ORIGINAL RESEARCH

Sick Sinus Syndrome After the Maze Procedure Performed Concomitantly With Mitral Valve Surgery

Min Soo Cho, MD; Ran Heo, MD; Xin Jin, MD; Jung-Bok Lee, PhD; Sahmin Lee, MD, PhD; Dae-Hee Kim, MD, PhD; Joon Bum Kim, MD, PhD; Jun Kim, MD, PhD; Sung-Ho Jung, MD, PhD; Suk Jung Choo, MD, PhD; Jong-Min Song, MD, PhD; Gi-Byoung Nam, MD, PhD; Kee-Joon Choi, MD, PhD; Duk-Hyun Kang, MD, PhD; Cheol Hyun Chung, MD, PhD; Jae Won Lee, MD, PhD; You-Ho Kim, MD, PhD; Jae-Kwan Song, MD, PhD

***Background*—**To characterize the development of sick sinus syndrome (SSS) after the additive maze procedure (MP) during mitral valve surgery.

***Methods and Results*—**Follow-up data (median, 3.6 years) of 750 patients with a prevalence of rheumatic cause of 57.6% were analyzed. SSS occurred in 35 patients with a time-dependent increase: the incidence rates at 1, 2, and 4 years after surgery were 2.9%, 3.7%, and 4.3%, respectively. The additive MP showed higher risks of SSS development (hazard ratio, 7.44; 95% confidence interval, 3.45–16.05; $P<0.001$) and pacemaker implantation (hazard ratio, 3.61; 95% confidence interval, 1.95–6.67; $P<0.001$). Patients who developed SSS showed higher 4-year rates of clinical events (death, stroke, and hospital admission) (67.5±8.5% versus 33.0±1.9%; $P<0.001$). After adjustment for age and preoperative peak systolic pulmonary artery pressure, the lesion extent (biatrial versus left atrial MP), not the underlying cause (rheumatic versus nonrheumatic), was independently associated with SSS development (hazard ratio, 3.58; 95% confidence interval, 1.08–11.86; $P=0.037$). The adverse effect of the biatrial MP was confirmed in patients with trivial or mild preoperative tricuspid regurgitation showing higher SSS incidence (4.6±1.4% versus 1.0±0.7%; $P=0.023$), not in those with moderate-to-severe tricuspid regurgitation (6.8±1.7% versus 3.8±3.8%; $P=0.337$). Recurrence of atrial fibrillation was not associated with the lesion extent of the MP.

***Conclusions*—**After the additive MP, the ongoing risk of SSS development should be acknowledged irrespective of the underlying cause. Considering additive risk of biatrial MP with similar atrial fibrillation recurrence rate, minimizing lesion extent is warranted.
(*J Am Heart Assoc*. 2018;7:e009629. DOI: 10.1161/JAHA.118.009629.)

Key Words: atrial fibrillation • maze procedure • mitral valve surgery • sick sinus syndrome

The Cox-maze procedure (MP) is a well-established method of rhythm control in patients with atrial fibrillation (AF).[1,2] In previous randomized trials or observational registries, this procedure has been demonstrated to have excellent efficacy in terms of rhythm control and adverse outcomes after mitral valve (MV) surgery (MVS).[3–7] The development of symptomatic bradyarrhythmia is a well-known major complication of the MP, which can be fatal or necessitate pacemaker implantation. Previous studies have reported a wide incidence of 2% to 21% during short-term follow-up after surgery; and age, extended lesion set, and microwave energy source were identified as predictors of sinus node dysfunction or sick sinus syndrome (SSS).[4,8–10] However, these observations are not sufficient to change practice patterns and several issues remain unresolved. Although rheumatic pathological characteristics reportedly show a high prevalence of anti–sinus node antibodies that may contribute to SSS development after cardiac surgery,[11] the underlying cause of the MV disease has not been adequately addressed. Moreover, most of the existing clinical studies had a relatively short clinical follow-up duration of 1 year.[4,10,12] Thus, it remains unknown whether there is a cumulative or time-dependent risk of SSS development after the MP, and the impact of age or lesion extent (biatral versus

From the Divisions of Cardiology, (M.S.C., R.H., X.J., S.L., D.-H.K., J.K., J.-M.S., G.-B.N., K.-J.C., D.-H.K., Y.-H.K., J.-K.S.) and Biomedical Statistics, (J.-B.L.), and Department of Thoracic and Cardiovascular Surgery (J.B.K., S.-H.J., S.J.C., C.H.C., J.W.L.), Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea.

Correspondence to: Jae-Kwan Song, MD, Asan Medical Center Heart Institute, University of Ulsan College of Medicine, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 05505, South Korea. E-mail: jksong@amc.seoul.kr

Received April 26, 2018; accepted August 16, 2018.

Clinical Perspective

What Is New?

- The additive maze procedure during mitral valve surgery showed higher risks of development of sick sinus syndrome and pacemaker implantation.
- The biatrial versus left atrial maze procedure, not the underlying cause of mitral valve disease, was associated with sick sinus syndrome development, without any additive benefit of rhythm control.
- The adverse effect of the biatrial maze procedure was statistically significant in the subgroup of patients with trivial or mild preoperative tricuspid regurgitation.

What Are the Clinical Implications?

- Tailored selection of lesion extent (biatrial versus left atrial) appears appropriate for the additive maze procedure during mitral valve surgery.

left atrial [LA] maze) has not been completely evaluated. These data are clinically important for defining the group of patients who would benefit the most from MPs. Therefore, in the current study, we sought to evaluate the pattern of SSS development by using clinical data with a relatively long follow-up duration and to determine whether the underlying cause of the MV disease and the lesion extent of the MP could affect SSS development.

Methods

We will make the data, methods used in the analysis, and materials used to conduct the research available to any researcher for purposes of reproducing the results or replicating the procedure. The data that support the findings of this study are available from the corresponding author on reasonable request.

Study Population

Between March 2006 and December 2014, 2584 patients underwent MVS at our institution (Asan Medical Center, Seoul, Republic of Korea), and 972 (37.6%) received a concomitant Cox-MP. Patients were excluded if they had undergone concomitant aortic valve surgery, had received a permanent pacemaker (PPM), or were diagnosed as having SSS before the surgery. Thus, the study population included 750 patients who underwent MVS with the MP and 1270 who underwent MVS only (Figure 1). This retrospective study was approved by our institutional review board, and the board waived the informed consent requirement.

