Risk factors and outcomes of intraoperative atrial fibrillation in patients undergoing thoracoscopic anatomic lung surgery

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Background: Atrial fibrillation (AF) is common after thoracoscopic anatomic lung surgery and can be associated with increased adverse outcomes. However, the incidence, risk factors, and related outcomes of intraoperative AF in thoracoscopic anatomical lung surgery are unknown.

Methods: We retrospectively analyzed the files of 14,986 patients who had presented to the Shanghai Chest Hospital for thoracoscopic anatomic lung operations between January 2016 and December 2018. Univariate and multivariate analyses were conducted to identify risk factors for intraoperative AF, and a 1:1 propensity score-matched (PSM) analysis was performed to compare postoperative outcomes.

Results: The incidence of intraoperative AF was 1.2% (177/14,986). Multivariate analysis identified age older than or equal to 60 years [odds ratio (OR) =1.872, P<0.001], male sex (OR =2.979, P<0.001), diabetes mellitus (OR =2.287, P=0.014), lesion diameter of 1.4 cm or larger (OR =1.855, P=0.002), clinical nodal involvement (OR =1.920, P=0.005), lobectomy resection (OR =2.958, P=0.001), and right resection (OR =1.475, P=0.021) as independent risk factors for intraoperative AF. After 1:1 PSM, we evaluated outcomes in 350 (175 pairs) patients with or without intraoperative AF. Patients who had intraoperative AF were associated with prolonged median ICU stay {28 [26–54] *vs.* 24 [22–44] hours, P=0.001} and length of stay (LOS) {6 [4–7] *vs.* 5 [4–6] days, P=0.009}. However, the differences in cardiovascular, pulmonary, and other complications were not significant. In the subgroup analysis, patients who recovered sinus rhythm during operation (n=16) had a shorter median LOS {4 [4–6] *vs.* 6 [4–7] days, P=0.031}, and a similar incidence of complications compared with patients who recovered sinus rhythm after surgery (n=159).

Conclusions: We identified 7 independent risk factors for intraoperative AF, which were associated with prolonged ICU and hospital stays. The findings may help clinicians identify high-risk patients and take preventive measures to minimize the incidence and adverse outcomes of intraoperative AF.

Keywords: Thoracic surgery; intraoperative atrial fibrillation; risk factors; video-assisted thoracoscopic surgery (VATS)

Introduction

Video-assisted thoracoscopic surgery (VATS) is a minimally invasive method which has been increasingly used for anatomical lung resection. VATS greatly reduces surgical stress, systemic inflammation and postoperative complications (1-3), and when accompanied by systematic lymph node dissection, is the best curative treatment for lung cancer. Postoperative atrial fibrillation (POAF) is a common surgical complication in thoracoscopic anatomic lung resection, with a reported incidence ranging from 12% to 32% (4-7) and is associated with increased short- and long-term adverse outcomes (6-11).

Several attempts at identifying risk factors for POAF have been made, and these studies have shown that advanced age, male sex, higher body mass index, race, higher preoperative rest heart rate, extent of surgical resection, history of congestive heart failure, history of arrhythmias, and brain natriuretic peptide are known as independent risk factors for POAF (4,6-9,12). The mechanism of POAF is mainly related to decreased cardiopulmonary reserve, systemic inflammatory response to surgery, enhanced sympathetic nervous system activity, postoperative high stress state, and peroxidative stress response (13,14), but whether the mechanism of intraoperative AF is consistent with POAF is still unclear. Although guidelines exist concerning the treatment of POAF (9), there is a lack of clinical experience in the management of intraoperative AF, especially when it causes significant hemodynamic fluctuations. Therefore, to provide evidence for the clinical practice of preventing intraoperative AF and related adverse outcomes in high-risk patients, we conducted this large sample study to explore the potential risk factors.

We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/atm-20-5035).

