diagnosis, preoperative comorbidities (chronic heart failure, hypertension, coronary heart disease, diabetes mellitus, chronic obstructive pulmonary disease, asthma, chronic renal failure and non-AF arrhythmia), main results of preoperative examination (including echocardiogram), and American Society of Anesthesiologist (ASA) classification. Perioperative data included type and duration of surgery, complexity [24] and cardiac risk [25] of surgery, type of anesthesia, intraoperative fluid balance, main laboratory test results after surgery (hemoglobin [HGB], cardiac troponin I [CTnI], brain natriuretic peptide [BNP], serum potassium, and serum magnesium), Acute Physiology and Chronic Health Evaluation (APACHE) II score at ICU admission, the worst physiological parameters during ICU stay, occurrence of postoperative complications, and pathological diagnoses (including the tumor, node and metastasis [TNM] stage for cancer [26]).

Postoperative major adverse cardiovascular events (MACEs) indicated those that occurred during hospital stay after surgery (up to 30 days) and included cardiovascular death, nonfatal cardiac arrest, acute myocardial infarction, congestive heart failure, and ischemic stroke. Cardiovascular death referred to any death caused by specific cardiovascular diseases (including myocardial infarction [I21.X in the

International Classification of Diseases-10th Revision code], heart failure [I50.X], arrhythmia [I49.900], and cardiogenic shock [R57.001]), which might be combined with other diseases. Non-fatal cardiac arrest (I46.9) referred to cardiac arrest (ventricular fibrillation, pulseless ventricular tachycardia, asystole, and pulseless electrical activity) caused by various reasons, followed by return of spontaneous circulation after cardiopulmonary resuscitation (CPR), and patient survived. Acute myocardial infarction (I21.X) was diagnosed when the CTnI concentration was higher than the diagnostic criteria for myocardial infarction, together with the emergence of new Q wave (≥0.03 s) or the persistent change of ST-T segment (≥4 days). Congestive heart failure (I50.X) referred to the acute attack or aggravation of the symptoms or signs of heart failure, accompanied by BNP elevation (>400 pg/ml), and required medical treatment. Ischemic stroke referred to a new-onset, persistent (>24 hours) focal neurologic deficit with computed tomography or magnetic resonance imaging evidence of cerebral infarction (I63.9).

Other postoperative complications were generally defined as new-onset complications other than MACEs during hospital stay (up to 30 days) after surgery, which were harmful for postoperative recovery and required therapeutic intervention.

3-year follow-up

The 3-year follow-up was carried out by telephone interview with patients and/or their family members. Prior to the follow-up, the investigator reviewed the patients' medical records within 3 years. During the follow-up interview, the condition of patients after discharge and the occurrence of MACEs were inquired and collected in detail. Long-term MACEs included cardiovascular death, nonfatal cardiac arrest, acute myocardial infarction, congestive heart failure, and ischemic stroke. For all patients, the diagnoses of MACEs were confirmed by another senior ICU physician who was not aware of patients' study group assignment. For patients who died within 3 years, the date of death was recorded.

Study endpoints

The primary endpoint was the incidence of MACEs within 3 years after surgery. Secondary endpoints included the incidences of MACEs and other complications during hospital stay (up to 30 days), lengths of stay in ICU and hospital, all-cause in-hospital mortality (up to 30 days), and 3-year overall survival after surgery.

Statistical Analysis

Continuous variables were compared with the independent samples t test or Mann-Whitney U test. Categorical variables were compared with the χ^2 test or Fisher exact test. Time-to-event variables were calculated with the Kaplan-Meier estimator, with differences between groups assessed by the log-rank test. To assess the risk adjusted association between the new-onset POAF and the occurrence of MACEs within 3 years, univariate logistic regression analyses were performed first; independent variables with $p<0.10$ were included in a multivariate logistic regression model with a backward (Wald) stepwise

procedure. A two-tailed *p* value <0.05 was considered as statistically significant. All statistical analyses were performed with SPSS 25.0 software package (SPSS Inc, Chicago, Ill, USA).