Data Collection and Analysis

The patients' baseline characteristics and electrocardiographic, echocardiographic, surgical, and outcome data were obtained by carefully reviewing their medical records in standardized case report forms. Data on baseline demographic characteristics and comorbidity status were gathered during admission for MVS. The patients usually attended follow-up visits at 1, 3, and 6 months after MVS and every 6 months thereafter. Holter monitoring was usually prescribed during admission and at the first outpatient visit. Twelve-lead electrocardiographic data were recorded at every outpatient visit. Follow-up data were collected via a direct telephone interview and through a detailed review of all medical records. The cause and date of death in mortality cases were confirmed using information in death certificates, along with a review of all available clinical records at the time of death. The median follow-up duration was 3.6 (interquartile range, 1.7–6.4) years. The cause of the MV disease was evaluated by 2 cardiologists (J.-K.S. and M.S.C.) by using the echocardiographic images, and the intraobserver and interobserver variabilities in rheumatic cause were found to be excellent, with κ values of 0.96 and 0.91, respectively. Discordant cases were resolved using surgical findings.

Surgical Procedure

All patients underwent MV replacement or repair concomitantly with the MP at the discretion of cardiac surgeons together with the recommendations of cardiologists. The decision on performing a tricuspid valve (TV) surgical intervention was made by the in-house cardiosurgical team, on the basis of the preoperative echocardiographic findings as well as on-site findings in the operation room. The extent and details of the MP were determined by the cardiac surgeons, and a detailed description of the surgical procedure has previously been reported by the surgical members of our team.[5,13] In brief, after aorta clamping and LA incision, LA ablation was performed endocardially before the MV procedure. LA ablation lesions included a single-box lesion for pulmonary vein isolation, a line from the box lesion to the left appendage, and a mitral isthmus line connecting the box lesion and the MV annulus. Additional epicardial coronary sinus ablation was performed on the opposite side of the mitral isthmus lesion. The right atrial (RA) lesion set consisted of a cavotricuspid isthmus line and a line from the isthmus lesion to the superior vena cava. This simplified modification of the Cox-MP was intended to minimize the area of isolation and avoid damage to the normal conduction system. The decision to perform the RA ablation was made on the surgeon's discretion, influenced by an individual patient's risk of recurrent AF, such as age, atrial size, AF wave pattern on

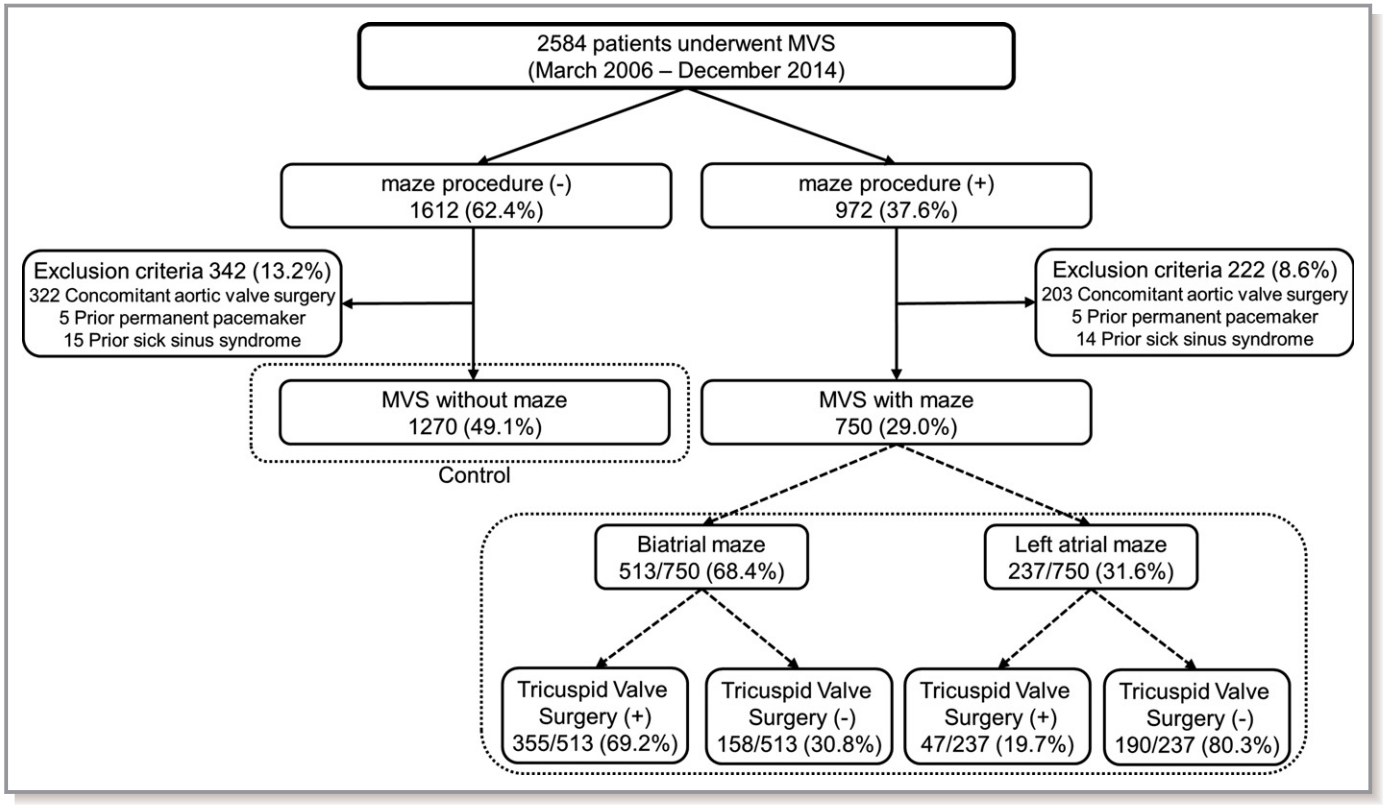

Figure 1. Flow diagram of the study population and summary of surgical procedures. MVS indicates mitral valve surgery; PPM, permanent pacemaker; and SSS, sick sinus syndrome.

ECG (fine or coarse), or necessity of surgical procedure for tricuspid regurgitation (TR).

Study Outcomes and Definitions

The primary outcome of the current study was SSS development, defined as symptomatic sinus bradycardia associated with documented sinus exit block, pause, or arrest in any type of electrocardiographic data, including 12-lead ECG, Holter monitoring, or telemetry record. Transient asymptomatic postoperative junctional rhythm, which disappeared during the convalescence period or by the first outpatient clinic visit, was not counted as a clinical event. The rate of high-degree atrioventricular block (AVB), including documented Mobitz type II or complete AVB, and PPM implantation were defined as secondary outcomes. For the evaluation of the efficacy of the MP, recurrent AF lasting ≥30 seconds in Holter monitoring or sufficiently long for a 12-lead ECG to be recorded after 90 days of blanking period from index surgery was also defined as a secondary outcome of the current study.[14,15] The rates of clinical outcomes, including death, stroke, and unexpected rehospitalization after surgery, were compared between patients with and those without SSS development throughout the follow-up period after the index surgery.

