Long-term results of atrial fibrillation surgery concomitant with mitral valve surgery: A propensity score–matched multicenter study

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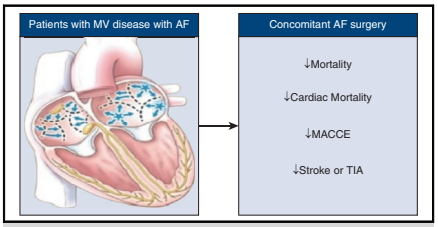
ABSTRACT

Objective: The aim of the study was to elucidate the long-term outcomes of atrial fibrillation surgery in patients with atrial fibrillation and mitral valve disease by comparing the patients who underwent mitral valve surgery with and without atrial fibrillation surgery.

Methods: Between 2005 and 2017, 2680 patients with atrial fibrillation who underwent mitral valve surgery (mitral valve surgery with atrial fibrillation surgery, n = 1841; mitral valve surgery without atrial fibrillation surgery, n = 839) at 5 centers were included. After propensity score matching, 1442 patients were extracted (atrial fibrillation surgery group, n = 721; non–atrial fibrillation surgery group, n = 721). All-cause mortality, cardiac mortality, major adverse cardiac and cerebrovascular events, stroke or transient ischemic attack, and permanent pacemaker implantation were compared between the atrial fibrillation surgery and non–atrial fibrillation surgery groups.

Results: Overall survivals at 5 and 10 years postoperatively were 91.0% and 80.7% in the atrial fibrillation surgery group and 86.5% and 75.9% in the non–atrial fibrillation surgery group, respectively ($P = .013$). Cardiac mortality-free survivals at 5 and 10 years postoperatively were 96.9% and 91.7% in the atrial fibrillation surgery group and 90.9% and 83.7% in the non–atrial fibrillation surgery group, respectively ($P < .001$). Cumulative incidence of reoperation, major adverse cardiac and cerebrovascular events, and stroke or transient ischemic attack was lower in the matched atrial fibrillation surgery group compared with the matched non–atrial fibrillation surgery group up to 15 years postoperatively ($P = .010$, $P < .001$, and $P = .012$, respectively). Cumulative incidence of permanent pacemaker implantation was higher in the matched atrial fibrillation surgery group compared with the matched non–atrial fibrillation surgery group ($P < .001$).

Conclusions: In patients with atrial fibrillation and mitral valve disease, mitral valve surgery concomitant with atrial fibrillation surgery was associated with lower mortality, cardiac mortality, major adverse cardiac and cerebrovascular events, and stroke or transient ischemic attack up to 15 years after surgery when compared with mitral valve surgery without atrial fibrillation surgery. (J Thorac Cardiovasc Surg 2024;168:821-31)



Long-term outcomes of concomitant AF surgery in patients with MV disease and AF.

CENTRAL MESSAGE

In patients with MV disease and AF, MV surgery concomitant with AF surgery significantly lowered mortality, cardiac mortality, MACCE, and stroke or TIA up to 15 years after surgery.

PERSPECTIVE

Although current guidelines recommend performing concomitant surgical AF ablation in patients undergoing MV surgery, only a few studies have enrolled a large patient cohort and had a long-term follow-up period. Concomitant AF surgery in patients with MV disease and AF is associated with better long-term clinical outcomes.

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ADULT

Abbreviations and Acronyms

ACC = aortic crossclamp
AF = atrial fibrillation
ARF = acute renal failure
CPB = cardiopulmonary bypass
HR = hazard ratio
MACCE = major adverse cardiac and cerebrovascular events
MV = mitral valve
TIA = transient ischemic attack

Atrial fibrillation (AF) is the most common form of arrhythmia, and its incidence and prevalence are increasing worldwide, with advancing age and increased survival with chronic disease of the population.[1] AF is associated with increased risk of cardioembolic stroke, systemic embolism, decompensation of heart function, and reduced survival.[2,3] More than one-third of patients with mitral valve (MV) disease have concomitant AF.[4,5] The benefits of concomitant AF surgery on clinical outcomes in patients undergoing MV surgery have been documented.[6-8] The Society of Thoracic Surgeons guidelines recommend surgical ablation for AF concomitant with MV surgery (Class I, Level A).[9] The American Association for Thoracic Surgery guidelines also recommend concomitant surgical ablation for AF because there are significant improvements in health-related quality of life and operative survival, the incidence of late stroke or transient ischemic attack (TIA) is unaffected or decreased, and long-term survival is unaffected or improved without increased perioperative morbidity.[10] However, only a few studies have enrolled a large patient cohort and examined patients over a long-term follow-up period.

The aim of the present study was to elucidate the long-term outcomes of AF surgery by comparing the patients with AF who underwent MV surgery with and without AF surgery using a propensity score–matched analysis from multicenter data.

MATERIAL AND METHODS

The study protocol was reviewed by the Institutional Review Board of each participating center and approved as a minimal-risk retrospective study (Approval Number: 4-2019-0971; approval date: November 19, 2019) that did not require individual consent based on the institutional guidelines for waiving consent.

Patient Characteristics

From January 2005 to December 2017, patients with AF who underwent MV surgery at 5 centers were included in the study. A total of 2680 patients (N = 114, 247, 622, 699, and 998 from 5 hospitals, respectively) were included in the study (MV surgery with AF surgery [AF surgery group], n = 1841; MV surgery without AF surgery [non-AF surgery group], n = 839). Patients who underwent AF surgery included patients who underwent biatrial maze (n = 1299) and left-sided maze procedures (n = 542). Energy sources used were cryoablation (n = 1813), radiofrequency ablation (n = 15), and cut-and-sew method (n = 13). Patients who needed concomitant myocardial revascularization were excluded.

A propensity score–matched analysis was performed to adjust differences in preoperative characteristics between the 2 groups, and 721 patients in each group were extracted by 1:1 matching (Figure 1). The non-AF surgery group had more female patients ($P = .002$), was older ($P < .001$), and had more frequent comorbidities such as coronary artery disease ($P < .001$), diabetes mellitus ($P = .005$), left ventricular dysfunction ($P = .012$), dyslipidemia ($P < .001$), and chronic kidney disease ($P = .023$) compared with the AF surgery group. Duration of AF was longer in the non-AF surgery group ($P = .007$). After propensity score matching, all covariates were well balanced between the 2 groups with standardized mean difference 10% or less (Table 1).

