



Long-Term Outcomes of Preoperative Atrial Fibrillation in Cardiac Surgery

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Background: Atrial fibrillation (Afib) is a marker of increased cardiovascular morbidity and mortality. Owing to the increased prevalence of Afib in patients undergoing cardiac surgery, assessing the effect of Afib on postsurgical outcomes is important. We aimed to analyze the effect of preoperative Afib on clinical outcomes in patients undergoing cardiac surgery using a large surgical database.

Methods: This retrospective cohort study was based on the national health claims database established by the National Health Insurance Service of the Republic of Korea from 2009 to 2015. Diagnosis and procedure codes were used to identify diseases according to the International Statistical Classification of Diseases, 10th revision.

Results: We included 1,037 patients (0.1%) who had undergone cardiac surgery from a randomized 1,000,000-patient cohort, and 15 patients (1.5%) treated with isolated surgical Afib ablation were excluded. Of these 1,022 patients, 412 (39.7%), 303 (29.2%), and 92 (9.0%) underwent coronary artery bypass, heart valve surgery, and Cox-maze surgery, respectively. Preoperative Afib was associated with higher patient mortality ($p=0.028$), regardless of the surgical procedure. Patients with preoperative Afib ($n=190$, 18.6%) experienced a higher cumulative risk of overall mortality (hazard ratio [HR], 1.435; 95% confidence interval [CI], 1.263–2.107; $p=0.034$). Subgroup analysis revealed a reduced risk of overall mortality with Cox-maze surgery in Afib patients (HR, 0.500; 95% CI, 0.266–0.938; $p=0.031$). Postoperative cerebral ischemia or hemorrhage events were not related to Afib.

Conclusion: Preoperative Afib was independently associated with worse long-term postoperative outcomes after cardiac surgery. Concomitant Cox-maze surgery may improve the survival rate.

Keywords: Atrial fibrillation, Maze procedure, Database

Introduction

Atrial fibrillation (Afib) is the most common sustained cardiac arrhythmia in the general population. The prevalence of Afib has been projected to increase to 12 million people in the United States by 2050 and 17.9 million in Europe by 2060. Consequently, the healthcare burden related to Afib, which is mainly driven by hospitalizations, is growing considerably [1,2]. A few large cohort studies have recently recognized Afib as a marker of increased cardiovascular morbidity and mortality [3-6]. This, together with the increased prevalence of Afib in patients undergoing cardiac surgery [7], makes it important to assess the poten-

tial effect of arrhythmia on outcomes after cardiac surgery in a large cohort.

As a result of recent developments in cardiac intervention with improved pharmacological treatments, cardiac surgeons are increasingly operating on elderly patients with complicated, high-risk heart diseases. In such patients, Afib is often present before cardiac surgery, thus increasing the risk of surgery and the occurrence of postoperative complications. Preoperative Afib significantly worsens the postoperative hemodynamic function of the heart. This increases the chances of complications, which could result in a prolonged stay in the intensive care unit and hospital, as well as death [8-11]. In a multicenter study



involving 522 patients with end-stage renal disease who were undergoing cardiac surgery, preexisting Afib was associated with overall but not perioperative mortality [12, 13].

Findings from the Society of Thoracic Surgery national adult cardiac database revealed that the incidence of Afib in patients requiring coronary artery bypass grafting (CABG) was approximately 6% [14]. Although previous studies have examined the effects of preoperative Afib on mortality following cardiac surgery, the long-term outcomes were not studied [15]. In addition, previous studies have concentrated on a single type of cardiac surgery (e.g., CABG or mitral valve surgery) and did not evaluate other types of surgery, which might have an impact on the observed long-term outcomes.

The purpose of this study was to conduct a nationwide analysis of the impact of preoperative Afib on the long-term postoperative outcomes in patients who underwent heart surgery. Furthermore, we examined the extent to which a concomitant Cox-maze surgical procedure affected the postoperative outcomes in preoperative Afib patients.

Methods

This study was based on the national health claims database established by the National Health Insurance Service (NHIS) of the Republic of Korea and was approved by the Institutional Review Board of Yonsei University Health System (approval no., 4-2018-0603). The requirement for informed consent was waived. The procedures followed were in accordance with the Declaration of Helsinki (2013 version). We examined a randomized cohort of 1 million sampled patients from the NHIS database from January 2009 to December 2015 and selected those who underwent cardiac surgery using International Statistical Classification of Diseases, 10th revision (ICD-10) codes, including O1641-1642, OA641-642, O1781-1783, O1791-1793, O2031-2033, and O2006 (aortic valve replacement/repair, mitral valve replacement/repair, tricuspid replacement/repair, and aorta replacement, respectively). The details are presented in Table 1.