Statistical Analysis

Summary statistics are presented as frequencies and percentages or as means±SD. Differences between 2 groups were compared using unpaired Student *t* test or Mann-Whitney *U* test for continuous variables and χ^2 test or Fisher's exact test for categorical variables. To identify the factors associated with SSS development, univariate and multivariate Cox proportional hazard models were used. The proportional hazard assumption was tested by examining the log(-log[survival]) plot and partial Schoenfeld residuals. In multivariate analysis, backward elimination techniques were used to define the independent predictors of SSS development. Cumulative survival rate and event-free survival rate curves were generated using the Kaplan-Meier method and compared using the log-rank test. To compensate for the nonrandomized design of the current study and reduce the number of potential confounding factors, we used propensity scoring in the subgroup analysis in patients without moderate to severe TR. A logistic regression model was used to compute propensity scores. Covariates included age, sex, body mass index, hypertension, diabetes mellitus, congestive heart failure, cerebrovascular accident, coronary artery disease, prior cardiac surgery, rheumatic pathological features, LA and RA areas, left ventricular ejection fraction, TR pressure

gradient, moderate-to-severe mitral stenosis, and moderate-to-severe mitral regurgitation. Model discrimination was assessed using C-statistics, and model calibration was assessed using Hosmer-Lemeshow statistics. Weighted Cox's proportional hazards models were fitted using the inverse probability of treatment weighting method, and relative outcomes were analyzed accordingly. All *P* values were 2 sided, and $P<0.05$ was considered statistically significant. All statistical analyses were performed using R software version 3.2.2 (http://cran.r-project.org/).

Results

Between 2006 and 2014, 750 patients (age, 56.8±12.2 years) underwent MVS and the MP at our institution. The 2 most common causes of MV disease included rheumatic disease (n=431, 57.6%) and MV prolapse or chordae rupture (n=249, 33.2%). Moderate-to-severe mitral regurgitation was the most common valvular dysfunction and was observed in 523 patients (69.7%). MV replacement was performed in 446 patients (59.5%), and MV repair was performed in 304 patients (40.5%). The biatrial MP was performed in 513 patients (68.4%), and the LA MP was performed in 237 patients (31.6%) (Figure 1). Concomitant TV surgery was performed in 402 patients (53.6%), most of whom underwent TV repair (n=385, 95.8%).

SSS After the MP

During the follow-up period, SSS and AVB occurred in 35 (4.7%) and 7 (0.9%) patients, respectively, and PPM was implanted in 28 patients (80.0%) with SSS and in 6 patients (83.3%) with AVB. Compared with patients who underwent MVS only, those who underwent concomitant MVS and the MP showed higher risks of SSS development (hazard ratio [HR], 7.44; 95% confidence interval [CI], 3.61–12.46; $P<0.001$) and PPM implantation (HR, 3.61; 95% CI, 1.95–6.67; $P<0.001$). However, the risk of AVB development was not significant (HR, 1.49; 95% CI, 0.58–3.86; $P=0.411$) (Figure 2). The temporal pattern of symptomatic bradycardia development is also shown in Figure 2. AVB development was mostly confined to the immediate postoperative period, whereas SSS showed a gradual increase during follow-up after the surgery, with incidence rates at 1, 2, and 4 years after surgery of 2.9%, 3.7%, and 4.3%, respectively. In accordance with this pattern, the rate of PPM implantation also continuously increased during follow-up.

Patients who developed SSS showed a higher incidence of adverse clinical events (67.5±8.5% versus 33.0±1.9%; $P<0.001$) (Figure 3) driven by the higher incidence of rehospitalization (63.7±9.1% versus 23.5±1.8%; $P<0.001$) and stroke (15.1±6.2% versus 5.0±0.9%; $P=0.026$) than those who did not develop SSS. The mortality rate did not differ between patients who developed SSS and those who did not.

The baseline characteristics of patients with and without SSS are shown in Table 1. Patients with SSS were significantly older than those without SSS (64.0±9.0 versus 56.5±12.2 years; $P<0.001$), with a larger RA area, higher maximal TR pressure gradient, and higher incidence of moderate-to-severe TR. However, the dominant type of valvular dysfunction, underlying cause of MV disease, biventricular systolic function, and LA diameter or area did not significantly differ between the 2 groups. The biatrial MP was more frequently performed in patients with SSS than in those without SSS (91.4% versus 67.3%; $P=0.001$); patients with SSS also showed longer cardiopulmonary bypass and cross-clamp time than those without SSS. TV surgery concomitant with MVS was performed more frequently in patients with SSS than in those without SSS (71.4% versus 52.7%; $P=0.046$). The MP details, other than lesion extent, such as energy source, concomitant LA appendage resection/obliteration, or

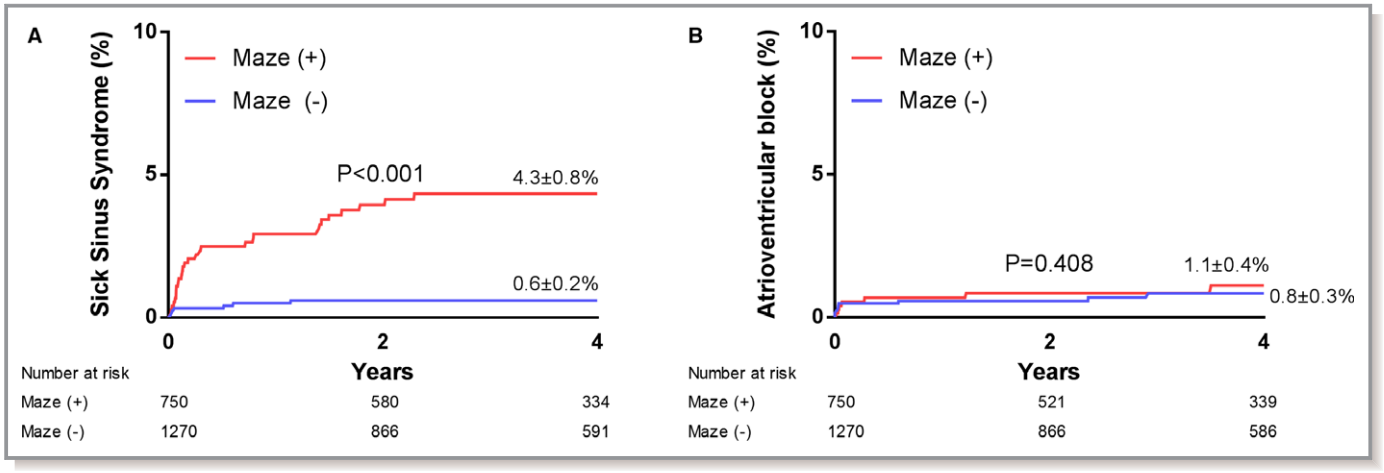

Figure 2. Impact of the additive maze procedure on the development of sick sinus syndrome (A) and atrioventricular block (B) and their temporal patterns.

