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ORIGINAL RESEARCH

Long-Term Outcomes of Surgical Ablation for Atrial Fibrillation

Impact of Ablation Lesion Sets

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ABSTRACT

BACKGROUND The lesion sets for surgical ablation of atrial fibrillation (AF) that provide optimal outcomes have remained controversial.

OBJECTIVES We evaluated the effects of left-atrial (LA) ablation of AF compared with bi-atrial (BA) ablation on the clinical and rhythm outcomes, and examined the predictors for AF recurrence and permanent pacing in consideration of ablation lesion sets.

METHODS Between 2001 and 2018, 1,965 patients underwent surgical ablation during cardiac surgery at our institution. Among these, 796 and 1,169 patients underwent LA and BA ablation, respectively. The clinical outcomes were evaluated after propensity score adjustment, with death accounting for a competing event. The probability of AF recurrence was estimated with the generalized estimating equations model.

RESULTS The patients with BA ablation had morbidities greater than those with LA ablation. The probability of AF recurrence at 1 and 5 years was 13.9% and 37.1% in patients with LA ablation, and 11.2% and 30.1% in those with BA ablation (hazard ratio [HR]: 1.24; 95% confidence interval [CI]: 0.96-1.61; $P = 0.100$). After adjustment, LA ablation was associated with a decreased risk of early death (<30 days) (odds ratio [OR]: 0.56; 95% CI: 0.31-0.96; $P = 0.041$) and new-onset dialysis (OR 0.47; 95% CI: 0.27-0.78; $P = 0.003$). However, the risk of overall mortality (HR: 1.03; 95% CI: 0.75-1.41; $P = 0.878$) and permanent pacing (HR: 0.68; 95% CI: 0.43-1.06; $P = 0.091$) was comparable between the 2 groups.

CONCLUSIONS The risk of AF recurrence and adverse events was comparable between the 2 ablation lesion sets. BA ablation was not related to an increased risk of permanent pacing. (JACC: Asia 2021;1:203–214) © 2021 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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ABBREVIATIONS AND ACRONYMS

AAD = anti-arrhythmic drug

AF = atrial fibrillation

BA = bi-atrial

LA = left atrial

PPM = permanent pacemaker

SA = surgical ablation

TR = tricuspid regurgitation

TV = tricuspid valve

Surgical ablation (SA) has been established as an effective therapeutic option to restore sinus rhythm in patients with atrial fibrillation (AF) during concomitant cardiac surgery, and the current guidelines from the cardiac surgical societies recommend SA for selected patients with preoperative AF undergoing cardiac surgery as a class I indication (1,2).

However, controversies still remain with respect to achieving optimal clinical and rhythm outcomes after SA. Bi-atrial (BA) Cox-maze procedure has been regarded as a gold standard for surgically treating AF, but several recent studies have demonstrated that left-atrial (LA) ablation may have similar efficacy compared with BA ablation in restoring AF to sinus rhythm (3-5). Furthermore, some observational studies have suggested that BA ablation may be associated with an increased risk of procedural complications, such as permanent pacing (6-8). Thus, the ablation lesion sets that provide optimal benefits to the patients and the predictors for ablation failure remain to be further clarified.

SA has been dedicatedly performed during cardiac surgery for the past 2 decades at our institution, and a large SA database was constructed (9). Using this database, we evaluated the effects of ablation lesion sets on the clinical and rhythm outcomes during cardiac surgery, and examined the risk factors that affected postablation permanent pacing and AF recurrence in consideration of the ablation lesion sets.

METHODS

STUDY COHORT. We reviewed the institutional cardiac surgery database of Asan Medical Center (Seoul, Korea) and retrieved the consecutive adult patients (age ≥18 years) with preoperative AF who underwent SA using radiofrequency or cryothermic energy during concomitant cardiac surgery from January 2001 to September 2018. Excluded were those who: 1) had a prior history of surgical/catheter ablation and active infective endocarditis at the time of surgery; 2) underwent SA using a microwave energy source; or 3) received an incomplete LA lesion set or right-atrial ablation only.

The decision to perform LA or BA ablation was left to the operating surgeons' discretion in consideration of the patient's clinical and surgical profiles and based on the best available evidence from our data or other studies (10,11). This study was approved by the Institutional Review Board of Asan Medical Center (study number: 2017-0172), which waived the requirement for informed consent due to the retrospective nature of the study design.