Study population and risk stratification

Among the randomized 1,000,000 sampled cohort patients, we identified 1,037 (0.1%) adult patients (≥ 18 years) who underwent cardiac surgery between January 2009 and December 2015. Of these, patients who had isolated Afib

Table 1. Operative characteristics of patients in preoperative Afib versus non-Afib groups in patients who underwent cardiac surgery (n=1,022)

| Characteristic | Non-Afib (n=832) | Afib (n=190) |
|-----------------------------------|------------------|--------------|
| CABG surgery | 382 (45.9) | 30 (15.8) |
| Valve surgery | 250 (30.0) | 53 (27.9) |
| Aorta surgery | 81 (9.7) | 7 (3.7) |
| CABG+valve surgery | 48 (5.8) | 3 (1.6) |
| CABG+aorta surgery | 24 (2.9) | 0 |
| Valve+aorta surgery | 23 (2.8) | 2 (1.1) |
| CABG+valve+aorta surgery | 24 (2.9) | 3 (1.6) |
| CABG+Cox-maze surgery | 0 | 2 (1.1) |
| Valve+Cox-maze surgery | 0 | 73 (38.4) |
| Aorta+Cox-maze surgery | 0 | 6 (3.2) |
| CABG+valve+Cox-maze surgery | 0 | 9 (4.7) |
| CABG+aorta+Cox-maze surgery | 0 | 0 |
| Valve+aorta+Cox-maze surgery | 0 | 0 |
| CABG+valve+aorta+Cox-maze surgery | 0 | 2 (1.1) |

Values are presented as number (%).

Afib, atrial fibrillation; CABG, coronary artery bypass graft.

surgery (n=15) were excluded. The resulting 1,022 patients were categorized into 2 groups according to their preoperative Afib status: no Afib (n=832, 81.4%) and Afib (n=190, 18.6%) (Appendix 1). For risk adjustment, the underlying diseases were identified, and primary diagnoses were defined using the corresponding ICD-10 codes. The preoperative data (baseline characteristics), including height, weight, body mass index, hypertension, serum fasting glucose or creatinine level, and lipid profiles, were analyzed. We also analyzed postoperative medications (e.g., anti-platelets, anticoagulants, anti-hypertensive drugs, and 3-hydroxy-3-methyl-glutaryl coenzyme A [HMG-CoA] reductase inhibitors) that could affect morbidity and mortality.

Primary and secondary endpoints

The primary endpoint was overall mortality after cardiac surgery, which was obtained from the NHIS. The secondary endpoint was a postoperative cerebrovascular accident (CVA), such as stroke or non-traumatic cerebral hemorrhage. Incident CVA was identified according to the following ICD-10 codes: I60.0-9, I61.0-9, I62.0,1,9, I63.0-9, I64, I65.0,1,2,3,8,9, I66.0,1,2,3,4,8,9 (subarachnoid hemorrhage, intracerebral hemorrhage, non-traumatic intracranial hemorrhage, cerebral infarction, stroke, occlusion and stenosis of the cerebral artery, respectively).

Statistical methods

Baseline demographic characteristics, preoperative risk factors, and outcomes of interest were compared between patients with and without preoperative Afib. Continuous variables were categorized, and all variables were described as frequencies, with the chi-square test used for comparisons between the groups. We used a Cox proportional hazard model to examine the associations between Afib and hard endpoints, including major morbidities (e.g., CVA) and mortality. We first performed unadjusted comparisons followed by an analysis adjusted for patients' preoperative characteristics, which included age, sex, hypertension, diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), coronary artery obstructive disease, peripheral arterial obstructive disease (PAOD), renal failure, hyperlipidemia, and heart failure.

We investigated whether significant interactions existed between Cox-maze surgery and mortality. Furthermore, we estimated the adjusted hazard ratios (HRs) with 95%

confidence intervals (CIs) for the relationships with mortality, stroke, cerebral hemorrhage, and Cox-maze surgery after adjusting for postoperative medications (anti-coagulant, anti-platelets, and HMG-CoA reductase inhibitors). A p-value ≤ 0.05 was considered statistically significant. All analyses were performed with SAS ver. 7.1 (SAS Institute Inc., Cary, NC, USA) and R software ver. 3.3.3 (https://www.r-project.org).

Results

Comparison of long-term survival between patients with and without Afib who underwent cardiac surgery

Among patients who underwent cardiac surgery, the overall mortality was significantly higher in patients with preoperative Afib than in those without preoperative Afib ($p=0.028$) (Fig. 1A). The relationship between preoperative characteristics and overall survival is shown in Table 2.