Methods

We conducted a single-center retrospective study of 15,419 patients who had undergone thoracoscopic anatomic lung surgery between January 2016 and December 2018. Patients who met any of the following criteria were excluded from the study: preoperative AF (n=90), non-sinus rhythm (n=22), conversion to thoracotomy from VATS (n=195), thoracoscopic sleeve lobectomy (n=67), pneumonectomy (n=39), or bilateral lung resection (n=20). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and was approved by the Institutional Review Board at Shanghai Chest Hospital (No. KS1230). Informed consent was waived because of the retrospective nature of the study.

Data collection, outcomes, and definitions

Perioperative medical data were extracted from the electronic recording system of our institution, including patient demographics, medical history, surgical procedures, cancer clinical stage, and outcomes. Outcomes included postoperative pulmonary complications (PPCs), cardiovascular complications and other related surgical complications, intensive care unit (ICU) stay, and the length of hospital stay (LOS). PPCs are defined according to the European Perioperative Clinical Outcome (EPCO) (15). The definition for intraoperative AF was based on 2014 American Association for Thoracic Surgery (AATS) guidelines (9), and included the onset of intraoperative AF recorded from the electrocardiogram (ECG) lasting at least 1 minute.

Technique of operation

The number of lung operations in the Shanghai Chest Hospital has approached 10,000 cases each year since 2016, of which VATS accounts for more than 80%. Our center has 13 surgical teams, each including a chief surgeon and 1–2 surgical assistants. Considering the surgeons perform an average of 384 cases per year, we divided the teams into two groups (<400/year vs. ≥400/year). In all patients, surgical resection with systematic lymph node dissection was considered as the best curative treatment for lung cancer.

Statistical analysis

Statistical analysis was performed using SPSS 25.0 software (SPSS Inc., IBM Corp., Armonk, NY, USA). Two-sample independent t-test or Wilcoxon rank-sum test were used to compare the potential differences of continuous variables, while chi-square or Fisher's exact test for small samples were used to compare the categorical variables. Kaplan-Meier estimates were used for ICU stay and LOS. All variables found to be significantly (P<0.1) associated with intraoperative AF by univariate analysis were selected for the multivariable logistic regression model. Discrimination (C index) and calibration (Hosmer-Lemeshow goodness-of-fit test) were adopted to assess the prediction model. To determine the thresholds for age and lesion diameter, receiving operator
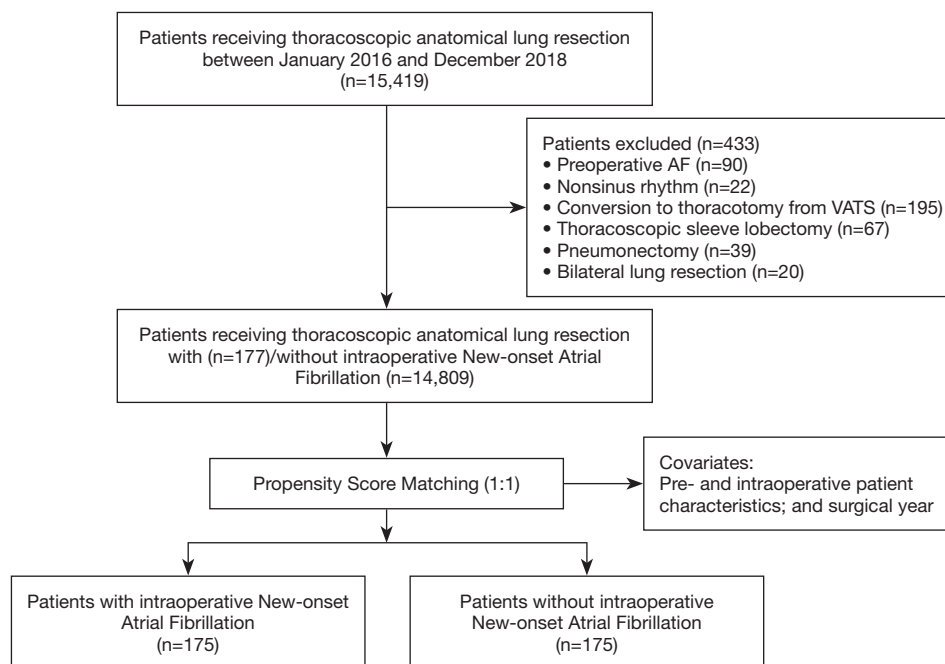
Figure 1 Patient flowchart.