Collection of Data

Data were collected based on electronic medical records in each hospital. Patients' preoperative demographic and echocardiographic data were retrospectively collected. Information on surgical treatment, such as type of MV surgery, concomitant surgery, whether and how AF surgery was performed, cardiopulmonary bypass (CPB) time, and aortic crossclamp (ACC) time, was collected. Presence of early postoperative complications was collected, including acute renal failure (ARF), need for tracheostomy, mediastinitis, reoperation, and stroke or TIA. ARF was defined as an increase of greater than 50% of serum creatinine level from the preoperative value or a need for renal replacement therapy irrespective of serum creatinine level. Mediastinitis was defined to be present when an organism was isolated from culture of mediastinal tissue or fluid, when evidence of mediastinitis was seen during operation, or when chest pain, sternal instability, or fever, and purulent drainage from the mediastinum or isolation of an organism were present in a blood culture or a culture of the mediastinal area. Stroke was defined as a new and sudden onset of neurologic deficits lasting more than 24 hours with no apparent nonvascular cause.

Follow-up and Evaluation of Long-Term Clinical Outcomes

Patients underwent regular postoperative follow-up examinations through the outpatient clinic, and their survival status and presence of cardiovascular events were collected by reviewing electronic medical records. Information on reoperation, occurrence of major adverse cardiac and cerebrovascular event (MACCE), stroke, permanent pacemaker implantation, and recurrence of AF was collected. The clinical follow-up examinations were closed on July 31, 2021. Median follow-up duration was 63.6 [32.8-103.3] months. Operative death was defined as death occurring within 30 days after surgery or during the same hospital stay. Cardiac death was defined as any death related to cardiac events, including sudden death during the follow-up. MACCE was a composite of all-cause mortality, myocardial infarction, TIA or stroke, and heart failure requiring hospital admission.

Statistical Analysis

Statistical analysis was performed with R software, version 4.1.2. Continuous data were expressed as the mean ± standard deviation for normally distributed variables or as medians [interquartile ranges] for non-normally distributed variables according to the Shapiro–Wilk test, and categoric data were expressed as count (percentage). For propensity score matching, 19 variables were used, including sex, age, body surface area, body mass index, New York Heart Association class, smoking status, chronic obstructive pulmonary disease, coronary artery disease, hypertension, diabetes mellitus, history of stroke, left ventricular dysfunction (left ventricular ejection fraction <50%), dyslipidemia,

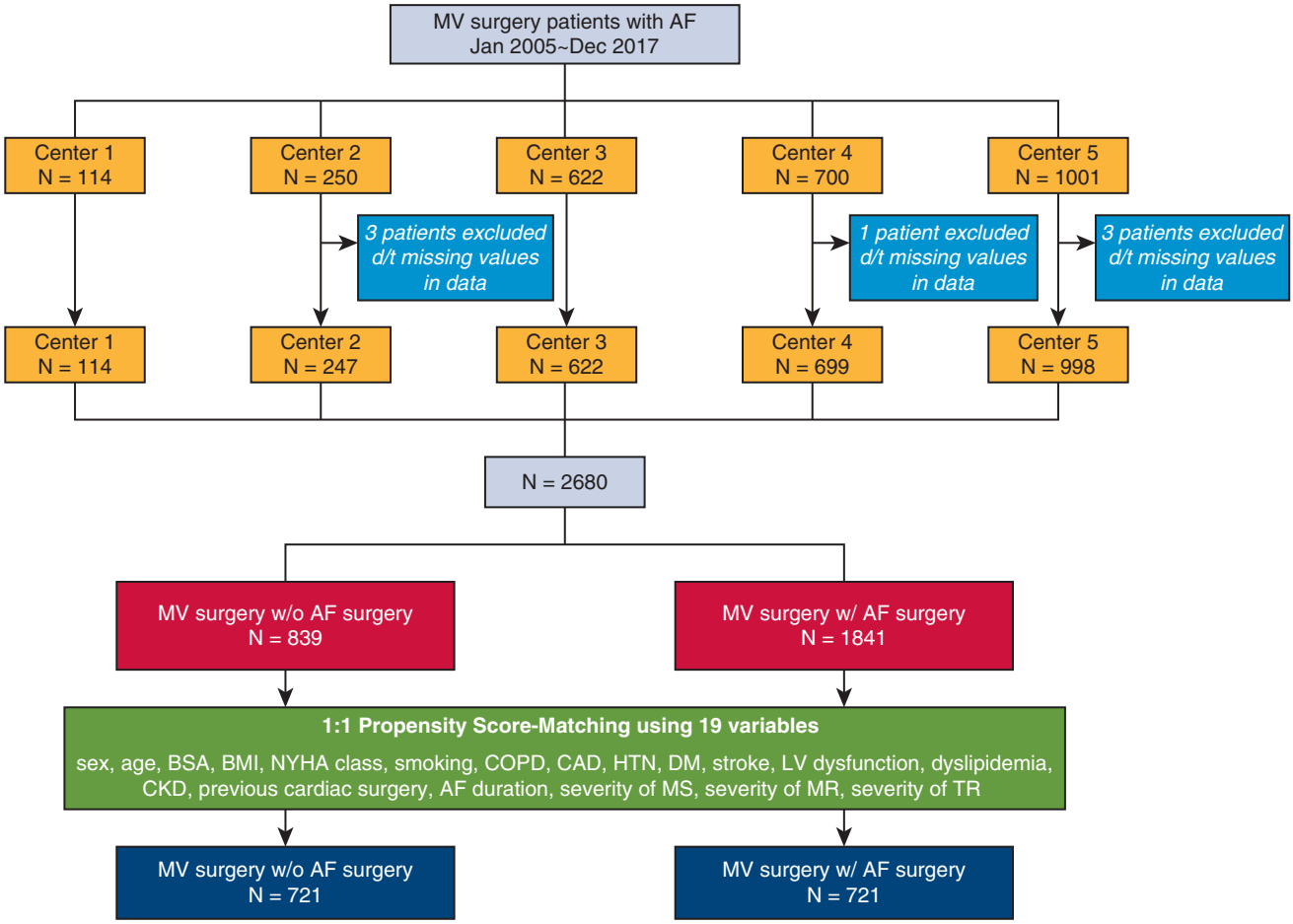

FIGURE 1. Summary flow diagram of patients. *MV*, Mitral valve; *AF*, atrial fibrillation; *BSA*, body surface area; *BMI*, body mass index; *NYHA*, New York Heart Association; *COPD*, chronic obstructive pulmonary disease; *CAD*, coronary artery disease; *HTN*, hypertension; *DM*, diabetes mellitus; *LV*, left ventricle; *CKD*, chronic kidney disease; *MS*, mitral stenosis; *MR*, mitral regurgitation; *TR*, tricuspid regurgitation.