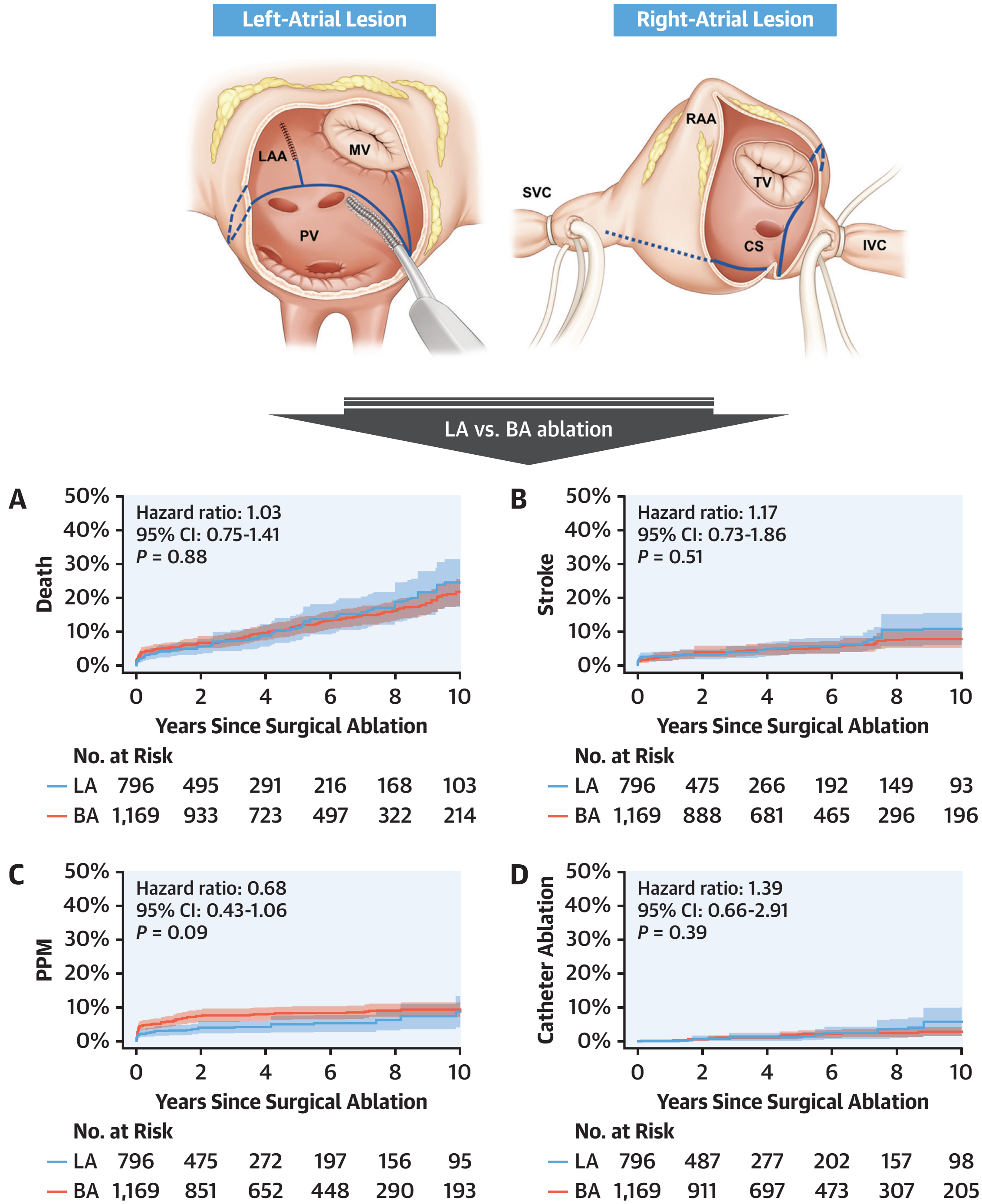
SURGICAL PROCEDURES. LA ablation was usually performed after the left atriotomy in the interatrial groove to approach the inside of the LA. The lesion sets for the LA included: 1) a box lesion encircling the pulmonary veins; 2) a mitral line from the box lesion to the mitral annulus; 3) a line from the box lesion to the LA appendage; and 4) an epicardial coronary sinus lesion. Right-atrial ablation lesion included cavotricuspid isthmus lesion and a line from the cavotricuspid isthmus lesion to the superior vena cava (Central Illustration, upper image). Argon-based cryoablation was most commonly used, whereas bipolar epicardial radiofrequency ablation was performed for a limited number of patients (n = 54).

The size of the LA was usually reduced for the patients with a LA diameter ≥5 cm to prevent the macro-reentry circuit by resecting the enlarged atrial free wall between the right inferior pulmonary vein and the posterior mitral valve annulus. The LA appendage was treated by external resection (n = 360), endocardial obliteration using running sutures (n = 74), or an occlusion clip (n = 50). Concomitant cardiac surgery was performed using a median sternotomy or minimally invasive approach (n = 639) depending on the surgeon's preference and the procedural type.

POSTOPERATIVE MANAGEMENT. Monitoring for AF recurrence was mainly performed at the outpatient clinic visit postoperatively. At the end of a 3-months blanking period, the restoration of sinus rhythm was usually assessed by 24-hour Holter monitoring or electrocardiography (ECG). Thereafter, rhythm status of the patients was screened every 6 months for 2 years after surgery, and then annually after 2 years from surgery. Patients who demonstrated any episodes of AF, atrial flutter, or atrial tachycardia ≥30 seconds were regarded to have AF recurrence (12), and usually treated with electrical cardioversion or class I or III anti-arrhythmic drugs (AADs).

Patients who underwent mechanical valve replacement were anticoagulated with warfarin to maintain a target international normalized ratio of 2.0 to 3.0, whereas patients who received annuloplasty rings or bioprosthetic valve were routinely maintained with warfarin for 3 to 6 months. The decision to continue with anticoagulation thereafter was determined by the individual patient's estimated thromboembolic risk and the restoration of sinus rhythm encompassing effective atrial contraction. Permanent pacemaker (PPM) was mainly indicated for patients who developed sinus node dysfunction or

CENTRAL ILLUSTRATION **Comparison of Clinical Outcomes Between Left-Atrial and Bi-Atrial Ablation in the Inverse-Probability-of-Treatment Weighting-Adjusted Population**



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(Upper image) Lesion set diagram of the left-atrial **(left)** and right-atrial **(right)** ablation **(blue lines)**. **(Lower image)** Adjusted time-to-event curves for death **(A)**, stroke **(B)**, permanent pacemaker (PPM) implantation **(C)**, and catheter ablation **(D)** according to the ablation lesion sets. CS = coronary sinus; IPTW = inverse-probability-of-treatment weighting; IVC = inferior vena cava; LAA = left-atrial appendage; MV = mitral valve; PV = pulmonary vein; RAA = right-atrial appendage; SVC = superior vena cava; TV = tricuspid valve.

high-degree atrioventricular block; all patients who showed persistent symptomatic bradyarrhythmia postoperatively were referred to cardiac electrophysiologists and were evaluated for the feasibility of PPM implantation.

OUTCOMES OF INTEREST AND CLINICAL FOLLOW-UP. The primary outcomes of interest were the probability of AF recurrence after a 3-months blanking period; early recurrence was defined as that occurring within the blanking period (12). The secondary outcomes of interest were all-cause mortality and adverse events (PPM implantation, stroke, and catheter ablation). Stroke was defined as the occurrence of neurologic deficits, which was validated on imaging studies; all patients who showed newly developed neurologic deficits were examined by a neurologist and subsequently evaluated by brain imaging studies (13). For further assessment, early postoperative complications (those occurring within 30 days of surgery) and serial postoperative echocardiographic parameters were evaluated.

Follow-up data were obtained until May 31, 2019. Patients without AF and clinical events were censored at the end of the follow-up. Vital status was obtained from the National Population Registry of the Korea National Statistical Office, and all-cause mortality was followed up in 100% of the study cohort. For other time-related events, the completeness of follow-up was 80.7% in the patients with LA ablation (3,343 patient-years), and 82.2% in those with BA ablation (6,771 patient-years).