characteristic (ROC) analysis was performed. A P value <0.05 was considered statistically significant.

Matching

Based on pre- and intraoperative variables and surgical years, a 1:1 propensity score matching (PSM) (16) with a caliper size of 0.001 was conducted to reduce the effects of confounding factors and compare outcomes between intraoperative AF and non-AF. After 1:1 PSM, all patient characteristics and surgical years were found to be comparable among the two groups. A subgroup analysis comparing patients with intraoperative AF who recovered sinus rhythm during the operation or after surgery was also carried out. All patients who failed to achieve sinus rhythm during the surgery eventually recovered sinus rhythm in the postoperative period.

Results

Between January 2016 and December 2018, 14,986 patients received thoracoscopic anatomical lung resection, with 22.0% (3,301 of 14,986) receiving segmentectomy resection and 78.0% (11,685 of 14,986) receiving lobectomy resection. Of these, 1.2% of patients (177 of 14,986) experienced AF during the operation (*Figure 1*).

The incidence of intraoperative AF dropped from 81 of 4,340 (1.9%), to 51 of 5,069 (1.0%), to 45 of 5,577 (0.8%) (P<0.001) over 3-year intervals.

Risk factors for intraoperative AF

The univariate analysis found 10 significant variables related to intraoperative AF (*Table 1*). Multivariate analysis identified age older than or equal to 60 years [odds ratio (OR) =1.872, P<0.001], male sex (OR =2.979, P<0.001), diabetes mellitus (OR =2.287, P=0.014), lesion diameter of 1.4 cm or larger (OR =1.855, P=0.002), clinical nodal involvement (OR =1.920, P=0.005), lobectomy resection (*vs.* segmentectomy resection, OR =2.958, P=0.001), and right resection (*vs.* left resection, OR =1.475, P=0.021) as independent risk factors for intraoperative AF (*Table 2*). The multivariable logistic regression model had good calibration (Hosmer-Lemeshow test, P=0.875) and discrimination (C statistic, 0.756). The ROC analysis showed similar area under the curve threshold values of 0.644 (P<0.05) for age and lesion diameter.

Outcomes after PSM (1:1)