Results

Patients

Of the 213 patients enrolled in our previous study (71 in the POAF group and 142 in the control group), 11 (5.2%) were lost to follow-up at 3 years after surgery. The remaining 202 patients completed the 3-year follow-up and were included in the final analysis; of these, 68 were in the POAF group and 134 in the control group. Postoperative 3-year follow-up was performed between January 1, 2014 and December 31, 2016 (Figure 1).

Baseline characteristics and perioperative data

Baseline characteristics were comparable between the two groups (Table 1). Compared with patients in the control group, those in the POAF group had higher proportion of emergency surgery (p=0.005) and higher APACHE II score at ICU admission (p=0.003); they had lower levels of hemoglobin (p=0.003), serum potassium (p<0.001) and serum magnesium (p=0.005), but higher levels of troponin I (p<0.001) and brain natriuretic peptide (p<0.001) during ICU stay (Table 2). There were no significant differences regarding the proportion of pathologically diagnosed cancer and the distribution of cancer stages between the two groups (Table 3).

Results of 3-year follow-up

The incidence of 3-year MACEs was higher in the POAF group than in the control group (64.7% [44/68] vs. 23.1% [31/134], odds ratio [OR] 6.091, 95% confidence interval [CI] 3.215-11.543, p<0.001). Among individual incidences of MACEs, those of congestive heart failure (p<0.001) and ischemic stroke (p=0.032) were higher in the POAF group than in the control group.

The incidences of in-hospital MACEs and other complications after surgery were higher in the POAF group than in the control group (both p<0.001). The duration of mechanical ventilation in patients who were admitted to the ICU with endotracheal intubation was longer (p<0.001), the lengths of stay in ICU and hospital after surgery in all patients were also longer (both p<0.001) in the POAF group than in the control group. All-cause in-hospital mortality was higher (p=0.006), whereas 3-year overall survival was shorter (p=0.043) in the POAF group than in the control group (Table 4; Figure 2).

Association between new-onset POAF and 3-year MACEs

Apart from new-onset POAF, univariable analyses identified 9 other factors that were associated with 3-year MACEs (p<0.10), including preoperative coronary heart disease, non-AF arrhythmia and left atrial enlargement, emergency surgery, APACHE II score at ICU admission, as well as hemoglobin <110 g/L, troponin I >0.04 ng/ml, brain natriuretic peptide >100 pg/ml and occurrence of other complications after

surgery (Supplement 1). After correction for confounding factors, new-onset POAF was associated with an increased risk of 3-year MACEs (OR 5.448, 95% CI 2.202-13.481, p<0.001). Among other factors, preoperative coronary heart disease (OR 2.974, 95% CI 1.126-7.858, p=0.028) and postoperative troponin I >0.04 ng/ml (OR 19.137, 95% CI 5.642-64.909, p<0.001) were also associated with increased risks of 3-year MACEs (Table 5).

Discussion

Results of the present study showed that, in patients admitted to the ICU after non-cardiac surgery, those who developed new-onset POAF had a higher incidence of MACEs and a shorter overall survival within 3 years after surgery. New-onset POAF was independently associated with an increased risk of 3-year MACEs.

A large database study from the United States revealed that, between 2004 and 2013, 1 of every 33 patients hospitalized for non-cardiac surgery developed perioperative major adverse cardiovascular and cerebrovascular events [27]. Different from cardiac surgery patients [16-19], available evidence regarding the impact of new-onset AF on the long-term outcomes after non-cardiac surgery are still controversial. For example, Gialdin and colleagues [10] found that perioperative AF was associated with an increased risk of long-term ischemic stroke; others also reported that patients with new-onset AF after cancer surgery were at increased risk of cardiovascular events within 1 year [12,13]. On the other hand, results of Meierhenrich and colleagues [23] showed that new-onset AF did not increase 2-year mortality in septic shock patients; long-term follow-ups of Cormack and colleagues [11] also showed that new-onset POAF did not affect oncologic outcomes. Differences in patient populations and surgical types may be responsible for different results.