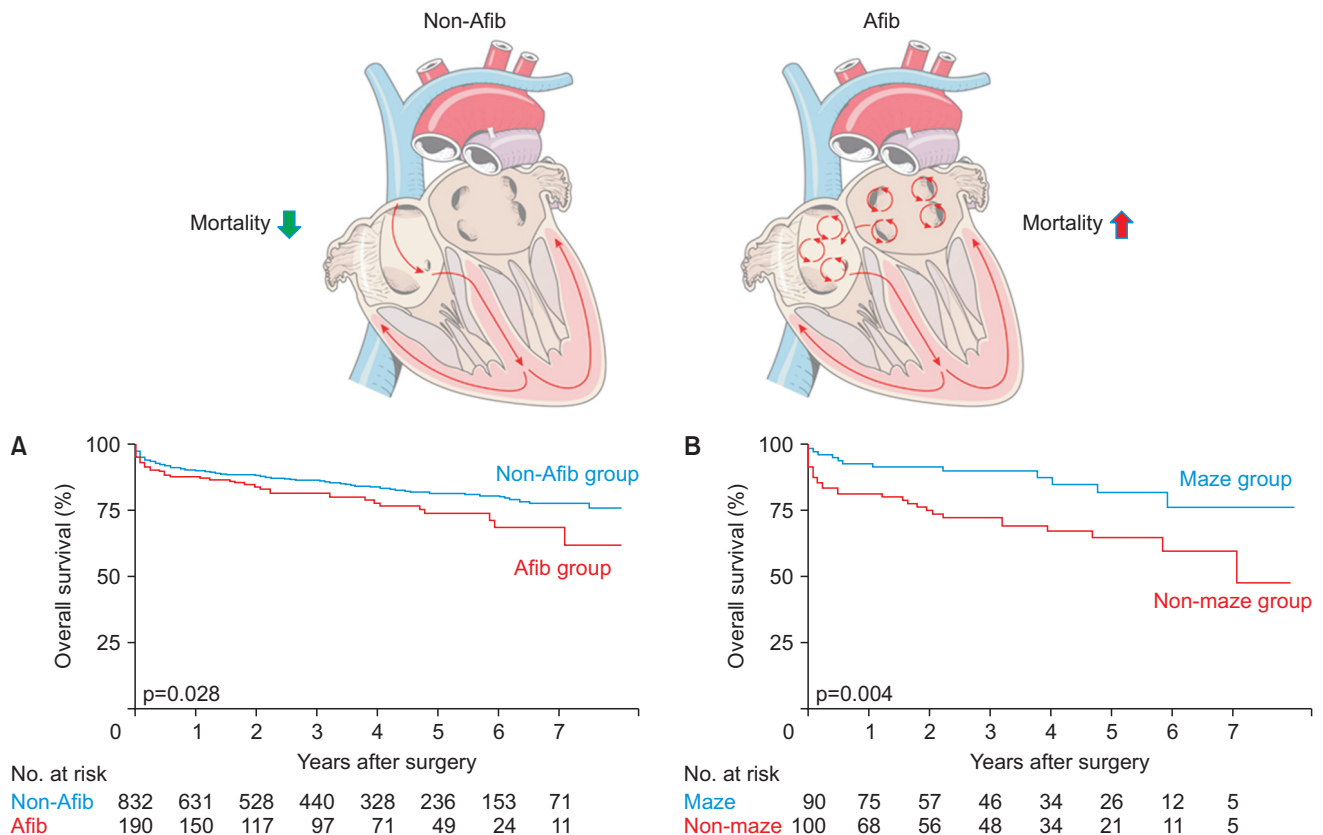


Fig. 1. (A) Kaplan-Meier curves of overall mortality in patients with and without preoperative atrial fibrillation (Afib) who underwent cardiac surgery ($p=0.028$); Cox regression, adjusted (hazard ratio [HR], 1.435; 95% confidence interval [CI], 1.263–2.107; $p=0.034$). (B) Kaplan-Meier curves of overall survival after concomitant Cox-maze surgery versus non-Cox-maze surgery in preoperative Afib patients ($p=0.004$); Cox regression, adjusted (HR, 0.500; 95% CI, 0.266–0.938; $p=0.031$).