After 1:1 PSM, all patient characteristics and surgical

Table 1 Pre- and intraoperative patient characteristics

Variables[a]	ALL (n=14,986)	AF (n=177)	No AF (n=14,809)	P value
Age, years	57.8±10.7	63.0±7.7	57.7±10.7	<0.001[b]
Sex				<0.001[b]
Male	6,031 (40.2)	125 (2.1)	5,906 (97.9)	
Female	8,955 (59.8)	52 (0.5)	8,903 (99.5)	
BMI, kg/m^2	23.3±3.0	23.3±2.7	23.3±3.0	0.916
ASA grade				0.013[b]
I	1,278 (8.6)	5 (0.3)	1,273 (99.7)	
II	12,157 (81.1)	148 (1.2)	12,009 (98.8)	
III/IV	1,551 (10.3)	24 (1.5)	1,527 (98.5)	
Comorbidity				
Hypertension	1,106 (7.4)	20 (1.8)	1,086 (98.2)	0.045[b]
Diabetes mellitus	285 (1.9)	10 (5.6)	275 (94.4)	0.002[b]
Coronary artery disease	103 (0.69)	1 (0.6)	102 (99.4)	0.999
Malignant disease	13,812 (92.2)	166 (1.2)	13,646 (98.8)	0.420
Lesions diameter, cm	1.8±1.1	2.3±1.3	1.8±1.1	<0.001[b]
Clinical stage	13,812 (92.2)	166 (1.2)	13,646 (98.8)	<0.001[b]
T1a	3,973 (26.5)	17 (0.4)	3,956 (99.6)	
T1b	5,836 (38.9)	72 (1.2)	5,764 (98.8)	
T1c	2,615 (17.4)	39 (1.5)	2,576 (98.5)	
T2a	897 (6.0)	26 (2.9)	871 (97.1)	
T2b	311 (2.1)	6 (1.9)	305 (98.1)	
T3	146 (1.0)	4 (2.7)	142 (97.3)	
T4	34 (0.3)	2 (5.9)	32 (94.1)	
Lymph nodes calcification	711 (4.7)	22 (3.1)	689 (96.9)	<0.001[b]
Clinical nodal involvement	664 (4.4)	23 (3.5)	641 (96.5)	<0.001[b]
Pleural adhesions	303 (2.0)	6 (2.0)	297 (98.0)	0.273
Type of resection				<0.001[b]
Segmentectomy resection	3,301 (22.0)	10 (0.3)	3,291 (99.7)	
Lobectomy resection	11,685 (78.0)	167 (1.4)	11,518 (98.6)	
Uni-portal VATS	1,241 (8.2)	12 (0.1)	1,229 (99.9)	0.466
Approach				0.871
VATS	14,357 (95.8)	170 (1.2)	14,187 (98.8)	
Robotic-assisted VATS	629 (4.2)	7 (1.1)	622 (98.9)	
Location of resection				0.006[b]
Left	5,805 (38.7)	51 (0.9)	5,754 (99.1)	
Right	9,181 (61.3)	126 (1.4)	9,055 (98.6)	
Surgical experience				0.169
<400/year	4,866 (32.5)	66 (1.4)	4,800 (98.6)	
≥400/year	10,120 (67.5)	111 (1.0)	10,009 (99.0)	

[a], continuous data are shown as mean ± standard deviation and categoric data as number (%). [b], statistically significant (P<0.05). AF, atrial fibrillation; ASA, American Society of Anesthesiology; BMI, body mass index; VATS, video-assisted thoracoscopic surgery.

Table 2 [a]Multivariable logistic regression analysis of risk factors for AF

Variables	OR (95% CI)	P value
Age ≥60 years	1.872 (1.343–2.610)	<0.001[b]
Male sex	2.979 (2.144–4.140)	<0.001[b]
Diabetes mellitus	2.287 (1.185–4.414)	0.014[b]
Lesions diameter ≥1.4 cm	1.855 (1.261–2.729)	0.002[b]
Clinical nodal involvement	1.920 (1.215–3.034)	0.005[b]
Type of resection		
Segmentectomy (reference)		
Lobectomy	2.958 (1.538–5.686)	0.001[b]
Location of resection		
Left (reference)		
Right	1.475 (1.059–2.054)	0.021[b]

[a], Hosmer-Lemeshow test P=0.875; C statistic: 0.756; CI, confidence interval; OR, odds ratio. [b], statistically significant (P<0.05). AF, atrial fibrillation.

years were comparable among the two groups (*Table 3*). We evaluated outcomes in 350 (175 pairs) patients with or without intraoperative AF. Patients who had intraoperative AF were associated with prolonged median ICU stay {28 [26–54] *vs.* 24 [22–44] hours, P=0.001} and LOS {6 [4–7] *vs.* 5 [4–6] days, P=0.009}. However, the differences in cardiovascular, pulmonary, and other complications were not significant (*Table 4*).