In the present study, we followed up patients included in a previous retrospective case-control study at 3 years after surgery. In our previous results, 95.8% of new-onset POAF were transient, and only 4.2% became persistent [15]. But even so, new-onset POAF was significantly associated with an increased risk of 3-year MACEs. Our results provide further evidence that new-onset POAF may produce negative effects on long-term outcomes of patients admitted to the ICU after non-cardiac surgery. Considering that POAF is an easily diagnosed and preventable arrhythmia, whether the prevention of POAF can improve the long-term outcomes in this patient population deserves further study.

The exact mechanisms leading to increased long-term MACEs by new-onset POAF remain not totally clear but may include the following. Firstly, the effect of inflammation and stress response [28-31]. New-onset AF is often seen in patients with more intense inflammation and stress response [6,23,29,32,33], including sepsis [15] and septic shock [34]. POAF is usually triggered by surgery-related inflammation and stress response in elderly patients with comorbid cardiac disease [30]. Although POAF is transient in most cases, the intense and persistent inflammation and stress response might have worsened the long-term outcomes. Secondly, the effect of recurrent or chronic AF. It was found that recurrent or chronic AF is more likely to occur in patients with new-onset POAF [17, 20, 21, 35]. And even a short period (>6 minutes)

of subclinical fibrillation is associated with an increased risk of stroke and embolism [36], and subsequently affects late survival [16]. In our previous study, only a small part of patients with new-onset POAF (4.2%) had persistent AF during hospital stay. However, it was possible that AF reoccurred or even became persistent in some patients after hospital discharge, and increased long-term MACEs after surgery.

In the present study, the 3-year overall survival was shorter in patients with new-onset POAF. The occurrence of MACEs might have led to a shortened survival time [35]. In addition, other factors might also have exerted impact, such as cancer. In the present study, 78.2% of all patients underwent surgery for cancer. Although the staging of cancers did not differ significantly between the two groups, the proportions with advanced-stage cancer were slightly higher in patients in the POAF group. The confounding effect of cancer stage on long-term survival cannot be excluded. The impact of new-onset POAF on long-term survival requires further study.

There are several limitations of the present study. Firstly, because of the low incidence of POAF, our previous study was a case-control study with a small sample size and single-center data. This limited the generalizability of the present results. Secondly, the long-term outcome data was collected through telephone interview. Although detailed diagnostic criteria were set to define the endpoints, there might be some bias. Lastly, as results of 3-year follow-up of a case-control study, the effects from unidentified confounding factors could not be excluded. Nevertheless, the results from the present study provide important clues for further interventional trials.

Conclusions

Our study found that, for adult patients admitted to the ICU after non-cardiac surgery, those with new-set POAF had higher incidence of 3-year MACEs and shorter overall survival. New-onset POAF was independently associated with an increased risk of 3-year MACEs. Interventional studies are required to elucidate whether prevention of new-onset POAF can improve long-term outcomes.

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Tables

Table 1. Baseline data

	POAF group (n=68)	Control group (n=134)	*p* value
Age (years)	72.3 ± 10.8	72.7 ± 10.2	0.768
Male	36 (52.9%)	72 (53.7%)	0.915
Body mass index (kg/m^2)	23.2 ± 4.3	22.8 ± 3.2	0.498
Preoperative complicated diseases			
Chronic heart failure [a]	1 (1.5%)	6 (4.5%)	0.486
Hypertension	39 (57.4%)	82 (61.2%)	0.599
Coronary heart disease	18 (26.5%)	33 (24.6%)	0.776
Diabetes mellitus	9 (13.2%)	25 (18.7%)	0.330
Chronic obstructive pulmonary disease	3 (4.4%)	3 (2.2%)	0.674
Asthma	3 (4.4%)	5 (3.7%)	>0.999
Chronic kidney disease [b]	4 (5.9%)	9 (6.7%)	>0.999
Non-AF arrhythmia [c]	4 (3.0%)	7 (10.3%)	0.066
Preoperative echocardiographic abnormality			
Left atrial enlargement	19 (35.8%)	22 (24.7)	0.157
Pulmonary arterial systolic pressure (mmHg)	32.6 ± 10.1	30.8 ± 11.0	0.195
Left ventricular ejection fraction <50%	6 (11.1%)	10 (10.6)	0.929
Cardiac valves abnormality	52 (98.1%)	86 (96.6)	>0.999
Preoperative ASA classification			0.498
I	23 (34.3%)	37 (27.4%)	
II	26 (38.8%)	67 (49.6%)	
III	11 (16.4%)	21 (15.6%)	
IV	7 (10.2%)	10 (7.4%)	
Duration from surgery to interview (month)	36.6 ± 1.3	36.3 ± 0.9	0.086