STATISTICAL ANALYSIS. Categorical variables, summarized as number (%), were compared with chi-square test or Fisher's exact test. Continuous variables, summarized as the mean ± SD or median (interquartile range [IQR]), were compared using Student's *t*-test for data with normal distribution and Mann-Whitney *U* test for skewed data based on the normality test.

For the analysis of time-related events, a cumulative incidence function was generated using a competing risk model with all-cause death as a competing variable (14). Subdistribution hazard ratio (HR) was estimated by the Fine-Gray method. For the assessment of rhythm outcomes, a longitudinal logit model of the binary sequence of AF that was assessed at each time point (3, 6, 12, 36, and 60 months) was used to estimate the probability of AF recurrence. For patients who had catheter ablation postoperatively, only rhythm data before catheter ablation were included in the analysis. The repeated measures for AF recurrence was modeled with correlations using the generalized estimating equations method. The multivariable analysis included candidate variables listed in Table 1 and the use of AADs as a time-varying covariate. For serial echocardiographic parameters, we used a random coefficient model over time according to the ablation lesion sets with the fixed effects of time, group (LA vs BA ablation), and the interactions between time and group, and the random effects of patient (intercepts) and the interactions between patient and time (slopes).

The clinical and echocardiographic outcomes between the patients with LA and BA ablation were compared with a propensity score (PS)-weighting (inverse-probability-of-treatment weighting). The PS was defined as the probability of a patient undergoing LA ablation in either of 2 groups (conditional on baseline and operative profiles) and was estimated from the logistic regression analysis incorporating all the covariates in Table 1. The balance for all covariates in Table 1 was assessed using the standardized mean difference (SMD), for which a difference of <10% was deemed to indicate good balance. All reported *P* values were 2-tailed, and $P < 0.05$ was considered statistically significant. R software, version 3.4.0 (R Foundation for Statistical Computing) and SAS software version 9.4 (SAS Institute) were used for statistical analyses.

RESULTS

PATIENT CHARACTERISTICS. Among a total of 2,236 patients who underwent SA with concomitant cardiac surgery during a study period, we excluded patients (n = 271) who met the exclusion criteria, and 1,965 patients were enrolled. LA ablation was performed in 796 patients, whereas BA ablation was performed in 1,169 patients (Figure 1).

Table 1 (left column) summarizes the baseline characteristics of all patients. Persistent AF (92.0% vs 83.0%; $P < 0.001$) and chronic kidney disease (19.6% vs 15.5%; $P = 0.022$) were more prevalent in the patients with BA ablation, who also had a longer AF duration (<0.001) than those with LA ablation. For echocardiographic profiles, the patients with BA ablation had a larger left atrium (57.3 ± 10.2 mm vs 54.5 ± 9.0 mm; $P < 0.001$) and a higher peak tricuspid regurgitation (TR) velocity (37.5 ± 13.7 mm vs 35.3 ± 13.8 mm; $P < 0.001$). Significant TR (≥ moderate) was also more prevalent in the patients with BA ablation (57.1% vs 26.5%; $P < 0.001$); LA size reduction and tricuspid valve (TV) surgery were more frequently performed in these patients accordingly. Further operative profiles are presented in Supplemental Table 1.

TABLE 1 Baseline Characteristics Between Left Atrial and Bi-Atrial Groups

	Original				IPTW-adjusted			
	Left Atrial (n = 796)	Bi-Atrial (n = 1,169)	P value	SMD, %	Left Atrial (n = 796)	Bi-Atrial (n = 1,169)	P value	SMD, %
Age, y	58.5 ± 12.1	58.8 ± 11.3	0.595	2.4	58.6 ± 12.2	58.6 ± 11.2	0.936	0.5
Female	387 (48.6)	685 (58.6)	<0.001	20.1	53.7	55.0	0.644	2.6
BMI, kg/m^2	23.7 ± 3.4	23.4 ± 3.2	0.045	9.2	23.5 ± 3.5	23.4 ± 3.2	0.798	1.4
AF type			<0.001	27.2			0.872	0.9
Paroxysmal	135 (17.0)	94 (8.0)			11.4	11.2		
Persistent	661 (83.0)	1075 (92.0)			88.6	88.8		
AF duration, y	1.5 [0.2-7]	0.7 [0.2-4]	<0.001	42.6	0.6 [0.1-4.6]	2.2 [0.3-6.9]	0.139	8.3
Hypertension	296 (37.2)	404 (34.6)	0.252	5.5	35.6	35.6	0.998	<0.1
Diabetes mellitus	126 (15.8)	170 (14.5)	0.472	3.6	15.0	15.1	0.959	0.3
Dyslipidemia	240 (30.2)	269 (23.0)	<0.001	16.2	26.8	26.7	0.944	0.4
Congestive heart failure	66 (8.3)	113 (9.7)	0.337	4.8	9.7	9.6	0.920	0.6
CKD	123 (15.5)	229 (19.6)	0.022	10.9	17.9	19.0	0.630	2.9
Hemodialysis	12 (1.5)	14 (1.2)	0.697	2.7	1.8	1.9	0.955	0.4
Chronic lung disease	68 (8.5)	91 (7.8)	0.602	2.8	8.2	7.8	0.748	1.7
History of CVA	105 (13.2)	162 (13.9)	0.721	2.0	12.6	13.7	0.553	3.2
Coronary artery disease	104 (13.1)	129 (11.0)	0.195	6.2	11.7	12.0	0.853	1.0
Previous PCI	25 (3.1)	31 (2.7)	0.616	2.9	2.8	2.5	0.677	2.3
Hemoglobin, mg/dL	13.4 ± 1.9	13.1 ± 1.9	<0.001	18.5	13.3 ± 1.9	13.2 ± 1.9	0.439	4.4
Peripheral arterial disease	98 (12.3)	95 (8.1)	0.003	13.8	10.2	10.3	0.956	0.3
Rheumatic heart disease	400 (50.3)	630 (53.9)	0.123	7.3	53.2	53.4	0.936	0.5
NYHA functional class III or IV	164 (20.6)	236 (20.2)	0.867	1.0	18.0	19.7	0.434	4.2
Previous cardiac surgery	35 (4.4)	54 (4.6)	0.903	1.1	4.1	4.3	0.803	1.3
Echocardiographic data								
LV ejection fraction, %	56.5 ± 9.6	56.1 ± 9.4	0.338	4.4	56.1 ± 9.4	56.2 ± 9.8	0.967	0.2
LVESD, mm	36.9 ± 8.3	36.6 ± 8.3	0.363	4.2	36.4 ± 8.1	36.4 ± 8.6	0.875	0.2
LVEDD, mm	54.7 ± 8.8	53.8 ± 9.5	0.044	9.3	53.7 ± 8.8	53.8 ± 9.6	0.975	0.9
LA diameter, mm	54.5 ± 9.0	57.3 ± 10.2	<0.001	28.5	55.9 ± 9.3	56.1 ± 10.1	0.655	2.5
Peak TRPG, mm Hg	35.3 ± 13.8	37.5 ± 13.7	<0.001	16.1	36.6 ± 14.4	36.8 ± 13.4	0.794	1.5
TR ≥ moderate	211 (26.5)	667 (57.1)	<0.001	65.1	44.0	44.8	0.789	1.6
Year of surgery			<0.001	70.9			<0.001	67.5
2001-2005	39 (4.9)	155 (13.3)			10.9	9.7		
2006-2010	209 (26.3)	306 (26.2)			33.3	21.8		
2011-2015	183 (23.0)	501 (42.9)			18.0	47.4		
2016-2018	365 (45.9)	207 (17.7)			37.8	21.1		
Concomitant cardiac surgery								
MV vs Non-MV surgery			0.029	10.4			0.919	0.6
MV surgery	674 (84.7)	944 (80.8)			82.3	82.1		
Non-MV surgery	122 (15.3)	225 (19.2)			17.7	17.9		
TV surgery	257 (32.3)	834 (71.3)	<0.001	84.9	54.2	55.5	0.648	2.6
Use of mechanical valve	380 (47.7)	592 (50.6)	0.223	5.8	50.0	50.8	0.759	1.7
LA appendage treatment	338 (42.5)	550 (47.0)	0.050	9.2	42.4	45.1	0.329	5.5
LA size reduction	289 (36.3)	662 (56.6)	<0.001	41.6	42.9	46.9	0.165	8.0
MICS	297 (37.3)	342 (29.3)	<0.001	17.2	29.5	29.8	0.918	0.6
Emergency or urgency	20 (2.5)	16 (1.4)	0.092	8.3	1.8	2.1	0.733	1.8