AF recovery during or after operation

Among the 175 patients with intraoperative AF, 16 recovered sinus rhythm during operation, including 8 patients who recovered automatically without intervention, 5 who recovered after cardioversion, and 3 who recovered after amiodarone intervention, which took 6.9±5.8, 4.0±1.0, and 37.7±27.6 (P=0.003) minutes, respectively (Table S1). In the subgroup analysis, patients who recovered sinus rhythm during operation (n=16) had a shorter duration of intraoperative AF (14.6±16.4 *vs.* 44.5±25.2, P<0.001) and median LOS {4 [4–6] *vs.* 6 [4–7] days, P=0.031}, but a similar incidence of complications compared with patients who recovered sinus rhythm after surgery (n=159) (Table S2).

Discussion

The overall incidence of intraoperative AF was 1.2%. Our study found 7 independent risk factors for intraoperative

AF which were associated with longer ICU and hospital stays. For patients with intraoperative AF, recovering sinus rhythm during operation may shorten hospital stay. The findings may help clinicians identify high-risk patients and take preventive measures to minimize the incidence and adverse outcomes of intraoperative AF.

Intraoperative AF has always been a concern for the surgical teams at our thoracic center. With the accumulation of unit experience, increase of cases, enhancement of confidence, and the identification of potential risk factors, intraoperative AF rates have decreased from 3.4% as previously reported (17) to 1.2% as found in our study. The incidence of intraoperative AF also dropped from 81 out of 4,340 (1.9%), to 51 out of 5,069 (1.0%), to 45 out of 5,577 (0.8%) over 3-year intervals.

Previous studies have suggested some risk factors for POAF, including advanced age, male sex, higher body mass index, race, higher preoperative rest heart rate, extent of surgical resection, history of congestive heart failure, history of arrhythmias, and brain natriuretic peptide (4,6-9,12). By comparison, our study also found that advanced age, male sex, and the extent of surgical resection were still independent risk factors for intraoperative AF. Elderly patients have decreased lung function reserves, increased comorbidities, and tissue vulnerability (13,18), accompanied by age-related myocardial apoptosis and fibrosis, which may contribute to the cardiac re-modelling, intra-atrial conduction delay, and re-entrant circuits

Table 3 Pre- and intraoperative patient characteristics after PSM (1:1)

Variables[a]	AF (n=175)	No AF (n=175)	P value
Age, years	62.8±7.7	63.3±8.9	0.567
Sex			0.906
Male sex	124 (70.9)	125 (71.4)	
Female sex	51 (29.1)	50 (28.6)	
BMI, kg/m^2	23.3±2.7	23.5±2.8	0.339
ASA grade			0.770
I	5 (2.9)	4 (2.3)	
II	148 (84.6)	144 (82.3)	
III/IV	22 (12.6)	27 (15.4)	
Comorbidity			
Hypertension	18 (10.3)	14 (8.0)	0.458
Diabetes mellitus	8 (4.6)	11 (6.3)	0.479
Coronary artery disease	1 (0.6)	3 (1.7)	0.623
Malignant disease	164 (93.7)	168 (96.0)	0.333
Lesions diameter, cm	2.3±1.3	2.2±1.3	0.645
Clinical stage	164 (93.7)	168 (96.0)	0.692
T1a	17 (10.4)	24 (14.3)	
T1b	71 (43.3)	74 (44.0)	
T1c	39 (23.8)	33 (19.6)	
T2a	25 (15.2)	20 (11.9)	
T2b	6 (3.7)	9 (5.4)	
T3	4 (2.4)	7 (4.2)	
T4	2 (1.2)	1 (0.6)	
Lymph nodes calcification	21 (12.0)	16 (9.1)	0.385
Clinical nodal involvement	22 (12.6)	14 (8.0)	0.159
Pleural adhesions	6 (3.4)	5 (2.9)	0.759
Type of resection			0.398
Segmentectomy resection	10 (5.7)	14 (8.0)	
Lobectomy resection	165 (94.3)	161 (92.0)	
Uni-portal VATS	12 (6.9)	8 (4.6)	0.357
Approach			0.792
VATS	168 (96.0)	167 (95.4)	
Robotic-assisted VATS	7 (4.0)	8 (4.6)	
Location of resection			0.472
Left	51 (29.1)	45 (25.7)	
Right	124 (70.9)	130 (74.3)	
Surgical experience			0.262
<400/year	66 (37.7)	56 (32.0)	
≥400/year	109 (62.3)	119 (68.0)	