Data are presented as mean ± SD or number (%).

POAF: postoperative atrial fibrillation; AF: atrial fibrillation; ASA: American Society of Anesthesiologist.

[a] Diagnosed according to the symptoms and signs of heart failure, including dyspnea, inability to lie flat at night, decreased activity tolerance, peripheral edema, signs of pulmonary congestion on chest X-ray, and/or elevated serum brain natriuretic peptide level. These symptoms and signs developed on the basis of underlying heart diseases. Diagnosis was confirmed by cardiologists and treatment was required before surgery.

[b] Glomerular filtration rate <60 ml/min/1.73 m^2 lasting for more than 3 months. Diagnosis was confirmed by nephrologists.

[c] Included sinus tachycardia (2 cases), sinus bradycardia (2 cases), atrial premature beat (2 cases), ventricular premature beat (1 case), supraventricular tachycardia (1 case), atrioventricular block (2 cases), and bundle branch block (1 case). Diagnosis was confirmed by preoperative electrocardiographic examination.

Table 2. Perioperative data

	POAF group (n=68)	Control group (n=134)	*P* value
Type of surgery			0.995
Intra-abdominal	41 (60.3%)	84 (62.7%)	
Intra-thoracic	14 (20.6%)	27 (20.1%)	
Transurethral	2 (2.9%)	3 (2.2%)	
Intra-cranial	3 (4.4%)	6 (4.4%)	
Spinal and extremital	8 (11.8%)	14 (10.4%)	
Duration of surgery (min)	196 (131, 357)	202 (147, 333)	0.966
Complexity of surgery [a]			0.907
Intermediate	3 (4.2%)	4 (3.0%)	
Major or complex	65 (95.6%)	130 (97.0%)	
Cardiac risk of surgery [b]			0.930
Low	3 (4.4%)	6 (4.5%)	
Intermediate	64 (94.1%)	125 (93.3%)	
High	1 (1.5%)	3 (2.2%)	
Type of anesthesia			0.639
Neuraxial	8 (11.8%)	22 (16.4%)	
General	56 (82.4%)	106 (79.1%)	
Combined epidural-general	4 (5.9%)	6 (4.5%)	
Intraoperative fluid balance			
Fluid infusion (ml)	2750 (1862, 4263)	2300 (1600, 3925)	0.162
Blood transfusion	24 (35.3%)	43 (32.1%)	0.648
Emergency operation	21 (30.9%)	19 (14.2%)	0.005
ICU admission with intubation	45 (66.2%)	85 (63.4%)	0.700
APACHE II score at ICU admission [c]	12 (9,17%)	10 (8,13%)	0.003
Laboratory test results during ICU stay [d]			
Hemoglobin (g/L)	98.9 ± 20.0	107.7 ± 18.8	0.003
Cardiac troponin I (ng/ml)	0.03 (0.01, 0.13)	0.01 (0.01, 0.02)	<0.001
Brain natriuretic peptide (pg/ml)	510 (186, 1194)	164 (90, 410)	<0.001
Serum potassium (mmol/L)	3.9 ± 0.6	4.2 ± 0.5	<0.001
Serum magnesium (mmol/L)	0.87 ± 0.16	0.94 ± 0.16	0.005

Data are presented as number (%), median (interquartile range) or mean ± SD.