Values are mean ± SD or n (%) unless otherwise indicated.

AF = atrial fibrillation; BMI = body mass index; CKD = chronic kidney disease; CVA = cerebrovascular accident; IPTW = inverse-probability-of-treatment weighting; LA = left atrium; LV = left ventricular; LVEDD = left ventricular end-diastolic dimension; LVESD = left ventricular end-systolic dimension; MICS = minimally invasive cardiac surgery; MV = mitral valve; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; PG = pressure gradient; SMD = standardized mean difference; TR = tricuspid regurgitation; TV = tricuspid valve.

CLINICAL AND RHYTHM OUTCOMES. The incidence of new-onset dialysis and early AF recurrence (<3 months) was significantly higher in the patients with BA ablation (Table 2). For overall adverse outcomes, the PPM-free rate was significantly higher in the patients with LA ablation (P = 0.004) during a median follow-up of 49.3 months (interquartile range [IQR]: 22.2-95.9 months), which appeared to be largely attributed to the lower incidence of sinus node dysfunction in these patients (0.6 vs 1.1%/

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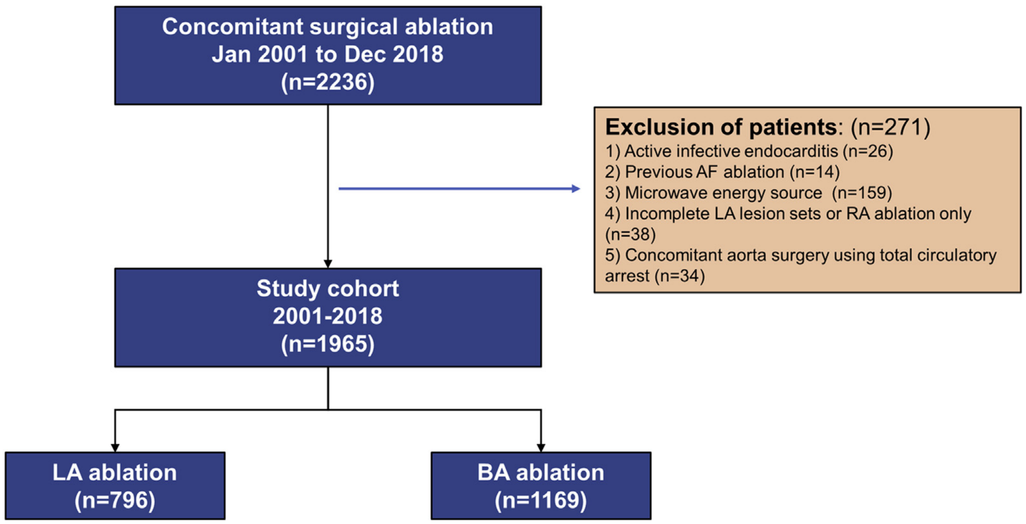
FIGURE 1 Study Flow Chart



AF = atrial fibrillation; BA = bi-atrial; LA = left atrial; RA = right atrial.

patient-year; P = 0.001). The freedom from other adverse events was comparable between the patients with LA and BA ablation.

The rate of non-AF patients without taking AADs at 12, 36, and 60 months after surgery was 79.1%, 76.1%, and 72.7%, respectively. The proportion of non-AF patients without AAD was significantly higher in the patients with LA ablation than those with BA ablation at 3, 6, 12, and 36 months postoperatively (Table 3).