[a], continuous data are shown as mean ± standard deviation and categoric data as number (%). PSM, propensity score matching; AF, atrial fibrillation; ASA, American Society of Anesthesiology; BMI, body mass index; VATS, video-assisted thoracoscopic surgery.

Table 4 Outcomes after propensity score matching (1:1)

Variables[a]	AF (n=175)	No AF (n=175)	P value
Any complications	51 (29.1)	49 (28.0)	0.813
PPCs	47 (26.9)	45 (25.7)	0.808
Atelectasis	26 (14.9)	20 (11.4)	
Pulmonary infection	25 (14.3)	26 (14.9)	
Respiratory failure	7 (4.0)	1 (0.6)	
Pleural effusion	1 (0.6)	2 (1.1)	
Cardiovascular			
Atrial arrhythmia	6 (3.4)	11 (6.3)	0.214
Acute cerebral infarction	1 (0.6)	0 (0)	0.999
Acute myocardial infarction	1 (0.6)	1 (0.6)	0.999
Air leakage >5 days	4 (2.3)	0 (0)	0.123
Chylothorax	1 (0.6)	1 (0.6)	0.999
Postoperative blood transfusion	2 (1.1)	0 (0)	0.499
Postoperative reoperation	1 (0.6)	0 (0)	0.999
ICU readmission	2 (1.1)	0 (0)	0.499
30-day readmission	2 (1.1)	1 (0.6)	0.999
ICU stay, h	28 [26–54]	24 [22–44]	0.001[b]
Length of stay, d	6 [4–7]	5 [4–6]	0.009[b]

[a], continuous data are shown as mean ± standard deviation and categoric data as number (%); [b], statistically significant (P<0.05). Length of stay and ICU stay, values as median (interquartile range). AF, atrial fibrillation; PPCs, postoperative pulmonary complications; ICU, intensive care unit.

responsible for AF. Furthermore, males have a higher risk of intraoperative AF. While the reasons for this are not fully understood, this may be due to their increased atrial size, higher pro-inflammatory immune response (19), and weaker congenital cardio-protection following surgical trauma compared to females (20-22). In addition, in accordance with other studies (4,6,7,9,17), we found that compared thoracoscopic segmentectomy resection, lobectomy resection was associated with higher rates of intraoperative AF, perhaps because of the increased lymph node removal, amount of adjacent tissues resection, higher risk of injury to the vagus nerve and its branches, and more operative time required (23,24).

Our research also identified other rarely reported underlying risk factors for intraoperation AF, including diabetes mellitus, lesion diameter ≥1.4 cm, clinical nodal involvement, and right resection. Although diabetes mellitus has been rarely reported as an independent risk

factor for POAF in thoracic surgery, Kalus *et al.* has demonstrated that patients with diabetes mellitus have a higher incidence of POAF during cardiac surgery (25), which is consistent with our study. The possible mechanism for atrial fibrillation (AF) in diabetic patients could be related to autonomic neuropathy which weakens parasympathetic activity and leads to relative sympathetic excess (24). Larger lesions (6,26) and clinical lymph node involvement (27) affected by inflammation and tumor invasion may directly mask regional anatomic areas near the vagus nerve and its branches, and increase surgical difficulty during endoscopic dissection (28,29). Interestingly, we found anatomic right lung resection to be more associated with higher intraoperative AF than left lung resection, which is in line with the observations of Roselli (30). This may be related to the distribution of the vagus nerve and its branches, especially the cardiac plexus and the area near the pulmonary veins during lymph node removal (14,23).