chronic kidney disease, previous cardiac surgery, duration of AF, severity of mitral stenosis, mitral regurgitation, and tricuspid regurgitation. A propensity score–matching analysis was performed using R software (MatchIt package), and nearest neighbor matching was used to match the groups in 1:1 manner. Comparisons between continuous variables were made using Student *t* test for normally distributed data or the Wilcoxon rank-sum test for non-normally distributed data based on the Shapiro–Wilk test. Categoric variables were compared using a chi-square test. When 20% or more of expected counts were 5 or less, the Fisher exact test was used. McNemar test and paired *t* test were used for the comparison between categoric and continuous variables, respectively, in the matched groups. Overall survival and cardiac mortality-free survival were analyzed using Kaplan–Meier survival curves, and cumulative incidence of reoperation, MACCE, and permanent pacemaker implantation was analyzed using cumulative incidence function with death as a competing risk. Comparisons between the matched groups were performed using the stratified log-rank test for overall and cardiac mortality-free survival, and robust standard errors in the Fine-Gray model for cumulative incidence functions. The univariable Cox proportional hazard model was used to identify risk factors that affect the all-cause mortality, cardiac mortality, MACCE, and stroke or TIA. The multivariable Cox regression model was selected by using Akaike information criterion.

RESULTS

Operative Data and Early Clinical Outcomes

In the matched AF surgery group, the biatrial maze and left-sided maze operations were performed in 508 patients (70.5%) and 213 patients (29.5%), respectively. AF surgery was performed using cryoprobe (n = 709, 98.3%) and radiofrequency probe (n = 9, 1.2%). Left atrial appendage was resected or obliterated in 1154 of 1442 patients (matched AF surgery group vs non-AF surgery group, 568 [78.8%] vs 586 [81.3%], $P = .263$). The matched AF surgery group had longer CPB time (149.0 [123.0-186.0] minutes vs 107.0 [82.0-149.0] minutes) and ACC time (106.0 [87.0-131.0] minutes vs 71.0 [55.0-102.0] minutes) than the matched non-AF surgery group ($P < .001$ and $P < .001$, respectively). Operative mortality was lower in the matched AF surgery group than in the non-AF surgery group (1.5% vs 3.3%, $P = .040$). Postoperative incidences of ARF (2.9% vs 6.0%, $P = .007$), need for tracheostomy (1.0% vs 2.8%, $P = .020$), and stroke or TIA (1.4% vs

TABLE 1. Comparison of preoperative characteristics of the non–atrial fibrillation surgery and atrial fibrillation surgery groups before and after propensity score matching

Group	AF surgery (−) N = 838	AF surgery (+) N = 1841	*P*	AF surgery (−), matched N = 721	AF surgery (+), matched N = 721	*P*	SMD
Female	536 (64.0%)	1062 (57.7%)	.002	451 (62.6%)	437 (60.6%)	.482	3.93%
Age, y	61.8 [53.1-70.0]	58.9 [51.4-67.1]	<.001	61.6 [51.8-69.6]	60.2 [52.7-68.0]	.181	1.77%
BSA, m^2	1.6 [1.5-1.7]	1.6 [1.5-1.8]	<.001	1.6 [1.5-1.7]	1.6 [1.5-1.7]	.067	7.43%
BMI, kg/m^2	22.2 [20.3-24.4]	23.2 [21.3-25.2]	<.001	22.4 [20.4-24.6]	22.6 [20.9-24.5]	.186	4.97%
NYHA class			<.001			.393	5.33%
1	111 (13.2%)	438 (23.8%)		110 (15.3%)	125 (17.3%)		
2	351 (41.9%)	822 (44.6%)		311 (43.1%)	319 (44.2%)		
3	302 (36.0%)	456 (24.8%)		240 (33.3%)	212 (29.4%)		
4	74 (8.8%)	125 (6.8%)		60 (8.3%)	65 (9.0%)		
Smoking			<.001			.475	5.63%
Never-smoker	637 (76.0%)	1236 (67.1%)		540 (74.9%)	524 (72.7%)		
Ex-smoker	111 (13.2%)	298 (16.2%)		98 (13.6%)	99 (13.7%)		
Current smoker	90 (10.7%)	307 (16.7%)		83 (11.5%)	98 (13.6%)		
COPD	74 (8.8%)	271 (14.7%)	<.001	73 (10.1%)	72 (10.0%)	>.999	0.39%
Coronary artery disease	235 (28.0%)	186 (10.1%)	<.001	151 (20.9%)	150 (208%)	>.999	0.46%
Hypertension	274 (32.7%)	643 (34.9%)	.278	238 (33.0%)	244 (33.8%)	.780	1.75%
Diabetes mellitus	140 (16.7%)	232 (12.6%)	.005	111 (15.4%)	114 (15.8%)	.885	1.25%
History of stroke	155 (18.5%)	289 (15.7%)	.080	134 (18.6%)	134 (18.6%)	>.999	<0.01%
LV dysfunction (LVEF <50%)	378 (45.1%)	450 (24.4%)	.012	88 (12.2%)	109 (15.1%)	.125	8.06%
Dyslipidemia	378 (45.1%)	450 (24.4%)	<.001	289 (40.1%)	279 (38.7%)	.628	3.23%
Chronic kidney disease	132 (15.8%)	229 (12.4%)	.023	107 (14.8%)	106 (14.7%)	>.999	0.42%
Previous cardiac surgery	148 (17.7%)	108 (5.9%)	<.001	98 (13.6%)	90 (12.5%)	.584	4.72%
AF duration, mo	49.2 ± 75.2	41.0 ± 65.1	.007	46.5 ± 72.6	46.0 ± 72.6	.897	0.76%
Severity of MS, grade 1-5	2.1 ± 2.2	1.8 ± 2.2	<.001	3.0 ± 2.2	3.0 ± 2.2	.688	2.14%
Severity of MR, grade 1-5	2.2 ± 1.9	2.6 ± 2.2	<.001	3.3 ± 2.0	3.4 ± 2.2	.369	4.38%
Severity of TR, grade 1-5	2.2 ± 1.8	2.0 ± 2.0	.064	3.2 ± 1.8	3.1 ± 2.0	.509	3.34%

AF, Atrial fibrillation; *SMD*, standardized mean difference; *BSA*, body surface area; *BMI*, body mass index; *NYHA*, New York Heart Association; *COPD*, chronic obstructive pulmonary disease; *LV*, left ventricle; *LVEF*, left ventricular ejection fraction; *MS*, mitral stenosis; *MR*, mitral regurgitation; *TR*, tricuspid regurgitation; *EF*, ejection fraction.