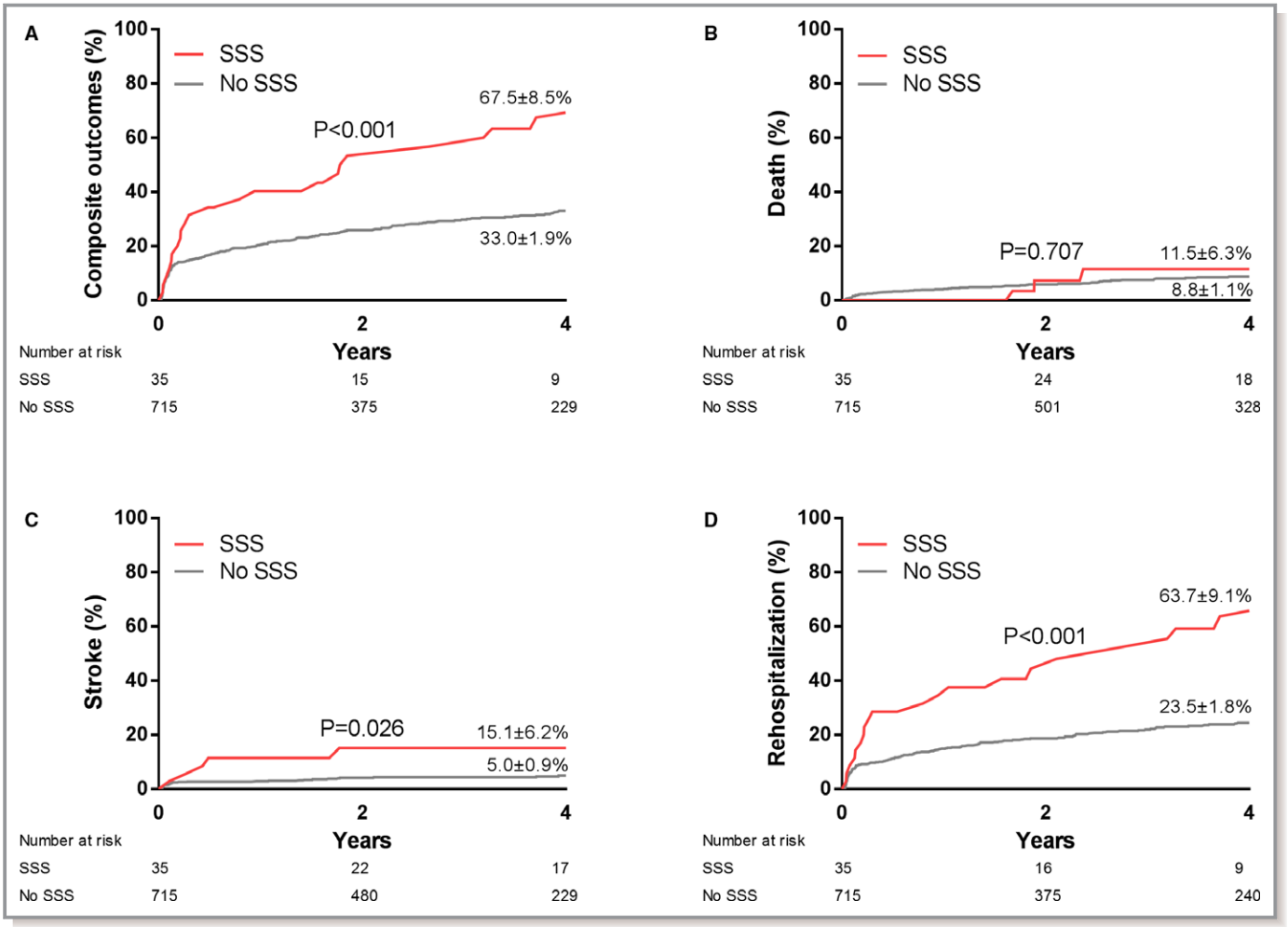

Figure 3. Time-to-event curves for adverse clinical events. The composite clinical outcomes included death, stroke, and hospital admission. A, Patients who developed sick sinus syndrome (SSS) during follow-up showed higher event rates during follow-up. The overall mortality was not significantly different (B); however, patients with SSS development showed higher rates of stroke (C) and rehospitalization (D).

LA volume reduction procedure, did not differ significantly between the 2 groups. The prescription rate of amiodarone in the discharge medication was not significantly different between those with or without AF, and the use rate of other types of antiarrhythmic drugs was almost negligible.

In the univariate Cox-proportional hazards model, age, moderate-to-severe TR, maximal TR pressure gradient, biatrial MP, and RA area were associated with SSS development (Table 2). After the backward elimination procedure, age (per 10 years: HR, 1.75; 95% CI, 1.26–2.43; $P<0.001$), maximal TR pressure gradient (per 10 mm Hg: HR, 1.24; 95% CI, 1.02–1.50; $P=0.032$), and biatrial MP (compared with left-sided MP: HR, 3.58; 95% CI, 1.08–11.86; $P=0.037$) were found to be independent predictors of SSS development.

Impact of Underlying Cause

To evaluate the impact of the underlying cause of MV disease, clinical data of patients with rheumatic disease (n=431) were compared with those of patients with nonrheumatic disease (n=319). Patients with rheumatic valvular heart disease were characterized by younger age, female predominance, lower prevalence of hypertension or congestive heart failure, larger atrial size, and a higher prevalence of moderate-to-severe TR than those without (Table 3). Mitral stenosis was a more common type of dominant valvular dysfunction in patients with rheumatic pathological characteristics, whereas mitral regurgitation was dominant in patients with nonrheumatic pathological characteristics. The underlying cause of MV disease demonstrated no difference in the rate of SSS development, pacemaker implantation, AF recurrence, and composite clinical events after the MP (Figure 4).