In our study, patients who had intraoperative AF were associated with prolonged median ICU and hospital stays, while cardiovascular, pulmonary, and other complications were not significantly different compared with patients who did not suffer from intraoperative AF. These results are consistent with other studies that reported POAF to be associated with increased ICU and hospital stays (6,7,9). In the subgroup analysis in this study, patients who recovered sinus rhythm during operation had a shorter duration of intraoperative AF, a shorter median hospital stay, and a similar incidence of complications compared with patients who recovered sinus rhythm after surgery. Among the 16 patients who recovered sinus rhythm during operation, cardioversion seemed to be an effective intervention based on the time required to restore sinus rhythm. For clinicians, who encounter AF during thoracoscopic anatomic lung resection, intraoperative intervention, especially through cardioversion, may be an effective measure to shorten hospital stay.

This study has several limitations. First, as a retrospective study, it has inherent design biases. Second, although the median ICU and hospital stay in patients with intraoperative AF were longer compared with those in patients without intraoperative AF, the two groups had similar short-term complications. On this basis more attention should be paid to perioperative care and the long-term prognosis of patients with intraoperative AF.

Conclusions

By conducting a retrospective analysis of 14,986 patients undergoing thoracoscopic anatomic lung operations, we identified 7 independent risk factors for intraoperative AF, which were associated with longer ICU and hospital stays. In addition, intraoperative recovery sinus rhythm may shorten hospital stay. Knowledge of these factors could help clinicians identify patients at high risk and take preventive measures to minimize the rate and adverse outcomes of intraoperative AF.

Acknowledgments

Footnote

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Table S1 AF recovery during or after operation

Variables	N=175	Percentage
AF recovery		
During operation	16	9.0
After operation	159	91.0
Intraoperative Intervention		
Cardioversion	5	31.2
Amiodarone	3	19.8
No	8	50.0
Time required for recovery, min, mean (SD)		
Cardioversion	4.0(1.0)	NA
Amiodarone	37.7(27.6)	NA
No	6.9(5.8)	NA
Duration of AF, time, mean (SD)		
Intraoperative recovery	14.6(16.4)	NA
Postoperative recovery	44.5(25.2)	NA

AF: Atrial fibrillation; NA: Not applicable

Table S2 Comparison of outcomes in AF recovery during or after operation

Variables [a]	During operation (n=16)	After operation (n=159)	P Value
Any complications	4 (25.0)	47 (29.6)	0.782
PPCs	2 (12.5)	45 (28.3)	0.242
Atelectasis	0 (0)	23 (14.5)	
Pulmonary infection	2 (12.5)	26 (14.9)	
Respiratory failure	0 (0)	7 (4.4)	
Pleural effusion	0 (0.6)	1 (0.6)	
Cardiovascular			
Atrial arrhythmia	2 (12.5)	4 (2.5)	0.095
Acute cerebral infarction	0 (0)	1 (0.63)	0.999
Acute myocardial infarction	1 (6.3)	0 (0)	0.091
Air leakage >5days	0 (0)	4 (2.5)	0.999
Chylothorax	0 (0)	1 (0.6)	0.999
Postoperative blood transfusion	1 (0.6)	1 (0.6)	0.999
Postoperative reoperation	0 (0)	1 (0.6)	0.999
ICU readmission	0 (0)	2 (1.3)	0.999
30-day readmission	0 (0)	2 (1.3)	0.999
ICU stay, h	30 [28-30]	28 [26-54]	0.503
Length of stay, d	4 [4-6]	6 [4-7]	0.031[b]

a Continuous data are shown as mean± standard deviation and categoric data as number (%); b Statistically significant (P<0.05). Length of stay and ICU stay, values as median (interquartile range). AF: Atrial fibrillation; PPCs: postoperative pulmonary complications; ICU: Intensive care unit.