Table 2. Cox regression with the predictors of overall survival (n=1,022)

| Variable | Univariable analysis | | Multivariable model | |
|---------------------|----------------------|---------|---------------------|---------|
| | HR (95% CI) | p-value | HR (95% CI) | p-value |
| CABG | 1.86 (1.009–3.432) | 0.047 | 1.010 (0.657–1.552) | 0.964 |
| Valve surgery | 1.017 (0.512–2.018) | 0.962 | 1.112 (0.746–1.656) | 0.602 |
| Aorta surgery | 2.760 (1.225–6.221) | 0.014 | 1.934 (1.236–3.027) | 0.004 |
| Cox-maze surgery | 0.347 (0.178–0.677) | 0.002 | 0.500 (0.266–0.938) | 0.031 |
| Atrial fibrillation | 1.466 (1.038–2.071) | 0.030 | 1.435 (1.263–2.107) | 0.034 |
| Age | 1.063 (1.047–1.080) | <0.001 | 1.048 (1.032–1.065) | <0.001 |
| Sex | 0.985 (0.727–1.334) | 0.921 | | |
| Diabetes mellitus | 2.396 (1.692–3.395) | <0.001 | 1.485 (1.024–2.155) | 0.037 |
| Hypertension | 1.634 (1.188–2.247) | 0.003 | 1.015 (0.727–1.416) | 0.931 |
| COPD | 2.390 (1.712–3.337) | <0.001 | 1.494 (1.048–2.130) | 0.026 |
| CAOD | 0.965 (0.715–1.301) | 0.814 | | |
| PAOD | 2.100 (1.504–2.932) | <0.001 | 1.473 (1.040–2.087) | 0.029 |
| Renal failure | 3.607 (2.481–5.243) | <0.001 | 2.424 (1.633–3.599) | <0.001 |
| Hyperlipidemia | 1.033 (0.756–1.411) | 0.840 | | |
| Heart failure | 1.927 (1.422–2.612) | <0.001 | 1.442 (1.034–2.012) | 0.031 |

HR, hazard ratio; CI, confidence interval; CABG, coronary artery bypass graft; COPD, chronic obstruction pulmonary disease; CAOD, coronary artery obstructive disease; PAOD, peripheral arterial occlusive disease.

Table 3. Subgroup analysis for overall mortality in patients with preoperative atrial fibrillation (n=190)

| Variable | Univariable analysis | | Multivariable model | |
|------------------------|----------------------|---------|---------------------|---------|
| | HR (95% CI) | p-value | HR (95% CI) | p-value |
| Cox-maze surgery | 0.386 (0.198–0.753) | 0.005 | 0.540 (0.272–0.753) | 0.032 |
| Age | 1.062 (1.025–1.100) | 0.001 | 1.045 (1.008–1.084) | 0.016 |
| Sex | 0.779 (0.428–1.418) | 0.414 | | |
| Diabetes mellitus | 2.374 (1.170–4.818) | 0.017 | 1.611 (0.772–3.362) | 0.204 |
| Hypertension | 1.739 (0.897–3.370) | 0.102 | | |
| COPD | 1.576 (0.750–3.308) | 0.230 | | |
| CAOD | 1.121 (0.610–2.060) | 0.713 | | |
| PAOD | 1.960 (1.029–3.734) | 0.041 | 1.358 (0.702–2.625) | 0.363 |
| Renal failure | 3.452 (1.753–6.796) | 0.001 | 2.446 (1.209–4.951) | 0.013 |
| Hyperlipidemia | 0.795 (0.435–1.454) | 0.457 | | |
| Heart failure | 1.823 (0.949–3.502) | 0.071 | | |
| Postoperative warfarin | 0.455 (0.105–1.981) | 0.294 | | |
| Postoperative aspirin | 0.918 (0.497–1.695) | 0.785 | | |
| Postoperative statin | 0.195 (0.026–1.458) | 0.111 | | |

HR, hazard ratio; CI, confidence interval; COPD, chronic obstruction pulmonary disease; CAOD, coronary artery obstructive disease; PAOD, peripheral arterial occlusive disease.

Univariable analysis identified the associations of predictor variables, including age, DM, COPD, PAOD, renal failure, and heart failure, with mortality (Table 2). In the multivariable model, which was adjusted for preoperative patient characteristics, overall mortality was significantly higher in the Afib group (HR, 1.435; 95% CI, 1.263–2.107; $p=0.034$). Multivariate analysis also showed significantly lower overall mortality in patients who underwent concomitant Cox-maze surgery than in those who did not (HR, 0.500; 95% CI, 0.266–0.938; $p=0.031$).

When we restricted the analysis to preoperative Afib ($n=190$), 12 mortality events (13.3%) were found in the concomitant Cox-maze surgery group, whereas 31 events (31.0%) were found in the non-Cox-maze surgery group ($p=0.004$) (Fig. 1B). Furthermore, in Cox regression, the Cox-maze procedure was significantly associated with a reduced risk of overall mortality (HR, 0.386; 95% CI, 0.198–0.753; $p=0.005$). After adjusting for preoperative characteristics (age, diabetes, PAOD, renal failure), Cox-maze surgery was significantly associated with a reduced likelihood of overall

mortality (HR, 0.540; 95% CI, 0.272–0.753; p=0.032) (Table 3).