POAF: postoperative atrial fibrillation; ICU: intensive care unit; APACHE II: Acute Physiology and Chronic Health Evaluation II.

[a] Rated according to routine preoperative tests for elective surgery: summary of updated National Institute for Health and Care Excellence (NICE) guidance [24].

[b] Rated according to American College of Cardiology/American Heart Association guideline update for perioperative cardiovascular evaluation for noncardiac surgery [25].

[c] The worst score within 24 hours after ICU admission.

[d] The last one before POAF in the POAF group. The worst one after ICU admission in the control group.

Table 3. Pathological diagnoses

	POAF group (n = 68)	Control group (n = 134)	P value
Pathologically diagnosed cancer	48 (70.6%)	110 (82.1%)	0.061
TNM stage of cancer [a]	(n = 48)	(n = 110)	
T stage			0.126
T0	0 (0.0%)	0 (0.0%)	
T1	5 (10.4%)	27 (24.5%)	
T2	12 (25.0%)	31 (28.2%)	
T3	22 (45.8%)	40 (36.4%)	
T4	9 (18.8%)	12 (10.9%)	
N stage			0.176
N0	26 (54.2%)	77 (70.0%)	
N1	13 (27.1%)	23 (20.9%)	
N2	5 (10.4%)	7 (6.4%)	
N3	4 (8.3%)	3 (2.7%)	
M stage			0.514
M0	41 (85.4%)	98 (89.1%)	
M1	7 (14.6%)	12 (10.9%)	
Cancer stage [a]	(n = 48)	(n = 110)	0.135
Stage 1	5 (10.4%)	26 (23.6%)	
Stage 2	21 (43.8%)	51 (46.4%)	
Stage 3	15 (31.3%)	21 (19.1%)	
Stage 4	7 (14.6%)	12 (10.9%)	

Data are presented as number (%).

POAF: postoperative atrial fibrillation; TNM: tumor, node and metastasis.

[a] Rated according to the American Joint Committee on Cancer (AJCC) Cancer Staging Manual-7th Edition [26].

Table 4. 3-year outcomes

	POAF group (n=68)	Control group (n=134)	Estimated effects (95% CI)	P value
Primary endpoint				
MACEs within 3 years after surgery	44 (64.7%)	31 (23.1%)	OR=6.091 (3.215-11.543)	<0.001
Cardiovascular death [a]	8 (11.8%)	10 (7.5%)	OR=1.653 (0.621-4.403)	0.311
Nonfatal cardiac arrest [b]	4 (5.8%)	3 (2.2%)	OR=2.729 (0.593-12.560)	0.228
Acute myocardial infarction [c]	17 (25.0%)	20 (14.9%)	OR=1.900 (0.919-3.927)	0.080
Congestive heart failure [d]	32 (47.1%)	10 (7.5%)	OR=11.022 (4.947-24.559)	<0.001
Ischemic stroke [e]	6 (8.8%)	3 (2.2%)	OR=4.226 (1.023,17.456)	0.032
Secondary endpoints				
MACEs in hospital after surgery	38 (55.9%)	10 (7.55%)	OR=15.707 (7.039-35.049)	< 0.001
Cardiovascular death [a]	1 (1.5%)	0 (0.0%)	---	---
Nonfatal cardiac arrest [b]	2 (2.9%)	2 (1.5%)	OR=2.000 (0.276-14.516)	0.604
Acute myocardial infarction [c]	12 (16.9%)	5 (3.7%)	OR=5.529 (1.860-16.434)	0.001
Congestive heart failure [d]	30 (44.1%)	8 (6.0%)	OR=12.434 (5.261-39.388)	< 0.001
Ischemic stroke [e]	1 (1.5%)	0 (0.0%)	---	---
Other postoperative complications in hospital	47 (69.1%)	25 (18.7%)	OR=9.758 (4.976-19.136)	< 0.001
Respiratory failure [f]	11 (16.2%)	1 (0.7%)	OR=25.667(3.237-203.505)	< 0.001
Severe sepsis or septic shock [g]	25 (36.8%)	10 (7.5%)	OR= 7.209 (3.203-16.226)	< 0.001
Circulatory insufficiency [h]	14 (20.6%)	12 (9.0%)	OR=2.636 (1.144-6.075)	0.020
New-onset arrhythmia (non-atrial fibrillation) [i]	27 (39.7%)	7 (5.2%)	OR=11.948 (4.844-29.468)	< 0.001
Acute kidney injury [j]	19 (27.9%)	3 (2.2%)	OR=16.932 (4.798-59.758)	< 0.001
Mechanical ventilation time [k] (hour)	36.0 (5.5, 168.5) (n=45)	7.0 (4.0, 13.5) (n=85)	Median D=29.0 (19.4, 41.7)	< 0.001
LOS in ICU after surgery (day)	5.0 (3.0, 11.0)	1.0 (1.0, 2.3)	Median D=4.0 (1.1, 10.4)	< 0.001
LOS in hospital after surgery (day)	17.5 (13.0, 31.0)	11.5 (8.0, 18.3)	Median D=6.0 (2.2, 13.1)	< 0.001
All-cause mortality in hospital	6 (8.5%)	1 (0.7%)	OR=13.015 (1.535, 110.325)	0.006
3-year overall survival after surgery (month)	25.8 (22.6, 28.9)	31.4 (30.1, 32.8)	HR=1.598 (1.007-2.538)	0.043