Impact of Lesion Extent

A subgroup analysis was performed to evaluate the relationship between the lesion extent of the MP and TR severity. Among patients without moderate-to-severe TR, 266 (56.3%)

Table 1. Baseline Characteristics of the Study Patients

Characteristic	Total (N=750)	Patients With SSS (n=35)	Patients Without SSS (n=715)	*P* Value
Age, y	56.8±12.2	64.0±9.4	56.5 ±12.2	<0.001
Men, n (%)	316 (42.1)	13 (37.1)	303 (42.4)	0.662
Body mass index, kg/m^2	23.9±3.3	23.8±3.2	23.9±3.3	0.793
Hypertension, n (%)	194 (25.9)	12 (34.3)	182 (25.5)	0.333
Diabetes mellitus, n (%)	69 (9.2)	6 (17.1)	63 (8.8)	0.172
Congestive heart failure, n (%)	67 (8.9)	2 (5.7)	65 (9.1)	0.704
Chronic renal disease, n (%)	10 (1.3)	1 (2.9)	9 (1.3)	0.960
Previous CVA, n (%)	34 (4.5)	2 (5.7)	32 (4.5)	>0.99
Previous CAD, n (%)	45 (6.0)	2 (5.7)	43 (6.0)	>0.99
Previous OHS, n (%)	38 (5.1)	4 (11.4)	34 (4.8)	0.173
Echocardiography				
LV end-diastolic dimension, mm	54.6±9.1	53.9±9.9	54.6±9.0	0.636
LA size, mm	57.5±9.5	59.2 ±13.1	57.4±9.3	0.425
LA area, mm^2	45.5±15.3	44.3±18.0	45.6±15.2	0.617
RA area, mm^2	25.8±10.6	29.7±12.0	25.6±10.5	0.026
LV ejection fraction, %	56.3±8.6	58.4±7.0	56.2 ± 8.6	0.138
Moderate-to-severe MS, n (%)	307 (40.9)	14 (40.0)	293 (41.0)	>0.99
Moderate-to-severe MR, n (%)	523 (69.7)	26 (74.3)	497 (69.5)	0.680
Rheumatic heart disease, n (%)	431 (57.6)	19 (54.3)	412 (57.6)	0.830
Moderate-to-severe TR, n (%)	278 (37.1)	21 (60.0)	257 (35.9)	0.007
TR PG, mm Hg	38.3±14.8	45.5 ±15.3	38.0 ±14.7	0.003
MV surgery				
MV surgery, n (%)				0.098
MV repair	304 (40.5)	9 (25.7)	295 (41.3)	
MV replacement	446 (59.5)	26 (74.3)	420 (58.7)	
Concomitant TV surgery, n (%)	402 (53.6)	25 (71.4)	377 (52.7)	0.046
Concomitant CABG, n (%)	60 (8.0)	4 (11.4)	56 (7.8)	0.655
CPB time, min	167.2±55.2	195.6±55.4	165.8 ±54.8	0.002
Cross-clamp time, min	108.7±45.5	124.2±41.3	108.0±45.6	0.040
Maze procedure, n (%)				
Biatrial maze	513 (68.4)	32 (91.4)	481 (67.3)	0.005
Cryoablation	721 (96.1)	35 (100.0)	686 (95.9)	0.478
Concomitant LA appendage resection/obliteration	315 (42.0)	16 (45.7)	299 (41.8)	0.779
Concomitant LA volume reduction	221 (29.5)	13 (37.1)	208 (29.1)	0.406
Discharge medication, n (%)				
Amiodarone	117 (15.6)	3 (8.6)	114 (15.9)	0.241
Other antiarrhythmics	5 (0.7)	0 (0)	5 (0.7)	0.787

Data are given as mean±SD unless otherwise indicated. CABG indicates coronary artery bypass grafting; CAD, coronary artery disease; CPB, cardiopulmonary bypass; CVA, cerebrovascular accident; LA, left atrial; LV, left ventricular; MR, mitral regurgitation; MS, mitral stenosis; MV, mitral valve; OHS, open-heart surgery; PG, pressure gradient; RA, right atrial; SSS, sick sinus syndrome; TR, tricuspid regurgitation; TV, tricuspid valve.

Table 2. Predictors of Development of SSS After MVS and MP

Variable	Univariable Analysis			Multivariable Analysis		
	HR	95% CI	*P* Value	HR	95% CI	*P* Value
Rheumatic cause of mitral disease	0.84	0.43–1.63	0.597	. . .	. . .	. . .
Biatrial maze (vs LA maze)	5.37	1.64–17.57	0.005	3.58	1.08–11.86	0.037
Age, per 10 y	1.07	1.04–1.11	<0.001	1.75	1.26–2.43	<0.001
Moderate-to-severe TR	2.65	1.35–5.22	0.005	. . .	. . .	. . .
TR PG, per 10 mm Hg	1.03	1.01–1.05	0.003	1.24	1.02–1.50	0.032
RA area, per mm^2	1.03	1.00–1.05	0.033	. . .	. . .	. . .

CI indicates confidence interval; HR, hazard ratio; LA, left atrial; MVS, mitral valve surgery; PG, pressure gradient; RA, right atrial; SSS, sick sinus syndrome; TR, tricuspid regurgitation.

Table 3. Characteristics of Study Patients With or Without Rheumatic Pathological Features

Characteristics	RHD (n=431)	No RHD (n=319)	*P* Value
Age, y	55.6±11.6	58.5±12.9	0.002
Men, n (%)	127 (29.5)	189 (59.2)	<0.001
LV end-diastolic dimension, mm	51.9±7.4	58.3±9.8	<0.001
LA size, mm	58.3±9.2	56.4±9.9	0.006
LA area, mm^2	47.1±15.6	43.4±14.8	0.001
RA area, mm^2	25.3±10.0	26.4±11.4	0.184
LV ejection fraction, %	54.7±7.7	58.4±9.2	<0.001
Moderate-to-severe MS, n (%)	298 (69.1)	9 (2.8)	<0.001
Moderate-to-severe MR, n (%)	210 (48.7)	313 (98.1)	<0.001
TR PG, mm Hg	38.0±13.6	38.9±16.4	0.421
MV surgery, n (%)			
MV repair	45 (10.4)	259 (81.2)	<0.001
MV replacement	386 (89.6)	60 (18.8)	
Concomitant TV surgery, n (%)	243 (56.4)	159 (49.8)	0.089
CPB time, min	106.0±51.3	112.5±36.2	0.043
Cross-clamp time, min	158.3±51.8	179.3±57.4	<0.001
Biatrial maze, n (%)	213 (66.8)	300 (69.6)	0.456
Cryoablation, n (%)	415 (96.3)	306 (95.9)	0.408
Concomitant LA appendage resection/obliteration, n (%)	218 (50.6)	97 (30.4)	<0.001
Concomitant LA volume reduction, n (%)	135 (31.3)	86 (27.0)	0.224

Data are given as mean±SD unless otherwise indicated. CPB indicates cardiopulmonary bypass; LA, left atrial; LV, left ventricular; MR, mitral regurgitation; MS, mitral stenosis; MV, mitral valve; PG, pressure gradient; RA, right atrial; RHD, rheumatic heart disease; TR, tricuspid regurgitation; TV, tricuspid valve.