TABLE 2 Early Complications and Overall Adverse Outcomes

	Left Atrial (n = 796)	Bi-Atrial (n = 1,169)	*P* Value[a]
Early complications, n (%)			
Early death	19 (2.4)	44 (3.8)	0.092
LCOS requiring MCS	18 (2.3)	38 (3.3)	0.248
Stroke	19 (2.4)	17 (1.5)	0.180
Bleeding	39 (4.9)	80 (6.8)	0.094
New-onset dialysis	19 (2.4)	68 (5.8)	<0.001
Sternal wound infection	7 (0.9)	11 (0.9)	1.000
Early AF recurrence (<3 months)	486 (61.1)	828 (70.8)	<0.001
AAD use (<3 months)	322 (40.5)	565 (48.3)	0.001
Overall adverse outcomes, n (%/PY)			
All-cause death	87 (2.5)	174 (2.5)	0.794
Stroke	42 (1.3)	56 (0.9)	0.114
PPM implantation	33 (1.0)	94 (1.5)	0.004
Atrioventricular block	12 (0.4)	16 (0.3)	0.650
Sinus node dysfunction	19 (0.6)	70 (1.1)	0.001
Others	2 (0.1)	8 (0.1)	0.238
Catheter ablation	14 (0.4)	23 (0.3)	0.497

[a]Chi-square test for early complications and log-rank test for overall outcomes. Early complications (early death, LCOS requiring MCS, stroke, bleeding, new-onset dialysis, and sternal wound infection) were defined as those occurring within 30 days of surgery.

AAD = anti-arrhythmic drug; LCOS = low cardiac output syndrome; MCS = mechanical circulatory support; PPM = permanent pacemaker; PY = patient-year.

EFFECT OF ABLATION LESION SETS AND PREDICTORS OF ABLATION FAILURE. After an adjustment with the PS, the baseline profiles were well balanced between the 2 groups with SMDs of <10% for all covariates except year of surgery in Table 1 (right column). The PS-adjusted analyses showed that the risk of early death (HR: 0.56; 95% confidence interval [CI]: 0.31-0.96; P = 0.041) and new-onset dialysis (HR: 0.47; 95% CI: 0.28-0.78; P = 0.003) was significantly lower in the patients with LA ablation (Table 4). However, the risk of other early complications as well as overall adverse outcomes including PPM implantation (P = 0.091) was comparable between the 2 groups (Central Illustration, lower image). When the analysis results after PS-weighting were further refined by covariate adjustment with year of surgery, which had not been adequately balanced after PS-weighting, but not found to interact with group (Supplemental Table 2), the risk analyses still showed similar outcomes. Furthermore, after accounting for early phase of death and adverse outcomes by a landmark analysis at 100 days, the risk of these outcomes still did not significantly differ between the 2 groups (Figure 2).

In the logit model with repeated measures, the probability of AF recurrence at 12 and 60 months was 13.9% and 37.1% in the patients with LA ablation, and

11.2% and 30.1% in those with BA ablation. The probability of AF recurrence at each time point was persistently higher with LA ablation than BA ablation, albeit not statistically significant (HR: 1.24; 95% CI: 0.96-1.61; $P = 0.100$) (**Figure 3**). The risk of AF recurrence increased with increasing follow-up duration (3 months vs 60 months; HR: 8.49; 95% CI: 6.46-11.16; $P < 0.001$) (**Table 5**). Early AF recurrence (HR: 2.09; 95% CI: 1.55-2.83; $P < 0.001$), large LA diameter (HR: 1.03; 95% CI: 1.02-1.05; $P < 0.001$), and significant TR (HR: 1.65; 95% CI: 1.20-2.28; $P = 0.002$) also significantly predicted the risk of later AF recurrence. As with AF recurrence, BA ablation was not associated with an increased risk of PPM implantation (**Table 6**). Rather, TV surgery (HR: 1.64; 95% CI: 1.02-2.62; $P = 0.042$) and increased age (HR: 1.02; 95% CI: 1.001-1.04; $P = 0.037$) significantly increased the risk of PPM implantation.

COMPARISON OF ECHOCARDIOGRAPHIC DIMENSIONAL AND FUNCTIONAL PARAMETERS. During a median follow-up of 12.7 (IQR 2.5-42.2) months, 10,703 echocardiographic measurements were performed. The median echocardiographic follow-up for the patients with LA and BA ablation was 11.3 (IQR 0.6-35.7) months and 14.3 (IQR 2.8-46.1) months, respectively. The PS-adjusted random coefficient model indicated that the patients in both groups showed a decreased left ventricular (LV) end-systolic dimension ($P < 0.001$) and an increased left ventricular ejection fraction (LVEF) ($P < 0.001$) (Supplemental Table 3).

TABLE 3 Longitudinal Rhythm Outcomes at Each Time Point

	Left Atrial (n = 796)	Bi-Atrial (n = 1,169)	*P* Value
Patients no. eligible for follow-up at 3 mo	734	1085	
With anticoagulation	480 (65.4)	791 (72.9)	
Warfarin	473 (64.4)	783 (72.2)	
DOAC	7 (1.0)	8 (0.7)	
Rhythm outcomes at 3 mo			0.001
Non-AF off AAD	648 (88.3)	907 (83.6)	
Non-AF on AAD	37 (5.0)	105 (9.7)	
Atrial fibrillation	49 (6.7)	73 (6.7)	
Patients no. eligible for follow-up at 6 mo	716	1066	
With anticoagulation	470 (65.7)	772 (72.4)	
Warfarin	458 (64.0)	754 (70.7)	
DOAC	12 (1.7)	18 (1.7)	
Rhythm outcomes at 6 mo			0.004
Non-AF off AAD	590 (82.4)	812 (76.2)	
Non-AF on AAD	40 (5.6)	97 (9.1)	
Atrial fibrillation	86 (12.0)	157 (14.7)	
Patients no. eligible for follow-up at 12 mo	614	994	
With anticoagulation	366 (59.6)	662 (66.6)	
Warfarin	353 (57.5)	648 (65.2)	
DOAC	13 (2.1)	14 (1.4)	
Rhythm outcomes at 12 mo			0.003
Non-AF off AAD	515 (83.9)	767 (77.2)	
Non-AF on AAD	23 (3.7)	65 (6.5)	
Atrial fibrillation	76 (12.4)	162 (16.3)	
Patients no. eligible for follow-up at 36 mo	387	846	
With anticoagulation	235 (60.8)	554 (65.5)	
Warfarin	227 (58.7)	535 (63.2)	
DOAC	8 (2.1)	19 (2.2)	
Rhythm outcomes at 36 mo			0.008
Non-AF off AAD	316 (81.7)	622 (73.5)	
Non-AF on AAD	13 (3.4)	44 (5.2)	
Atrial fibrillation	58 (15.0)	180 (21.3)	
Patients no. eligible for follow-up at 60 mo	236	585	
With anticoagulation	157 (66.5)	379 (64.8)	
Warfarin	153 (64.8)	362 (61.9)	
DOAC	4 (1.7)	17 (2.9)	
Rhythm outcomes at 60 mo			0.140
Non-AF off AAD	183 (77.5)	414 (70.8)	
Non-AF on AAD	9 (3.8)	27 (4.6)	
Atrial fibrillation	44 (18.6)	144 (24.6)	

Values are n (%).
AAD = anti-arrhythmic drug; AF = atrial fibrillation; DOAC = direct oral anticoagulant.