Data are expressed as n (%) or median/mean (95% CI).

POAF: postoperative atrial fibrillation; CI: confidence interval; MACEs: major adverse cardiovascular events; OR: odds ratio; D; difference; LOS: length of stay; ICU: intensive care unit; HR: hazard ratio; ICD-10: the International Classification of Diseases-10th revision.

[a] Any death caused by specific cardiovascular diseases (myocardial infarction [I21.X in the ICD-10 code], heart failure [I50.X], arrhythmia [I49.900], and cardiogenic shock [R57.001]), which might be combined with other diseases.

[b] Cardiac arrest (ventricular fibrillation, pulseless ventricular tachycardia, asystole, and pulseless electrical activity) caused by various reasons, followed by return of spontaneous circulation after cardiopulmonary resuscitation, and patient survived (I46.9).

[c] Diagnosed when the CTnI concentration was higher than the diagnostic criteria for myocardial infarction, together with the emergence of new Q wave (≥0.03 s) or the persistent change of ST-T segment (≥4 days) (I21.X).

[d] The acute attack or aggravation of the symptoms or signs of heart failure, accompanied by serum brain natriuretic peptide elevation (>400 pg/ml), and required medical treatment (I50.X).

[e] A new-onset, persistent (>24 hours) focal neurologic deficit with computed tomography or magnetic resonance imaging evidence of cerebral infarction (I63.9).

[f] Diagnosed when PaO_2 <60 mmHg (room air), oxygenation index <300, and/or arterial oxygen saturation <90%, and required oxygen therapy or mechanical ventilation for more than 48 hours.

[g] Systematic inflammatory response syndrome caused by a known or suspected infection, accompanied by at least one new organ dysfunction or required vasopressor therapy to maintain blood pressure.

[h] Requirement of vasopressors and/or inotropic therapy for more than 24 hours.

[i] New-onset arrhythmia other than atrial fibrillation. Diagnosis was confirmed by a 12-lead electrocardiogram. Medical treatment and/or electrical conversion were required.

[j] Serum creatinine increased to more than 26.5 nmol/L within 48 hours after surgery, or serum creatinine increased to more than 1.5 times baseline within 7 days, or urine output <0.5 ml/kg/hr for more than 6 hours.

[k] Results of those who were admitted to the ICU with endotracheal intubation.