underwent the biatrial MP and the remaining patients underwent the LA MP (n=206, 43.7%). The frequencies of concomitant TV repair in patients who underwent the biatrial MP and the LA MP were 46.6% and 8.3%, respectively. Those who underwent the biatrial MP had a higher mean age, larger LA and RA areas, and longer cardiopulmonary bypass and cross-clamp times (Table 4). In the overall population, patients who underwent biatrial maze surgery were at a higher risk of SSS development than those who underwent LA maze surgery (6.1±1.2% versus 1.4±0.8%; *P*=0.002; Figure 5A). Among patients without moderate-to-severe TR, the 4-year incidence of SSS development was higher after the biatrial MP than after the LA MP (4.6±1.4% versus 1.0±0.7%; *P*=0.023; Figure 5C), whereas the incidence of recurrent AF did not reach statistical significance (Figure 5D). After adjustment for baseline characteristics by propensity scoring using the inverse probability of treatment weighting method (Table 5), patients who underwent the biatrial MP showed a higher risk of SSS development (HR, 4.79; 95% CI, 1.62–14.15; *P*=0.005) than those who underwent the LA MP. However, the risk of recurrent AF did not reach statistical significance (HR, 1.31; 95% CI, 0.87–1.99; *P*=0.200). Of the patients with moderate-to-severe TR (n=278, 37.0%), most (n=261, 93.9%) underwent TV surgery (ie, either TV replacement [n=17] or TV repair [n=244]). In this group, the biatrial MP was concurrently performed for most patients (n=247, 88.8%), and the lesion extent of the MP revealed no difference in the rates of SSS development and recurrent AF (Figure 5E and 5F).

Efficacy of the MP

Early recurrence of AF during the 90-day blanking period was documented in 275 patients (36.7%). After the blanking period, AF recurrence was observed in 186 patients (24.8%) during follow-up, with the 4-year incidence rate of AF recurrence being 22.9%. The rate of recurrent AF was higher in patients who underwent the biatrial MP than in those who

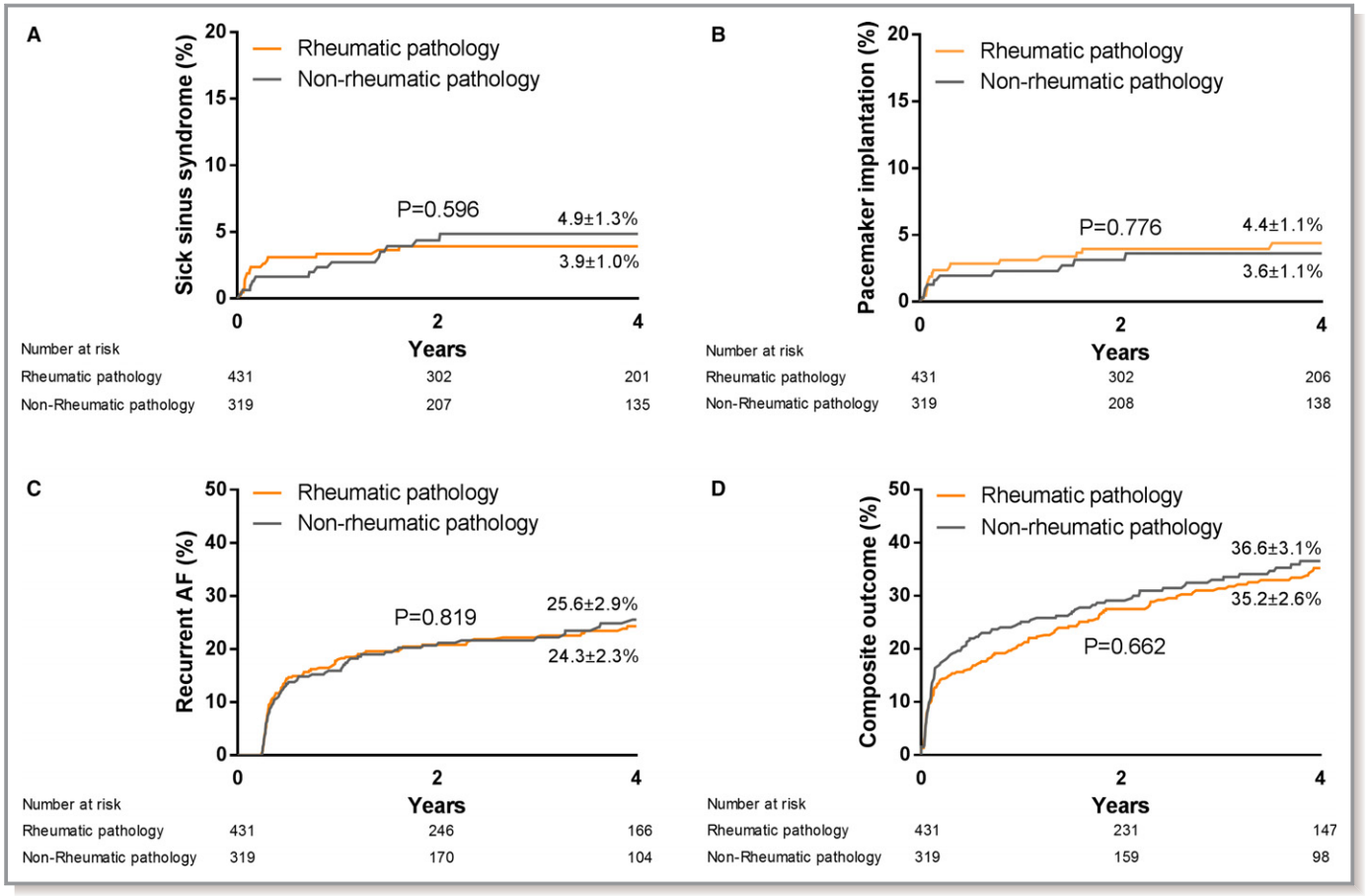

Figure 4. Time-to-event curves showing the impact of rheumatic pathological features on clinical outcomes. Patients with rheumatic mitral valve disease were not at a higher risk of sick sinus syndrome development (A), permanent pacemaker implantation (B), recurrent atrial fibrillation (AF; C), or composite clinical outcomes (death, stroke, and rehospitalization; D).

underwent the LA MP alone (28.2±2.3% versus 17.6±2.7%; *P*=0.002; Figure 5B). However, in multivariate adjustment, the lesion extent of the MP was not an independent factor associated with AF recurrence (HR, 1.19; 95% CI, 0.82–1.74; *P*=0.352; Table 6).