4.2%, $P = .002$) were also less frequent in the matched AF surgery group than in the non-AF surgery group. The matched AF surgery group demonstrated higher sinus rhythm rates on 12-lead electrocardiogram than the matched non-AF surgery group at discharge (62.4% vs 30.5%, $P < .001$) (Table 2).

Overall Survival, Cardiac Mortality-Free Survival

Among all the matched patients, all-cause mortality occurred in 218 patients (AF surgery group, n = 94; non-AF surgery group, n = 124), including 123 cardiac mortalities (AF surgery group, n = 40; non-AF surgery group, n = 83), during the follow-up period. Overall survival was higher in the matched AF surgery group (91.0% and 80.7% at 5 and 10 years postoperatively, respectively) compared with the matched non-AF surgery group (86.5% and 75.9% at 5 and 10 years postoperatively, respectively) ($P = .013$) (Figure 2, *A*). Cardiac mortality-free survival was higher in the matched AF surgery group (96.9% and 91.7% at 5 and 10 years postoperatively, respectively) compared with the matched non-AF surgery group (90.9% and 83.7% at 5 and 10 years postoperatively, respectively) ($P < .001$) (Figure 2, *B*).

Cumulative Incidences of Reoperation, Major Adverse Cardiac and Cerebrovascular Events, Stroke or Transient Ischemic Attack, Permanent Pacemaker Implantation, and Atrial Fibrillation Recurrence

Among all the matched patients, reoperations (n = 62; AF surgery group, n = 20 and non-AF surgery group n = 42), MACCE (n = 239; AF surgery group, n = 88 and non-AF surgery group, n = 151), stroke or TIA

TABLE 2. Operative data and early clinical outcomes between the matched non–atrial fibrillation surgery and the matched atrial fibrillation surgery groups

Group	AF surgery (−), matched N = 721	AF surgery (+), matched N = 721	*P*
MV surgery			<.001
Repair	59 (8.2%)	211 (29.3%)	
Replacement	662 (91.8%)	510 (70.7%)	
Concomitant TV surgery			.004
None	296 (41.1%)	292 (40.5%)	
Repair	378 (52.4%)	408 (56.6%)	
Replacement	47 (6.5%)	21 (2.9%)	
Concomitant CABG	30 (4.2%)	11 (1.5%)	.004
CPB time (min)	107.0 [82.0-149.0]	149.0 [123.0-186.0]	<.001
ACC time (min)	71.0 [55.0-102.0]	106.0 [87.0-131.0]	<.001
Operative mortality	24 (3.3%)	11 (1.5%)	.040
Postoperative morbidities			
ARF	43 (6.0%)	21 (2.9%)	.007
Tracheostomy	20 (2.8%)	7 (1.0%)	.020
Mediastinitis	3 (0.4%)	0 (0.0%)	.248
Bleeding reoperation	43 (6.0%)	43 (6.0%)	>.999
Stroke	30 (4.2%)	10 (1.4%)	.002
Sinus conversion at discharge	220 (30.5%)	450 (62.4%)	<.001

AF, Atrial fibrillation; *MV*, mitral valve; *TV*, tricuspid valve; *CABG*, coronary artery bypass grafting; *CPB*, cardiopulmonary bypass; *ACC*, aortic crossclamp; *ARF*, acute renal failure.

(n = 87; AF surgery group, n = 31 and non-AF surgery group, n = 56), permanent pacemaker implantation (n = 69; AF surgery group, n = 51 and non-AF surgery group, n = 18), and AF recurrence (n = 593; AF surgery group, n = 250 and non-AF surgery, n = 343) occurred during the follow-up period. Cumulative incidences of reoperation (P = .010), MACCE (P < .001), stroke or TIA (P = .012), and AF recurrence (P < .001) were significantly higher in the matched non-AF surgery group compared with the matched AF surgery group up to 15 years postoperatively. Cumulative incidence of permanent pacemaker implantation was higher in the matched AF surgery group compared with the matched non-AF surgery group (P < .001) (Figure 3).