DISCUSSION

In this contemporary real-world cohort of patients with AF who underwent cardiac surgery, we found that the patients with BA ablation had a longer duration of AF, a larger LA diameter, and more TV disease than those with LA ablation. The rate of non-AF without AAD was observed to be rather higher in the patients with LA ablation than those with BA ablation at each time point during follow-up. However, the probability of AF recurrence was numerically higher in the patients with LA ablation than those with BA ablation, and the ablation lesion sets were not associated with an increased risk of AF recurrence in the longitudinal analysis of AF. In the PS-weighted analysis, BA ablation was found to be associated with an increased risk of several early complications, such as new-onset dialysis. However, BA ablation did not significantly increase the risk of overall adverse outcomes including PPM implantation; a seemingly higher incidence of PPM implantation in these patients appeared to be largely attributed to the higher prevalence of underlying sinus nodal dysfunction. LV remodeling and improvement in LV function were equally observed in the patients with both LA and BA ablation.

Despite the electrophysiologic basis that strongly supports BA ablation and concerns for focal trigger sources located in the right atrium (15,16), recent observational studies (7,17) and meta-analyses (4,5) have shown comparable results with regard to the AF-free rate between patients who underwent LA and BA

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TABLE 4 Risk Analyses on the Clinical Outcomes

	Original			IPTW-Adjusted			IPTW + Year of Surgery		
	OR/HR	95% CI	*P* Value	OR/HR	95% CI	*P* Value	OR/HR	95% CI	*P* Value
Early complications									
Early death	0.63	0.35-1.06	0.092	0.56	0.31-0.96	0.041	0.56	0.32-0.98	0.041
LCOS requiring MCS	0.69	0.38-1.20	0.198	0.66	0.37-1.14	0.147	0.66	0.37-1.14	0.147
Early stroke	1.66	0.85-3.24	0.134	1.63	0.86-3.10	0.131	1.57	0.83-2.99	0.166
Bleeding	0.70	0.47-1.03	0.077	1.06	0.73-1.53	0.745	1.06	0.73-1.53	0.743
New-onset dialysis	0.40	0.23-0.65	< 0.001	0.47	0.28-0.78	0.003	0.47	0.27-0.77	0.004
Sternal wound infection	0.93	0.34-2.38	0.888	1.32	0.52-3.31	0.549	1.29	0.51-3.24	0.584
Overall adverse outcomes									
All-cause death	0.97	0.74-1.25	0.794	1.03	0.75-1.41	0.878	1.05	0.76-1.43	0.780
Stroke[a]	1.39	0.92-2.08	0.117	1.17	0.73-1.86	0.512	1.18	0.74-1.89	0.488
PPM implantation[a]	0.56	0.38-0.84	0.005	0.68	0.43-1.06	0.091	0.65	0.42-1.03	0.068
Catheter ablation[a]	1.24	0.63-2.45	0.529	1.39	0.66-2.91	0.386	1.56	0.74-3.29	0.240

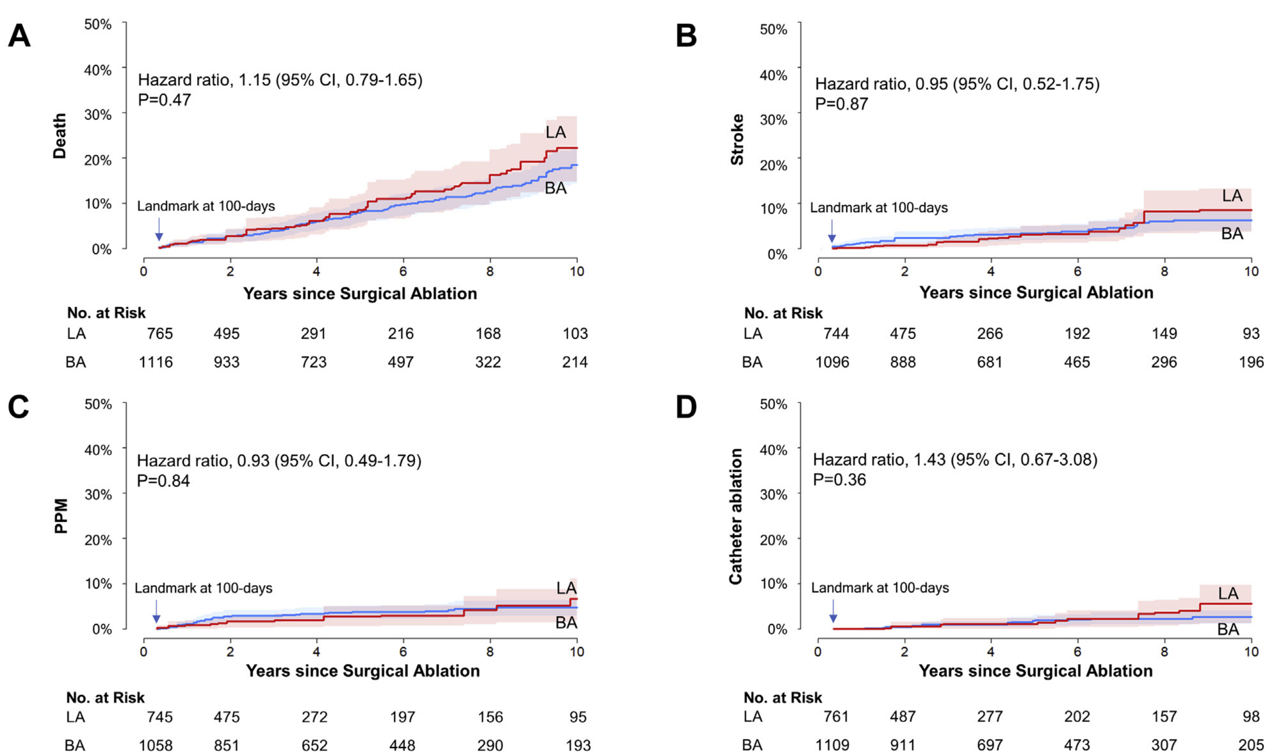
[a]Fine and Gray competing risk model was used to analyze the risk of stroke, PPM implantation, and catheter ablation as all-cause death as a competing risk. Early complications (early death, LCOS requiring MCS, stroke, bleeding, new-onset dialysis, and sternal wound infection) were defined as those occurring within 30 days of surgery. Bi-atrial ablation was used as a reference lesion. Early complications and atrial fibrillation (AF) recurrence are given as odds ratio (OR). Overall outcomes are given as hazard ratio (HR).