Discussion

This retrospective analysis focused primarily on the safety outcomes of the MP performed concomitantly with MVS and revealed the presence of an ongoing and cumulative risk of SSS development during follow-up after the index surgical procedure. The development of symptomatic bradycardia exhibited a characteristic temporal pattern on the basis of the type: SSS was the dominant form in the late postoperative period, whereas AVB was confined to the early postoperative period. The underlying cause of MV disease did not affect SSS development, and the biatrial MP was found to be an independent predictor of SSS development without any advantage of preventing AF recurrence, especially in patients without moderate-to-severe TR.

SSS After MVS and the MP

Most previous studies have focused on the efficacy of the MP; therefore, data about safety outcomes, especially the natural course from a chronological viewpoint, are lacking, even in a recently published study on late outcomes.[16] The limited data available on SSS development after the procedure demonstrate marked variations in the frequency of SSS development ranging from 6.8% to 21.5%.[17,18] Some studies included a relatively small numbers of patients (<300), and the reported incidence of SSS was usually the secondary outcome, outside the main findings.[13,19,20] In a recently published long-term follow-up study on 320 patients with a mean follow-up time of 111±44 months after the Cox-maze III procedure, pacing-dependent rhythm was observed in 10.6%; and among them, the prevalences of atrial, ventricular, and dual-chamber pacing were 6%, 1.6%, and 3% of patients, respectively.[21] The frequency of pacing-dependent rhythm at a 4-year follow-up duration after MVS and the MP in our study was 4.1%; and differing follow-up durations can explain the differing frequencies of pacing-dependent rhythm, which may reflect the

Table 4. Comparison of Clinical Characteristics According to the Type of MP in Patients With No or Mild TR

Characterstic	Biatrial Maze (n=266)	LA Maze (n=206)	*P* Value
Age, y	56.3 ±11.5	52.4 ±13.1	0.001
Men, n (%)	142 (53.4)	96 (46.6)	0.171
LV end-diastolic dimension, mm	55.2±9.2	55.4±9.1	0.861
LA size, mm	57.7±9.2	54.6±7.7	<0.001
LA area, mm^2	45.6±14.6	42.8±11.3	0.020
RA area, mm^2	23.0±8.1	21.1±7.5	0.007
LV ejection fraction, %	56.4±8.5	56.4±9.2	0.941
Moderate-to-severe MS, n (%)	169 (60.2)	121 (58.7)	0.829
Moderate-to-severe MR, n (%)	189 (71.1)	140 (68.0)	0.533
Rheumatic disease, n (%)	140 (52.6)	108 (52.4)	0.445
TR PG, mm Hg	35.6 ±12.2	33.4 ±12.3	0.054
MV surgery, n (%)			
MV repair	120 (45.1)	88 (42.7)	0.670
MV replacement	146 (54.9)	118 (57.3)	
Concomitant TV surgery, n (%)	124 (46.6)	17 (8.3)	<0.001
CPB time, min	111.0 ±34.7	96.3 ±32.0	<0.001
Cross-clamp time, min	173.8 ±54.7	149.4 ±52.3	<0.001
Cryoablation, n (%)	260 (97.7)	193 (93.7)	0.035
Concomitant LA appendage resection/obliteration, n (%)	123 (46.2)	70 (34.0)	0.010
Concomitant LA volume reduction, n (%)	85 (32.0)	27 (13.1)	<0.001

Data are given as mean±SD unless otherwise indicated. CPB indicates cardiopulmonary bypass; LA, left atrial; LV, left ventricular; MP, maze procedure; MR, mitral regurgitation; MS, mitral stenosis; MV, mitral valve; PG, pressure gradient; RA, right atrial; TR, tricuspid regurgitation; TV, tricuspid valve.

importance of follow-up duration in representing the ongoing risk of symptomatic bradyarrhythmia development after the MP.

Another variable to be considered in interpreting the frequency of SSS development was the underlying cardiac disease that needed a concomitant procedure. In a study with the longest follow-up duration,[21] MVS was performed only in 7% of patients, and 6% of patients underwent concomitant coronary artery bypass grafting. Thus, most patients underwent the MP alone. We excluded patients who underwent concomitant aortic valve surgery or the MP alone without MVS, thereby maintaining the homogeneity of the study subjects. To date, it is not known whether additional surgical procedures, such as mitral or aortic valve surgery, can contribute to an increased risk of SSS development after the MP. Further investigations using a more homogeneous patient population are necessary.

In addition to the ongoing risk of SSS development, our data revealed different temporal developmental patterns in SSS and AVB. Previous surgical series have demonstrated a predominance of AVB as an indication of PPM implantation in the early postoperative period,[4,9] and SSS development after the MP has not been adequately evaluated. In our study, SSS development was confirmed to be a more frequently encountered complication of the MP than AVB. This difference can be easily explained by the longer follow-up period of our study. The aging process itself is the main risk factor of sinus node dysfunction via the common mechanism of degeneration and fibrosis of the conduction system.[22,23] In a subgroup analysis of our data, 20 patients developed SSS >3 months after the surgery (late-onset group) and 15 patients developed SSS <3 months after the surgery (early-onset group). The late-onset group had a significantly higher mean age (67.3±7.3 versus 59.9±9.9 years; *P*=0.015), which suggested that age has an impact on the ongoing or cumulative risk of SSS development. Interestingly, some previous studies have described sinus node dysfunction from surgical damage as a transient phenomenon confined to the immediate postoperative period.[24,25] However, considering that surgery in the right atrium inevitably causes tissue damage and can alter the conduction system to some degree, a biatrial maze lesion set can make a substrate of conduction disturbance that can evolve into SSS development.[12] The contribution of these 2 potential mechanisms, aging and the substrate associated with surgical trauma, could be a plausible explanation for the difference in the frequency of SSS development after biatrial