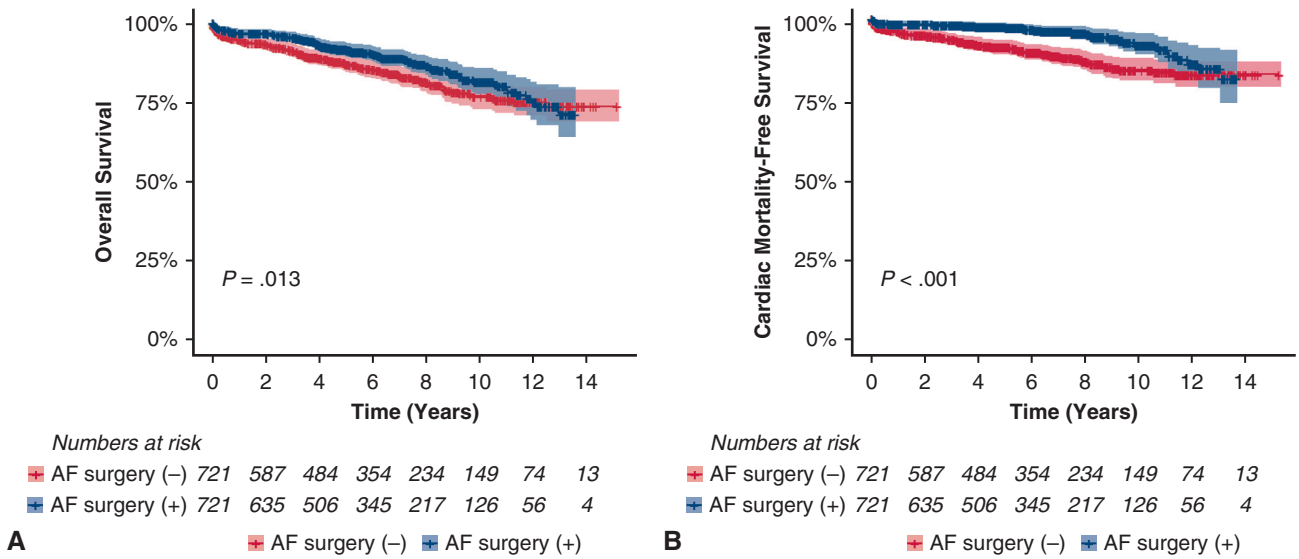

FIGURE 2. Overall survival (A) and cardiac mortality-free survival (B) between the matched AF surgery and the matched non-AF surgery groups. 95% CI is shown via shading. *AF*, Atrial fibrillation.

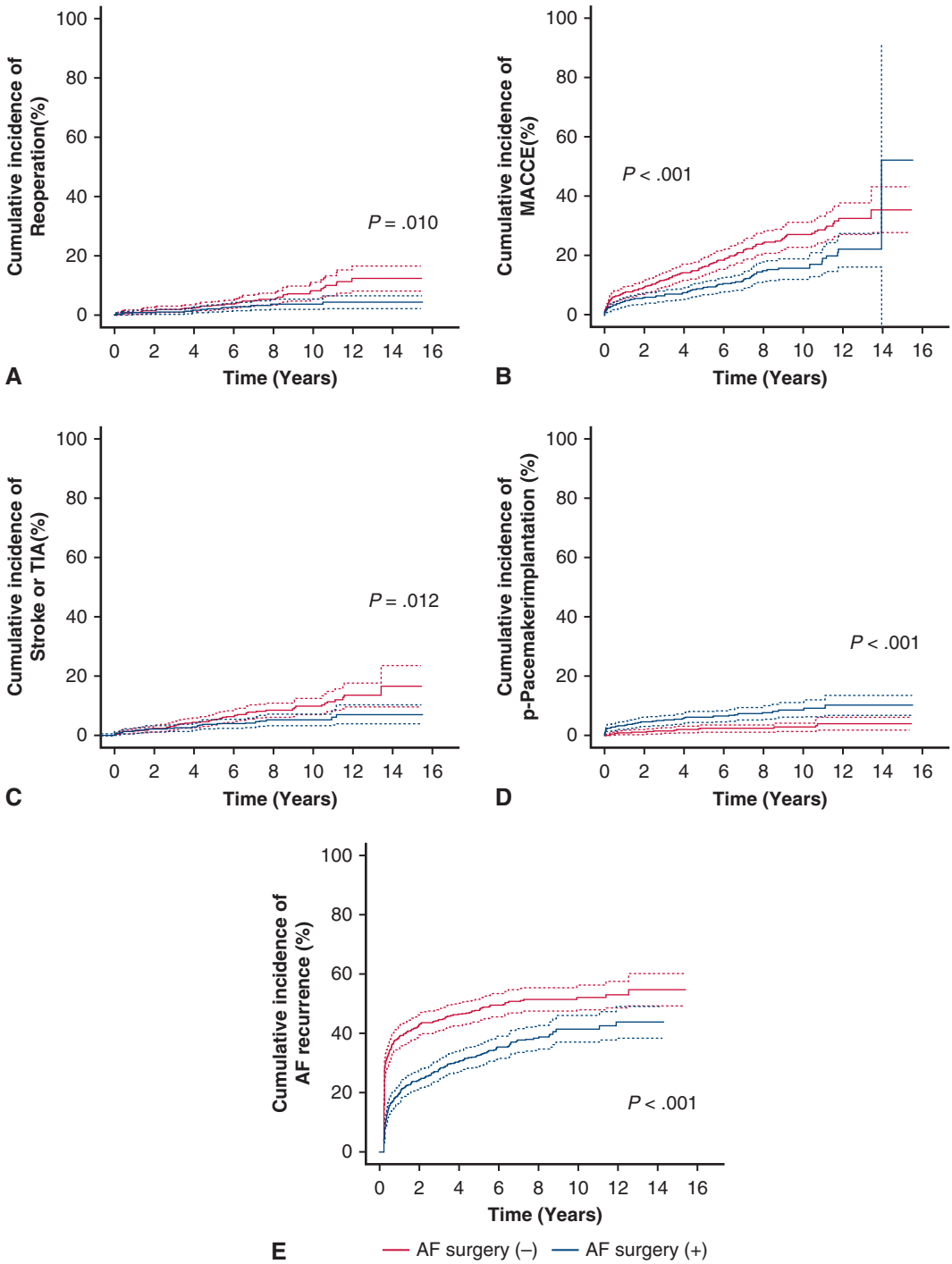

FIGURE 3. Cumulative incidence of reoperation (A), MACCE (B), stroke or TIA (C), permanent pacemaker implantation (D), and AF (E) recurrence between the matched AF surgery and the matched non-AF surgery groups. 95% CI. *AF*, Atrial fibrillation; *MACCE*, major adverse cardiac and cerebrovascular events; *TIA*, transient ischemic attack.

Predictors of All-Cause Mortality, Cardiac Mortality, Major Adverse Cardiac and Cerebrovascular Events, Stroke or Transient Ischemic Attack

AF surgery was a significant univariable predictor of all-cause mortality (hazard ratio [HR], 0.76; 95% CI, 0.58-0.99; $P = .043$), cardiac mortality (HR, 0.49; 95% CI, 0.33-0.71; $P < .001$), MACCE (HR, 0.57; 95% CI, 0.44-0.75; $P < .001$), and stroke or TIA (HR, 0.55; 95% CI, 0.36-0.86; $P = .008$). AF surgery was also analyzed as a significant predictor of MACCE (HR, 0.57; 95% CI, 0.44-0.74; $P < .001$) by the multivariable Cox regression model.