CI = confidence interval; IPTW = inverse-probability-of-treatment weighting; LCOS = low cardiac output syndrome; MCS = mechanical circulatory support; PPM = permanent pacemaker.

ablation. However, these results were mainly based on time-to-event analysis, and the recent study (18) that longitudinally analyzed AF recurrence after SA in the randomized trial showed that BA ablation was associated with a lower incidence of AF recurrence at 1 year.

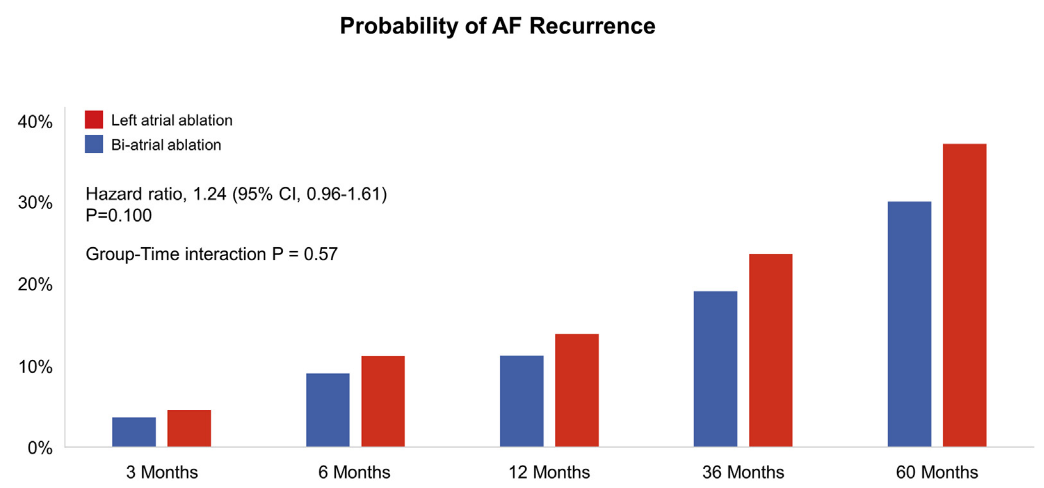
We also performed longitudinal analysis of AF recurrence with adjusting for relevant covariates over

FIGURE 2 Comparison of Clinical Outcomes According to the Ablation Lesion Sets (Landmark at 100 Days)



Adjusted time-to-event curves for death **(A)**, stroke **(B)**, permanent pacemaker (PPM) implantation **(C)**, and catheter ablation **(D)** according to the ablation lesion sets (landmark at 100 days).

FIGURE 3 **Estimated Recurrence of AF at 3, 6, 12, 36, and 60 Months**



AF = atrial fibrillation; CI = confidence interval.

an 18-year period in a large cohort. The probability of AF recurrence at 60 months in the patients with LA and BA ablation was 37.1% and 30.1%, respectively, which appears to be comparable to the rhythm outcomes of previous studies (17,19). The result showed that LA ablation was not associated with an increased risk of AF recurrence compared with BA ablation, suggesting that the difference in the rate of recurred AF between the 2 lesion sets may have been related more to the differences in the baseline and rhythm profiles rather than the ablation lesion sets. As atrial pathologic change that causes AF may occur earlier in the left side than the right side, complete LA ablation may be suitable for selected patients (7,15). However, given that the probability of AF recurrence was persistently higher in the patients with LA ablation (although not statistically significant), it should also be noted that the efficacy of LA ablation may not be as optimal as that of BA ablation under certain circumstances for patients at high risk for ablation failure (Table 5).

Similar to AF recurrence, the risk of mortality, stroke, and PPM implantation was found to unrelated to the ablation lesion sets (Table 4). In this study, the overall rate of PPM implantation in the patients with LA and BA ablation was 4.1% and 8.0%, respectively, which is comparable to the results of previous studies (5-7,17,20). It has remained controversial whether BA ablation is associated with an increased risk of PPM implantation compared with LA ablation only. Several observational series (6-8) and meta-analyses (5) have reported an increased risk of PPM implantation with BA ablation.

We also observed a higher PPM-free rate in the patients with LA ablation (Table 2); however, there was no significant difference in the rate of PPM implantation due to atrioventricular block ($P = 0.650$). The higher rate of PPM implantation in the patients with BA ablation was mainly attributed to sinus node dysfunction ($P = 0.001$). These findings can be largely explained by the arguments indicating that the postulated higher incidence of PPM implantation in patients undergoing BA maze procedure may be

TABLE 5 **Final Multivariable Repeated Measures Model of Atrial Fibrillation After a 3-Month Blanking Period**

	Odds Ratio	95% CI	*P* Value
Time, mo			
3	-	-	-
6	2.43	1.93-3.05	<0.001
12	3.11	2.46-3.93	<0.001
36	5.50	4.29-7.05	<0.001
60	8.83	6.69-11.65	<0.001
Early AF recurrence (<3 mo)	2.16	1.59-2.95	<0.001
Age (by 1-y increment)	1.03	1.02-1.05	<0.001
Persistent AF	1.61	1.07-2.41	0.022
AF duration (by 1-y increment)	1.04	1.02-1.06	<0.001
LA size (by 1-mm increment)	1.03	1.02-1.05	<0.001
Significant TR (≥grade 3)	1.66	1.19-2.30	0.003
AAD use (<3 mo)	2.16	1.68-2.77	0.001

Candidate variables were initially screened with univariable analyses. Significant variables with a $P < 0.05$ in univariable models were used to build a full multivariable model. The full multivariable model was built with all variables screened from univariable analyses (time, early AF recurrence, age, AF type, AF duration, congestive heart failure, chronic kidney disease, history of CVA, hemoglobin, peripheral arterial disease, significant TR, TV surgery, use of mechanical valve, LA appendage treatment, LA size reduction, AAD use). Only variables with a $P < 0.05$ in the full multivariable model were retained in the final multivariable model.