Association between postoperative stroke and preoperative Afib

Overall, 157 stroke events were found in 1,022 patients who underwent cardiac surgery, and 32 of these patients (20.4%) were in the preoperative Afib group. Fig. 2A shows the subgroup analysis for postoperative stroke according to

preoperative Afib (p=0.690). Multivariable regression analysis revealed that preoperative Afib did not influence the occurrence of stroke (HR, 0.951; 95% CI, 0.569–1.590; p=0.849). Moreover, Cox-maze surgery did not significantly affect the incidence of postoperative stroke (HR, 1.514; 95% CI, 0.809–2.835; p=0.195) (Table 4).

In the multivariate analysis, we observed that stroke was associated with age (p=0.027), DM (p=0.006), warfarin use (p=0.043), and statin use (p=0.019) (Table 4). In the analysis of patients with preoperative Afib (n=190), 17 stroke

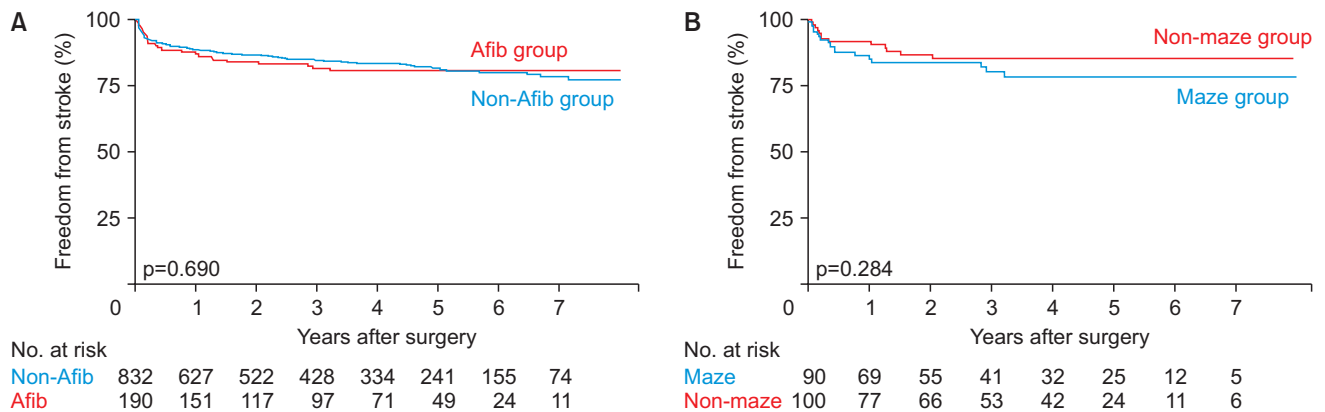


Fig. 2. (A) Kaplan-Meier curves of stroke incidence in patients with preoperative atrial fibrillation (Afib) who underwent cardiac surgery (p=0.690); Cox regression, adjusted (hazard ratio [HR], 0.951; 95% confidence interval [CI], 0.569–1.590; p=0.849). (B) In a subgroup analysis of preoperative Afib, Kaplan-Meier curves for stroke after concomitant Cox-maze surgery versus non-Cox-maze surgery (p=0.284); Cox regression, adjusted (HR, 1.885; 95% CI, 0.904–3.930; p=0.091).

Table 4. Subgroup analysis of postoperative stroke by Cox regression (n=1,022)

| Variable | Univariable analysis | | Multivariable model | |
|---------------------|----------------------|---------|---------------------|---------|
| | HR (95% CI) | p-value | HR (95% CI) | p-value |
| CABG | 1.561 (0.753–3.239) | 0.231 | 1.450 (0.914–2.299) | 0.114 |
| Valve surgery | 0.727 (0.344–1.537) | 0.405 | 1.079 (0.695–1.676) | 0.735 |
| Aorta surgery | 1.167 (0.355–3.832) | 0.799 | 1.318 (0.762–2.277) | 0.323 |
| Cox-maze surgery | 1.473 (0.727–2.983) | 0.202 | 1.514 (0.809–2.835) | 0.195 |
| Atrial fibrillation | 1.082 (0.734–1.596) | 0.690 | 0.951 (0.569–1.590) | 0.849 |
| Age | 1.025 (1.011–1.038) | 0.001 | 1.017 (1.002–1.032) | 0.027 |
| Sex | 0.931 (0.676–1.281) | 0.659 | | |
| Diabetes mellitus | 2.278 (1.586–3.272) | <0.001 | 1.715 (1.165–2.524) | 0.006 |
| Hypertension | 1.490 (1.076–2.063) | 0.016 | 1.414 (0.992–2.018) | 0.056 |
| COPD | 1.364 (0.916–2.030) | 0.127 | | |
| CAOD | 1.183 (0.864–1.619) | 0.295 | | |
| PAOD | 1.440 (0.989–2.097) | 0.057 | | |
| Renal failure | 1.356 (0.820–2.244) | 0.236 | | |
| Hyperlipidemia | 1.823 (1.264–2.628) | 0.001 | | |
| Heart failure | 0.914 (0.643–1.298) | 0.615 | 1.084 (0.708–1.661) | 0.710 |
| Warfarin | 1.288 (0.721–2.091) | 0.450 | 1.826 (1.020–3.269) | 0.043 |
| Aspirin | 1.649 (1.116–2.437) | 0.012 | 1.440 (0.949–2.186) | 0.087 |
| Statin | 2.179 (1.565–3.034) | <0.001 | 1.612 (1.083–2.401) | 0.019 |