Moreover, biatrial AF surgery was analyzed to be a significant predictor of lowering all-cause mortality, cardiac mortality, and stroke or TIA by the multivariable Cox regression model. MV replacement and type of prosthetic valves were not shown to be predictors of all-cause mortality, MACCE, and stroke or TIA by the multivariable Cox regression model (Tables 3 and 4).

DISCUSSION

The present study demonstrated 3 main findings. First, AF surgery concomitant with MV surgery did not increase the risk of operative mortality and postoperative complications, whereas there was significantly greater sinus conversion rate at discharge. Second, patients who underwent MV surgery concomitant with AF surgery showed significantly lower cumulative incidence of MACCE, stroke or TIA, and AF recurrence, and significantly higher overall and cardiac mortality-free survival up to 15 years postoperatively compared with the patients who underwent MV surgery without AF surgery. Third, concomitant AF surgery was a significant predictor of lowering MACCE, and concomitant biatrial AF surgery was a significant predictor of lowering all-cause mortality, cardiac mortality, and stroke or TIA.

Since the introduction of the Maze procedure by Cox and associates,[11] several modifications have been made to improve outcomes of the procedure.[12-16] However, the basic concept was largely the same, in that the procedures

TABLE 3. Univariable and multivariable predictors of all-cause mortality and cardiac mortality

	All-cause mortality				Cardiac mortality			
	Univariable analysis		Multivariable model*		Univariable analysis		Multivariable model*	
Variables	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Male sex	1.32 (1.01-1.73)	.041			1.17 (0.81-1.67)	.404		
Age	1.09 (1.07-1.10)	<.001	1.06 (1.05-1.08)	<.001	1.07 (1.05-1.10)	<.001	1.05 (1.03-1.07)	<.001
BSA	0.42 (0.19-0.94)	.034			0.37 (0.13-1.07)	.068		
BMI	0.99 (0.94-1.03)	.586			0.97 (0.92-1.03)	.391		
NYHA	1.13 (0.96-1.32)	.137			1.11 (0.90-1.37)	.316		
Smoking	1.34 (1.13-1.58)	.001	1.39 (1.16-1.66)	<.001	1.22 (0.96-1.54)	.102	1.23 (0.97-1.58)	.087
COPD	2.20 (1.54-3.14)	<.001			1.39 (0.79-2.43)	.251		
Coronary artery disease	1.18 (0.85-1.63)	.324			1.02 (0.65-1.60)	.940		
Hypertension	1.66 (1.27-2.17)	<.001			1.31 (0.91-1.89)	.151		
Diabetes mellitus	1.71 (1.25-2.36)	.001			1.43 (0.92-2.24)	.116		
History of stroke	0.70 (0.48-1.03)	.068	0.75 (0.51-1.12)	.160	0.80 (0.49-1.30)	.372		
LV dysfunction	1.72 (1.24-2.40)	.001	1.70 (1.21-2.39)	.002	2.18 (1.44-3.29)	<.001	2.02 (1.33-3.07)	.001
Dyslipidemia	0.38 (0.27-0.53)	<.001	0.57 (0.40-0.81)	.001	0.31 (0.19-0.50)	<.001	0.49 (0.30-0.81)	.004
Chronic kidney disease	2.51 (1.86-3.39)	<.001	1.75 (1.28-2.40)	<.001	1.91 (1.25-2.94)	.003	1.41 (0.90-2.21)	.133
AF duration	1.00 (1.00-1.00)	.029			1.00 (1.00-1.00)	.032		
Severity of MS	0.83 (0.77-0.88)	<.001	0.93 (0.87-1.01)	.077	0.81 (0.74-0.89)	<.001	0.87 (0.80-0.96)	.005
Severity of MR	1.13 (1.06-1.21)	<.001			1.12 (1.03-1.22)	.010		
Severity of TR	1.27 (1.18-1.36)	<.001	1.13 (1.05-1.22)	<.001	1.39 (1.26-1.53)	<.001	1.26 (1.14-1.40)	<.001
MV replacement > MV repair	0.59 (0.43-0.79)	<.001	0.48 (0.25-0.91)	.025	1.00 (0.63-1.58)	.993		
MV replacement; Biological > mechanical	1.37 (1.08-1.74)	.010	1.38 (0.95-2.00)	.088	1.92 (1.39-2.64)	<.001	1.27 (0.96-1.67)	.094
AF surgery; (+) > (−)	0.76 (0.58-0.99)	.043			0.49 (0.33-0.71)	<.001		
AF surgery; Biatrial > left-sided	0.90 (0.82-1.00)	.042	0.88 (0.79-0.97)	.014	0.77 (0.66-0.89)	<.001	0.77 (0.66-0.89)	<.001

HR, Hazard ratio; *BSA*, body surface area; *BMI*, body mass index; *NYHA*, New York Heart Association; *COPD*, chronic obstructive pulmonary disease; *LV*, left ventricle; *AF*, atrial fibrillation; *MS*, mitral stenosis; *MR*, mitral regurgitation; *TR*, tricuspid regurgitation; *MV*, mitral valve. *The multivariable Cox regression model selected by Akaike information criterion.

TABLE 4. Univariable and multivariable predictors of major adverse cardiac and cerebrovascular events and stroke or transient ischemic attack