AAD = anti-arrhythmic drug; AF = atrial fibrillation; CI = confidence interval; CVA = cerebrovascular accident; LA = left atrium; TR = tricuspid regurgitation.

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TABLE 6 Final Multivariable Model for Pacemaker Implantation

	HR	95% CI	*P* Value
Age (by 1-y increment)	1.02	1.001-1.04	0.037
TV surgery	1.64	1.02-2.62	0.042
LA size (by 1-mm increment)	1.02	1.00-1.04	0.055
NYHA functional class III or IV	1.47	0.98-2.20	0.064
LA vs BA ablation	0.71	0.43-1.18	0.187

Candidate variables were initially screened with univariable analyses. Clinically significant variables with a $P < 0.10$ in univariable models were used in the final multivariable model (LA vs BA ablation, age, AF duration, diabetes mellitus, chronic kidney disease, hemoglobin, NYHA functional class III or IV, LA diameter, significant TR, year of surgery, MV surgery, TV surgery, LA appendage treatment). Variables that remained in the multivariable model using backward elimination technique were retained in the final multivariable model. A model for permanent pacemaker implantation (PPM) was built using Fine and Gray competing risk analyses that accounted for all-cause death as a competing risk.

BA = bi-atrial; CI = confidence interval; HR = hazard ratio; LA = left atrium; MV = mitral valve; NYHA = New York Heart Association; TV = tricuspid valve.

attributed to the unmasking of preoperative sinus node dysfunction rather than the damage of the conduction system by adding right-atrial ablation (15). After adjustment, BA ablation was not related to the increased risk of PPM implantation in this study (**Table 4**), which implies that a seemingly higher rate of PPM implantation in the patients with BA ablation may be primarily attributed to the baseline and procedural profiles such as advanced age or more frequent TV surgery (**Table 6**), rather than BA ablation itself. In particular, concomitant TV surgery at the time of mitral valve surgery may increase the rate of conduction disturbance and subsequent pacemaker implantation (21); of 28 patients with postablation pacemaker implantation, 18 (64.8%) underwent concomitant TV surgery in this study.

Improvement in LV function by restoring sinus rhythm after the maze procedure has been well documented (22), and we also observed an improvement in LVEF and LV remodeling equally in the patients with both LA and BA ablations (Supplemental Table 3). Although these functional and dimensional improvements may not be solely explained by SA, these benefits that were equally observed in patients with LA ablation as well as BA ablation imply that LA ablation may be as efficacious as BA ablation for selected patients.

Despite the clinical benefits of SA during concomitant cardiac surgery, SA has been underused in a real-world practice partially due to concerns over increased operative risks (23). In this context, it may be worthwhile to note that BA ablation was related to an increased risk of several early complications in this study. As the patients with BA ablation had greater morbidity and more TV surgery than those with LA ablation, such complications may not be solely accounted for by the addition of right-atrial lesions. Notwithstanding, as BA ablation can lead to longer cardiopulmonary bypass and aortic cross-clamping time, which is related to an increased risk of early mortality and morbidities (Supplemental Table 1), a judicious use of LA ablation may be considered as an efficient approach for selected patients who are at high risk for postoperative mortality and morbidities.

This study is subject to the inherent limitations of a retrospective and observational design. The selection bias in the choice of the ablation lesion sets may have affected our study results. This study included the patients who received SA by 11 surgeons over an 18-year period; unmeasured confounders such as different levels in surgical expertise and learning curves, and evolvement of ablation devices may have not been fully accounted for. Also, the proportion of patients with LA versus BA ablation differed over the study period, and year of surgery may have acted as a confounder even after statistical adjustment, although we demonstrated that the incidence of overall events showed a similar trend between the 2 groups during each quarter of the study period (Supplemental Figure 1).

The reported incidence of AF recurrence after SA may have been deflated with a discrepancy in follow-up durations between the patients with LA and BA ablation. As a diagnostic yield for AF can be increased with a prolonged monitoring modality, this study may be limited by the prevailing use of ECG as a modality that may have led to the possible underestimation of AF.

Finally, it should also be noted that this study was performed in a high-volume center where SAs have been dedicatedly performed, which decreases the generalizability. Therefore, these results may not be reproduced in other settings and should be interpreted with caution. Further studies are warranted to investigate the effect of additional right-atrial lesion sets, and our study findings should be confirmed or refuted through randomized trials with large sample sizes and long-term follow-up.

CONCLUSIONS

LA ablation has been mainly performed on patients with fewer morbidities than BA ablation. The risk of AF recurrence and other clinical outcomes, such as overall mortality or stroke, was comparable between the 2 ablation lesion sets. In particular, BA ablation was not related to an increased risk of PPM implantation. As both LA and BA ablations showed comparable long-term outcomes and improvements in cardiac function, LA ablation may be a viable therapeutic option for selected patients with AF undergoing cardiac surgery. Further research should be performed to determine the patient cohorts in whom better outcomes can be expected from BA ablation than LA ablation.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Surgical ablation is an effective therapeutic option to restore sinus rhythm in patients with AF undergoing cardiac surgery. However, it has remained controversial whether LA ablation is as efficacious as traditional BA ablation in the surgical treatment of AF.

COMPETENCY IN PATIENT CARE: We evaluated the clinical and rhythm outcomes between the patients undergoing LA and BA ablation. We showed that the risk of several early complications was higher in the patients with BA ablation than those with LA ablation; however, the risk of overall outcomes including permanent pacing and AF recurrence was comparable between the 2 groups. Tricuspid valve surgery, rather than BA ablation, independently increased the risk of PPM implantation.

TRANSLATIONAL OUTLOOK: LA ablation may be a viable therapeutic option for selected patients with AF undergoing cardiac surgery. Further research should be performed to determine the subgroup of patient cohorts in whom better outcomes can be expected from BA ablation than LA ablation.

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KEY WORDS atrial fibrillation, pacemaker, stroke, surgical ablation

APPENDIX For supplemental tables and a figure, please see the online version of this paper.