Table 5. Factors in association with 3-year MACEs [a]

	Univariate analysis		Multivariate analysis [b]	
	OR (95% *CI*)	*p* value	OR (95% *CI*)	*p* value
New-onset POAF	6.091 (3.215-11.543)	<0.001	5.448 (2.202-13.481)	<0.001
Preoperative coronary heart disease	1.942 (1.019-3.703)	0.044	2.974 (1.126-7.858)	0.028
Preoperative non-AF arrhythmia [c]	4.935 (1.267-19.225)	0.021	---	---
Left atrial enlargement	2.307 (1.102-4.831)	0.027	---	---
Emergency operation	3.733 (1.814-7.683)	<0.001	---	---
APACHE II score at ICU admission	1.065 (1.008-1.125)	0.025	---	---
Hemoglobin <110 g/L	2.606 (1.368-4.965)	0.004	---	---
Cardiac troponin I >0.04 ng/ml	12.675 (5.759-27.894)	<0.001	19.137 (5.642-64.909)	<0.001
Brain natriuretic peptide >100 pg/ml	5.483 (2.199-13.667)	<0.001	---	---
Other complications in hospital (within 30 days) [d]	4.115 (2.230-7.585)	<0.001	---	---

MACEs: major adverse cardiovascular events; OR: odds ratio; CI: confidence interval; POAF: postoperative atrial fibrillation; AF: atrial fibrillation; APACHE II: Acute Physiology and Chronic Health Evaluation II; ICU: intensive care unit.

[a] Include cardiovascular death, nonfatal cardiac arrest, acute myocardial infarction, congestive heart failure, and ischemic stroke.

[b] Factors with $p<0.10$ in univariate analyses are included in the multivariate Logistic regression model. Multivariate Logistic regression analysis was performed by using a Backward (Wald) stepwise procedure. Hosmer-Lemeshow test: $\chi^2=4.207$, df=6, $p=0.649$.

[c] Includes sinus tachycardia (2 cases), sinus bradycardia (2 cases), atrial premature beat (2 cases), ventricular premature beat (1 case), supraventricular tachycardia (1 case), atrioventricular block (2 cases), and bundle branch block (1 case).

[d] Include respiratory failure, severe sepsis or septic shock, circulatory insufficiency, new-onset non-AF arrhythmia, and acute kidney injury.

Figures

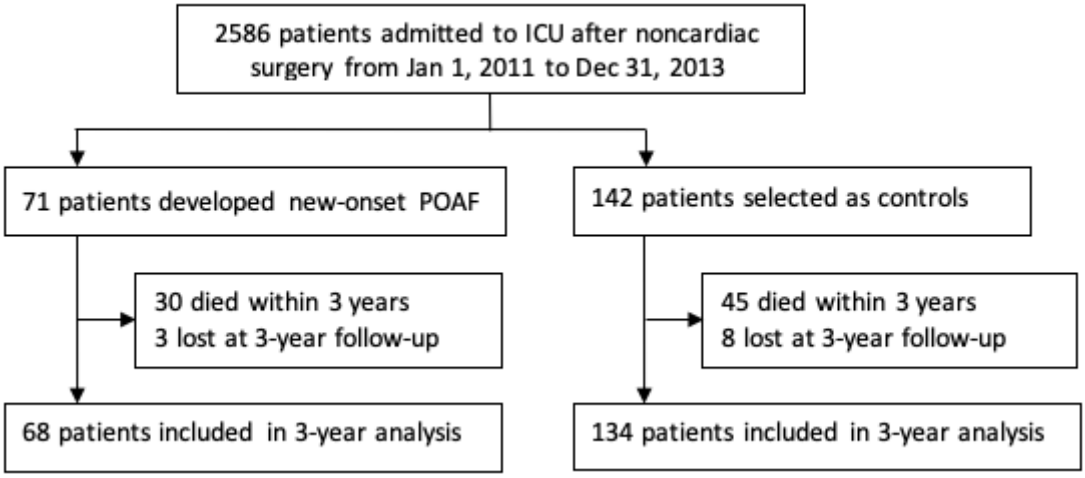

Figure 1

Flowchart of the study.