	MACCE				Stroke or TIA			
	Univariable analysis		Multivariable model*		Univariable analysis		Multivariable model*	
Variables	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Male sex	0.85 (0.65-1.11)	.224			0.78 (0.50-1.22)	.281	0.61 (0.37-1.00)	.051
Age	1.03 (1.02-1.05)	<.001	1.02 (1.01-1.03)	.006	1.01 (0.99-1.03)	.354		
BSA	0.37 (0.17-0.79)	.011	0.30 (0.10-0.85)	.023	0.61 (0.17-2.12)	.434		
BMI	1.00 (0.96-1.04)	.938	1.04 (0.99-1.10)	.151	0.99 (0.92-1.06)	.811		
NYHA	1.08 (0.93-1.26)	.310			1.15 (0.89-1.47)	.281		
Smoking	1.05 (0.87-1.26)	.607			1.18 (0.89-1.57)	.249	1.37 (1.01-1.87)	.046
COPD	1.46 (0.98-2.17)	.602			0.80 (0.35-1.84)	.604		
Coronary artery disease	1.28 (0.94-1.74)	.115	1.30 (0.94-1.80)	.108	2.17 (1.38-3.42)	.001	2.30 (1.46-3.61)	<.001
Hypertension	1.16 (0.89-1.52)	.282			0.86 (0.53-1.37)	.515		
Diabetes mellitus	1.44 (1.04-1.98)	.027			1.34 (0.78-2.31)	.288		
History of stroke	0.93 (0.67-1.30)	.661			1.22 (0.74-2.04)	.434		
LV dysfunction	1.40 (1.00-1.96)	.050	1.47 (1.05-2.07)	.026	0.88 (0.46-1.70)	.704		
Dyslipidemia	0.75 (0.57-0.98)	.033			1.33 (0.87-2.02)	.188		
Chronic kidney disease	1.74 (1.27-2.38)	.001	1.36 (0.98-1.90)	.065	1.18 (0.65-2.13)	.586		
AF duration	1.00 (1.00-1.00)	.039			1.00 (1.00-1.00)	.246		
Severity of MS	0.88 (0.83-0.94)	<.001	0.89 (0.84-0.95)	<.001	0.99 (0.90-1.09)	.861		
Severity of MR	1.03 (0.97-1.10)	.312			0.93 (0.84-1.04)	.193		
Severity of TR	1.18 (1.11-1.26)	<.001	1.13 (1.05-1.21)	<.001	1.04 (0.94-1.17)	.439		
MV replacement > MV repair	1.18 (0.83-1.68)	.345			1.68 (0.87-3.24)	.125		
MV replacement; Biological > mechanical	1.45 (1.16-1.83)	.001			1.36 (0.93-1.98)	.115		
AF surgery; (+) > (−)	0.57 (0.44-0.75)	<.001	0.57 (0.44-0.74)	<.001	0.55 (0.36-0.86)	.008		
AF surgery; Biatrial > left-sided	0.83 (0.75-0.92)	<.001			0.80 (0.67-0.95)	.009	0.79 (0.67-0.93)	.006

MACCE, Major adverse cardiac and cerebrovascular events; *TIA*, transient ischemic attack; *HR*, hazard ratio; *BSA*, body surface area; *BMI*, body mass index; *NYHA*, New York Heart Association; *COPD*, chronic obstructive pulmonary disease; *LV*, left ventricle; *AF*, atrial fibrillation; *MS*, mitral stenosis; *MR*, mitral regurgitation; *TR*, tricuspid regurgitation; *MV*, mitral valve. *The multivariable Cox regression model selected by Akaike information criterion.

tried to interrupt all the reentrant circuits to restore normal sinus rhythm. The efficacy and safety of the Maze procedure have been well documented, and concomitant AF surgery in patients with AF undergoing valve surgeries is recommended by the recent American and European guidelines as class IIaA and IIaB classifications, respectively.[17,18] The current guidelines by the Society of Thoracic Surgeons have upgraded the surgical ablation for AF concomitant with MV surgery to class IA classification.[9] Despite the well-established results demonstrating patient benefits, however, performance of AF surgery concomitant with MV surgery has been variable among centers and surgeons. Hesitation of the concomitant AF surgery might be related to the concerns of prolonged CPB and ACC times, as well as failure of the AF surgery. The present study demonstrated that performing concomitant AF surgery prolonged the CPB and ACC times without increasing operative mortality and postoperative morbidities such as ARF, need for tracheostomy, and stroke, whereas the patients who underwent concomitant AF surgery showed higher sinus rhythm at discharge than patients without AF surgery.

However, lower rates of mortality, ARF, and need for tracheostomy in the matched AF surgery group are not easily explained. Successful AF surgery resulting in atrioventricular synchrony might have assisted cardiac function positively and lowered the postoperative morbidities. However, the conclusion should be drawn cautiously and the results of the current study should be interpreted as concomitant AF surgery not having increased rather than decreasing operative mortality and early postoperative morbidity rates. In another study analyzing 569 patients who underwent mechanical valve replacement with or without the Maze procedure, no significant differences have been documented in terms of early mortality, early postoperative morbidities such as stroke, low cardiac output