HR, hazard ratio; CI, confidence interval; CABG, coronary artery bypass graft; COPD, chronic obstruction pulmonary disease; CAOD, coronary artery obstructive disease; PAOD, peripheral arterial occlusive disease.

events (18.9%) were found in the concomitant Cox-maze group, whereas 13 events (13.0%) were found in the non-Cox-maze surgery group ($p=0.284$) (Fig. 2B). Furthermore, multivariable Cox regression analysis showed that Cox-maze surgery itself did not significantly reduce postoperative stroke events (HR, 1.885; 95% CI, 0.904–3.930; $p=0.091$).

Association between postoperative cerebral hemorrhage and preoperative Afib

The relationship between preoperative Afib and postop-

erative non-traumatic cerebral hemorrhage is shown in Fig. 3A. According to the Kaplan-Meier analysis, the risk of occurrence of postoperative cerebral hemorrhage was not significantly different between patients with and without preoperative Afib ($p=0.863$). Table 5 shows a risk analysis, including preoperative and perioperative factors, for postoperative cerebral hemorrhage. Multivariable Cox analysis also revealed that preoperative Afib was not related to postoperative cerebral hemorrhage (HR, 0.887; 95% CI, 0.499–1.576; $p=0.685$), and Cox-maze surgery did not have any impact on the occurrence of cerebral hemorrhage (HR,

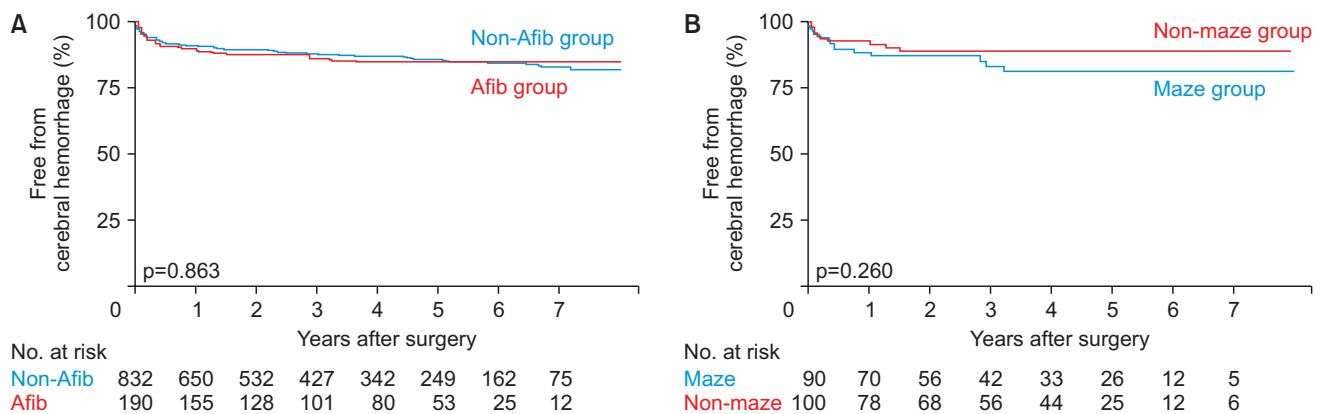


Fig. 3. (A) Kaplan-Meier curves of cerebral hemorrhage according to preoperative Afib in patients who underwent cardiac surgery ($p=0.863$); Cox regression, adjusted (hazard ratio [HR], 0.887; 95% confidence interval [CI], 0.499–1.576; $p=0.685$). (B) Kaplan-Meier curves of cerebral hemorrhage after a concomitant Cox-maze operation versus non-Cox-maze operation in preoperative Afib patients ($p=0.260$); Cox regression, adjusted (HR, 1.763; 95% CI, 0.880–3.531; $p=0.110$).