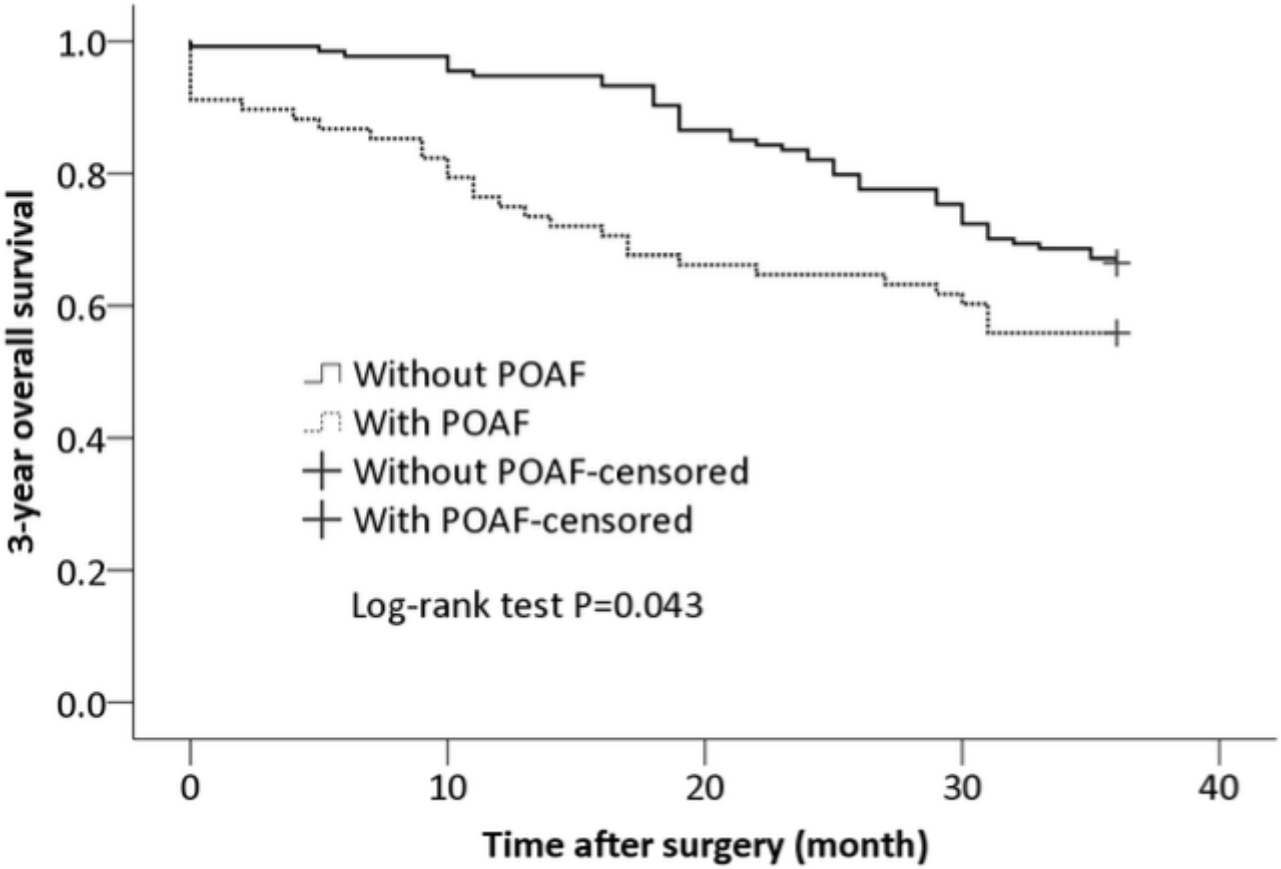

Figure 2

The 3-year overall survival in patients with or without now-onset POAF.

Supplementary Files

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- SubmitSupplement1.Factorsunivariateanalyses.docx
- SubmitSTROBEChecklist.docx