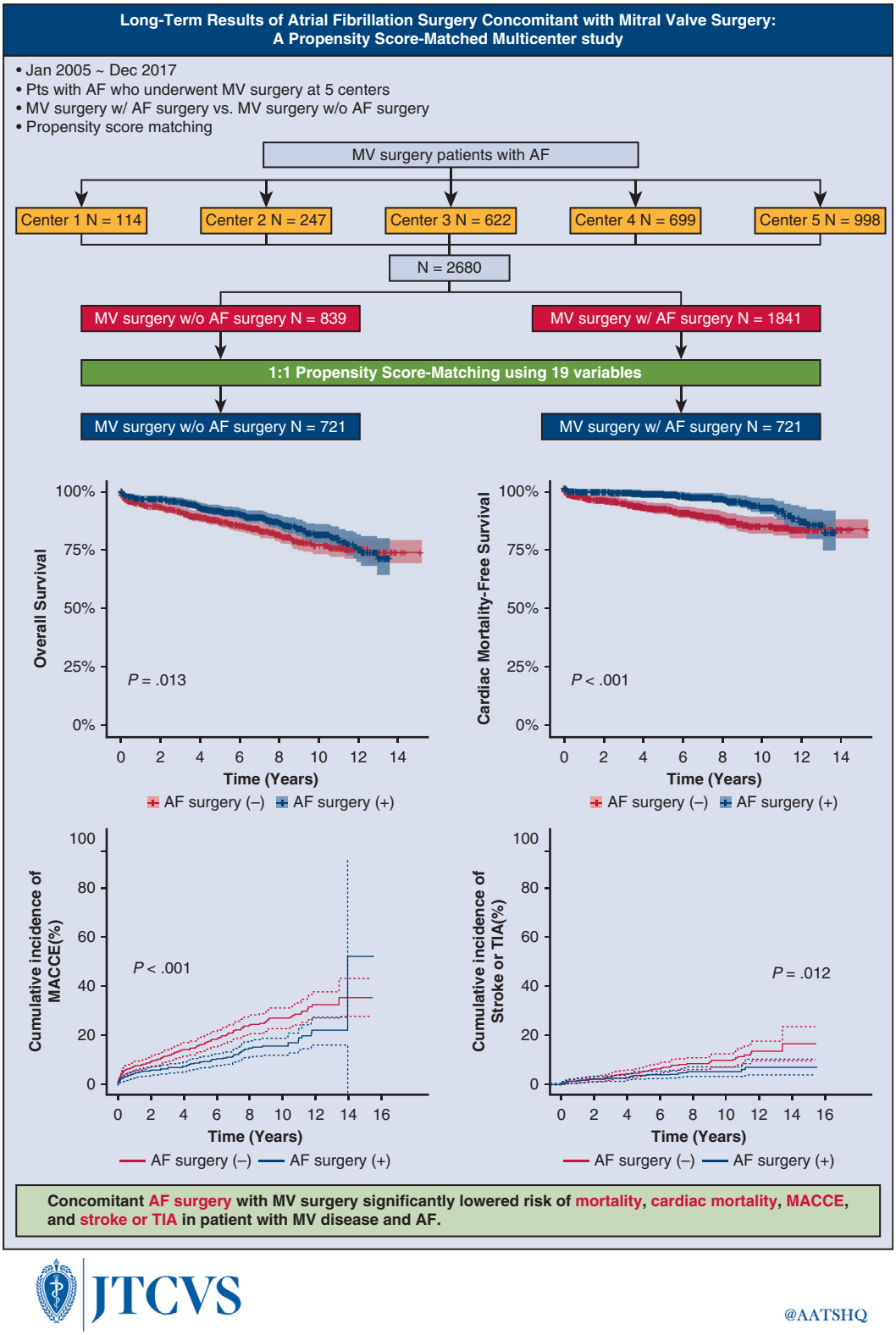

FIGURE 4. Graphical abstract. In patients with AF with MV disease, MV surgery concomitant with AF surgery significantly lowered mortality, cardiac mortality, MACCE, and stroke or TIA up to 15 years after surgery when compared with MV surgery without AF surgery. *AF*, Atrial fibrillation; *MV*, mitral valve; *MACCE*, Major adverse cardiac and cerebrovascular events; *TIA*, transient ischemic attack.

syndrome, requirement of new dialysis, pericardial effusion, and mediastinitis.[19]

Successful AF surgery concomitant with MV surgery is known to be associated with superior survival and greater freedom from stroke and cardiac events,[20] which are similar to the findings in the present study. The low stroke rate during the early postoperative period also could be expected in the AF surgery group because the left atrial appendage was resected or obliterated during the Maze procedure. One previous study analyzing 2140 patients enrolled in the international registry for AF surgery demonstrated that the achievement of stable sinus rhythm after AF surgery and concomitant MV surgery was a predictor of lower thromboembolic events and better survival at 48 months' follow-up.[21] The present study also demonstrated lower cumulative incidences of stroke or TIA and higher overall and cardiac mortality-free survival up to 15 years postoperatively in the matched AF surgery group than in the matched non-AF surgery group. The beneficial results in the AF surgery group could be explained by the lower incidence of AF recurrence compared with the non-AF surgery group. However, the higher survival curve in the AF surgery group showed a waning effect 10 years after surgery. One long-term follow-up study after AF surgery concomitant with MV surgery showed that the rate of freedom from AF was shown to decrease to 93% at 1 year, 82% at 3 years, 71% at 5 years, and 63% at 7 years.[22] Another midterm follow-up study after AF surgery and concomitant MV surgery demonstrated that the attrition rate for losing stable sinus rhythm was 3% per year.[21] The decreased long-term effect of the AF surgery might cause patients' survival to wane (Figure 2), although further study is warranted.

In a prospective, randomized study including 260 patients, Gillinov and colleagues[23] showed that the addition of AF ablation to MV surgery significantly increased the rate of freedom from AF, but also increased the risk of permanent pacemaker implantation. This finding was similar to the present study showing higher cumulative incidence of permanent pacemaker implantation up to 15 years postoperatively in the matched AF surgery group compared with the matched non-AF surgery group. The incidence of sick sinus syndrome and requirement of pacemaker implantation are known to be related to the Maze procedure in patients undergoing MV surgery, and the lesion extent is analyzed to be independently associated with the development of sick sinus syndrome.[24] Although the risk of permanent pacemaker implantation after AF surgery is a troublesome morbidity, the superiority of AF surgery in such morbidities as MACCE and stroke should be considered when performing AF surgery. The lower cumulative incidence of reoperations shown in the present study is not easily explained, and further study is warranted.

Although Gillinov and associates[23] showed a low AF recurrence in patients who underwent AF ablation and MV surgery, they failed to demonstrate survival benefits in patients who underwent ablation probably because of the short follow-up period of 1 year. However, another propensity score–matched study that included 3568 patients who underwent MV surgery with or without surgical ablation[25] showed improved survival in patients with concomitant surgical ablation. The present matched study also showed higher overall survival and cardiac mortality-free survival up to 15 years of follow-up in the matched AF surgery group than in the non-AF surgery group.

Study Limitations

The present study has several limitations that must be recognized. First, this study was a retrospective analysis, although it was a multicenter study with propensity score–matched analysis. The decision for performing concomitant AF surgery might be influenced by the center's or surgeon's preferences, which could be a source of a bias. Second, surgical factors such as surgeon factor, lesion sets, and energy sources used in the AF surgery were heterogenous among centers. Third, postoperative management strategies such as anticoagulation, antiarrhythmic, and beta-blocker medications were different among centers and not included in the analysis. Fourth, postoperative Holter monitoring was not performed in all patients for determination of the rhythm status. A longer period of Holter monitoring, such as 48 or 72 hours, has been performed recently. Fifth, there are limitations in interpreting the study results such as lower rates of mortality, ARF, need for tracheostomy, and cumulative incidence of reoperations in the matched AF surgery group, which requires further study.

CONCLUSIONS

AF surgery was not associated with increased operative mortality and postoperative morbidities when performed with MV surgery. The patients who underwent MV surgery concomitant with AF surgery was associated with a significantly lower cumulative incidence of MACCE, stroke or TIA, and AF recurrence, and significantly higher overall and cardiac mortality-free survival up to 15 years postoperatively when compared with the patients who underwent MV surgery without AF surgery (Figure 4). Concomitant AF surgery should be performed positively in patients with surgical MV disease and AF.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict

of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: atrial fibrillation, atrial fibrillation surgery, mitral valve

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