Table 5. Subgroup analysis of postoperative cerebral hemorrhage by Cox regression (n=1,022)

| Variable | Univariable analysis | | Multivariable model | |
|---------------------|----------------------|---------|---------------------|---------|
| | HR (95% CI) | p-value | HR (95% CI) | p-value |
| CABG | 1.308 (0.568–3.009) | 0.528 | 1.519 (0.914–2.524) | 0.107 |
| Valve surgery | 0.747 (0.325–1.718) | 0.493 | 0.983 (0.608–1.589) | 0.943 |
| Aorta surgery | 0.908 (0.215–3.842) | 0.896 | 1.430 (0.779–2.624) | 0.249 |
| Cox-maze surgery | 1.615 (0.733–3.561) | 0.234 | 1.763 (0.880–3.531) | 0.110 |
| Atrial fibrillation | 1.039 (0.677–1.596) | 0.861 | 0.887 (0.499–1.576) | 0.685 |
| Age | 1.029 (1.014–1.045) | 0.001 | 1.020 (1.003–1.038) | 0.018 |
| Sex | 0.903 (0.637–1.280) | 0.565 | | |
| Diabetes mellitus | 2.667 (1.766–4.027) | <0.001 | 1.940 (1.251–3.008) | 0.003 |
| Hypertension | 1.583 (1.109–2.259) | 0.011 | 1.476 (1.002–2.175) | 0.049 |
| COPD | 1.493 (0.978–2.280) | 0.063 | | |
| CAOD | 1.288 (0.914–1.817) | 0.149 | | |
| PAOD | 1.469 (0.977–2.207) | 0.064 | | |
| Renal failure | 1.318 (0.757–2.294) | 0.329 | | |
| Hyperlipidemia | 1.658 (1.122–2.451) | 0.011 | 0.843 (0.534–1.331) | 0.463 |
| Heart failure | 0.985 (0.675–1.435) | 0.936 | | |
| Warfarin | 1.204 (0.667–2.170) | 0.538 | 1.975 (1.033–3.778) | 0.040 |
| Aspirin | 1.716 (1.119–2.630) | 0.013 | 1.460 (0.926–2.301) | 0.103 |
| Statin | 2.557 (1.764–3.707) | <0.001 | 1.983 (1.266–3.105) | 0.003 |

HR, hazard ratio; CI, confidence interval; CABG, coronary artery bypass graft; COPD, chronic obstruction pulmonary disease; CAOD, coronary artery obstructive disease; PAOD, peripheral arterial occlusive disease.

1.763; 95% CI, 0.880–3.531; $p=0.110$). In a subgroup analysis of patients with preoperative Afib ($n=190$), we did not observe any relationship between Cox-maze surgery and cerebral hemorrhage ($p=0.260$) (Fig. 3B).

Discussion

In our study, preoperative Afib was common among patients undergoing cardiac surgery (18.3%) and was associated with overall mortality ($p=0.028$). The patients in the Afib group were older, had more comorbidities (COPD, PAOD, renal failure, and heart failure) than those in the non-Afib group, and showed worse overall mortality (HR, 1.435), even after adjusting for other risk factors. Cox-maze surgery significantly reduced long-term mortality in patients with preoperative Afib (HR, 0.540). Therefore, we should consider preoperative Afib as a serious risk factor for long-term outcomes in all types of cardiac surgery and concomitantly perform Cox-maze surgery in patients with Afib when they undergo cardiac surgery.

Most previous studies on patients with preoperative Afib undergoing CABG have shown associations of preoperative Afib with higher perioperative mortality (odds ratio, 1.39–2.77). A recent report found that preoperative Afib was independently associated with both worse overall mortality and marked morbidity in CABG patients [16–20]. A prospective study of CABG patients also found that patients with preoperative Afib had a higher burden of comorbidities and lower short- and long-term survival following surgery [21]. Our data support these prior studies on preoperative Afib in patients who underwent CABG. Furthermore, in a study investigating new-onset Afib in patients who underwent cardiac surgery, Afib was found to have an effect on outcomes [22–26]. These findings provide an overall understanding of the pattern of such complications. Moreover, understanding the effect of Afib on the outcomes of cardiac surgery can provide insights into potential preventative strategies to reduce the burden of these mortality and morbidity outcomes.

Thus, surgical ablation for Afib can be performed without an additional risk of operative mortality or major morbidity, and it is recommended during a concomitant mitral operation to restore the sinus rhythm. Furthermore, surgical ablation is recommended at the time of concomitant isolated aortic valve replacement (AVR), isolated CABG, and AVR with CABG to restore the sinus rhythm. It is also reasonable to perform left atrial appendage excision or exclusion in conjunction with surgical ablation for longitudinal prevention of thromboembolic morbidity [27].

The Cox-maze procedure is increasingly performed as a surgical strategy to treat preoperative Afib patients. The data supporting the use of this procedure showed a success rate of 90% with low postoperative risk. In addition, this procedure also showed significantly lower costs than medical therapy alone [28]. Our data confirm the findings from prior studies and add new information regarding the importance of Cox-maze surgery by revealing its association with a reduced risk of overall mortality in Afib patients [17].

In a previous multicenter study, Albage et al. reported a low incidence of perioperative and long-term postoperative ischemic stroke after the Cox-maze III procedure. They assessed the stroke incidence associated with the CHA₂DS₂-VASc score [29]. We did not demonstrate a meaningful correlation between Cox-maze surgery and CVA, which may indicate that the Cox-maze procedure itself did not solely influence the prevention of CVA; instead, the incidence of CVA may have been affected by postoperative anticoagulation (warfarin) or statin.

The most important finding of our study is the clinical association between preoperative Afib and overall mortality after cardiac surgery. These randomly selected NHIS patients from the database comprise representative population-based cohort data, which have strong statistical significance for estimating clinical results in the overall population. Nonetheless, we should obtain a larger sample of cardiac surgery population data to prevent missing data that may have resulted as part of the collection of a randomized sample.

There were a few limitations to our study. First, we did not include all patients undergoing cardiac surgery during the study period. Our findings represented a large sample from South Korea, but may not be generalizable to the entire Korean population or the populations of other countries. Second, the NHIS database has a paucity of information on surgeon and hospital characteristics. The NHIS collects several clinician-related variables, but does not release them to investigators. Thus, investigators generally cannot study the relationship between clinicians' characteristics and outcomes or adjust for potential confounding from these variables. Of particular note, in preoperative Afib patients, maze procedures might have been selectively performed in low-risk patients with a shorter disease duration, whereas Cox-maze surgery may have been skipped in high-risk patients. Third, the NHIS data are composed of ICD-10 codes and a basic physical examination database, so information about patients is limited. In particular, the NHIS does not capture mortality information, but only

presents insurance status, in which the loss of status (or expiration) does not always mean death. Hence, we estimated the correlations between ICD-10 codes and hard endpoints (mortality or critical morbidity such as CVA) because we could not access individual medical records. Moreover, the disease codes listed in the cohort may not represent participants' true disease status because the codes were created for the purposes of a health insurance claims database. Fourth, our data did not include information about the success of the Cox-maze surgery; therefore, the information on the postoperative rhythm status may not have been accurate. However, within these limitations, we believe our work provides important observations that will stimulate more research into preventative strategies and the aggressive use of the concomitant Cox-maze procedure when treating patients with preoperative Afib.

In conclusion, preoperative Afib is very common in patients undergoing cardiac surgery and is associated with high overall mortality regardless of the surgery type. A concomitant Cox-maze procedure at the time of cardiac surgery in patients with Afib could significantly reduce postoperative mortality. Therefore, we recommend that clinicians should consider Afib surgical treatment in all types of cardiac surgery.

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Conflict of interest

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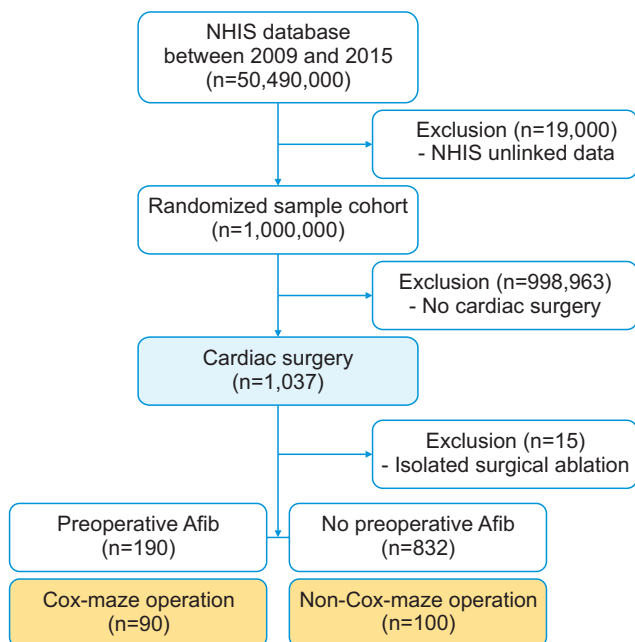
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Appendix 1. Flow diagram for patients undergoing concomitant Cox-maze surgery with preoperative atrial fibrillation (Afib) from January 2009 to December 2015. NHIS, National Health Insurance Service.