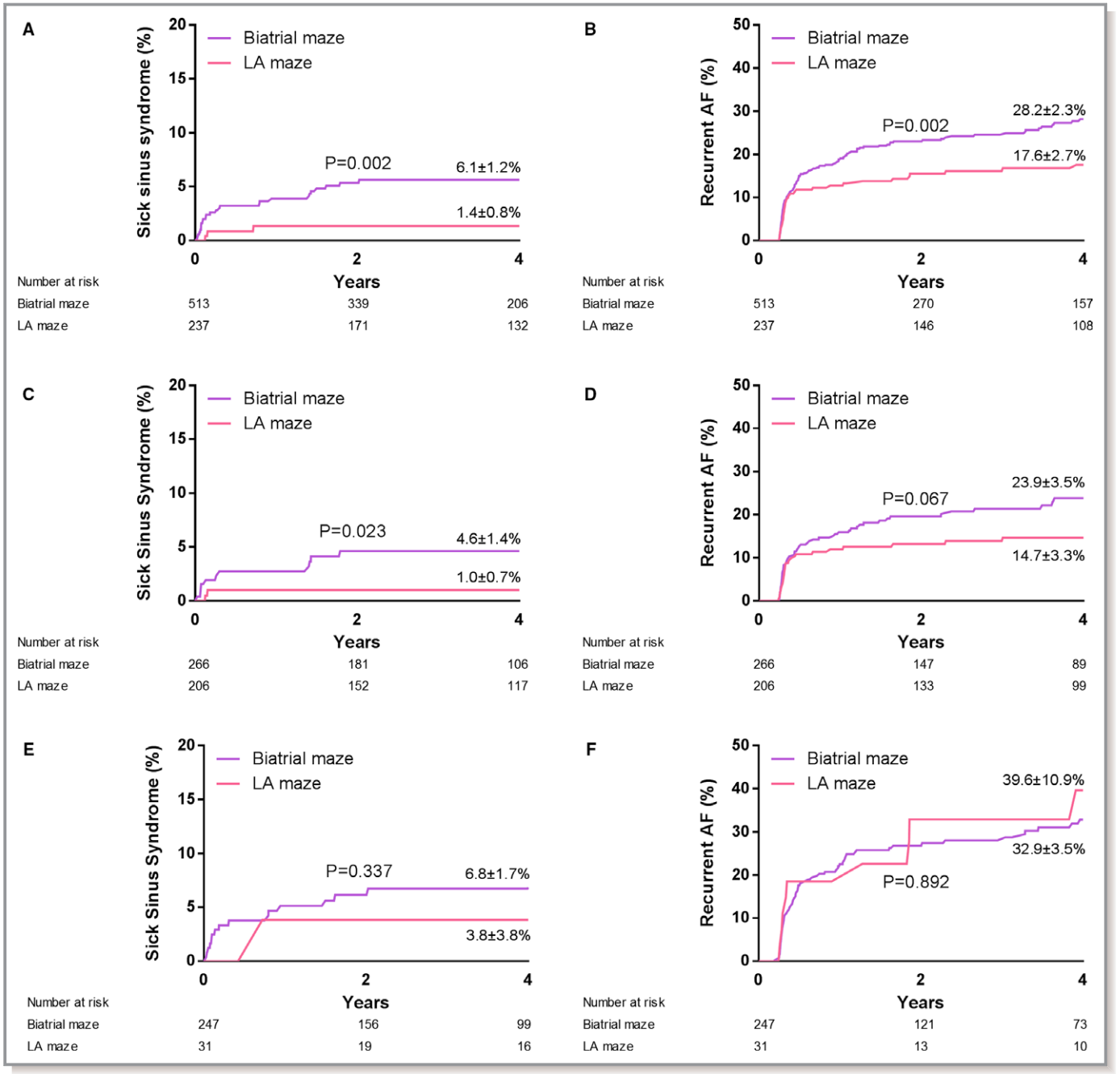

Figure 5. Impact of the lesion extent of the maze procedure (biatrial vs left atrial [LA]) on the long-term outcomes stratified according to the presence of moderate-to-severe tricuspid regurgitation (TR). Overall, the biatrial maze procedure resulted in higher rates of sick sinus syndrome (SSS) development (A) and atrial fibrillation (AF) recurrence (B). C and D, In patients with mild or no TR, the biatrial maze procedure resulted in a higher rate of SSS development with a similar rate of recurrent AF. E and F, In patients with moderate-to-severe TR, there was no difference in the SSS development or recurrent AF according to the lesion extent of the maze procedure.

versus LA MP during the follow-up period, with SSS being a predominant indication of PPM implantation in the late postoperative period. The absence of any impact of rheumatic pathological features on SSS development suggested that surgical injury is more powerful than a presurgical substrate change.

Another interesting finding in our study is that the effect of lesion extent of the MP on development of SSS is dependent on underlying TR severity. It has been well recognized that severe TR does not necessarily regress after MVS, and persistence or development of late significant TR after uneventful MVS with its poor long-term clinical and surgical outcome remains a challenging issue.[26–34] Because AF has been proved to be an important risk factor of development of late significant TR and the beneficial effect of the MP to prevent late TR development after MVS has been

Table 5. SMD of Variables Included in the Propensity Scoring Model Before and After Weighting

Variable	Biatrial Maze (n=266)	LA Maze (n=206)	SMD Before Weighting	SMD After Weighting
Age, y	56.3 ±11.5	52.4 ±13.1	0.319	0.003
Men, n (%)	142 (53.4)	96 (46.6)	0.136	0.015
Body mass index, kg/m^2	23.6 ±3.4	23.8 ±3.2	0.051	0.010
Hypertension	152 (48.9)	226 (49.9)	0.187	0.004
Diabetes mellitus	19 (7.1)	9 (4.4)	0.119	0.001
CHF, n (%)	21 (7.9)	14 (6.8)	0.042	0.004
Previous CVA, n (%)	9 (3.4)	10 (4.9)	0.074	0.001
Previous CAD, n (%)	17 (6.4)	7 (3.4)	0.139	0.001
Previous OHS, n (%)	16 (6.0)	6 (2.9)	0.150	0.001
Rheumatic pathological feature, n (%)	140 (52.6)	108 (52.4)	0.015	0.012
LA area, mm^2	45.6±14.6	42.8±11.3	0.213	0.025
RA area, mm^2	23.0±8.1	21.1±7.5	0.253	0.015
LV ejection fraction, %	56.4±8.5	56.4±9.2	0.007	0.008
TR PG, mm Hg	35.6 ±12.2	33.4 ±12.3	0.194	0.021
Moderate-to-severe MS, n (%)	169 (60.20)	121 (58.7)	0.029	0.010
Moderate-to-severe MR, n (%)	189 (71.1)	140 (68.0)	0.067	0.013

Data are given as mean±SD unless otherwise indicated. CAD indicates coronary artery disease; CHF, congestive heart failure; CVA, cerebrovascular accident; LA, left atrial; LV, left ventricular; MR, mitral regurgitation; MS, mitral stenosis; OHS, open-heart surgery; PG, pressure gradient; RA, right atrial; SMD, standardized mean difference; TR, tricuspid regurgitation.

confirmed,[35,36] the MP has been more widely performed during MVS. In addition, some surgeons believe that remodeling annuloplasty of the TV on the basis of tricuspid dilation improves functional status irrespective of the TR grade.[37] A concomitant TV repair during MVS in patients without moderate-to-severe TR is still controversial, and the current guidelines do not provide definite recommendations on TV repair for these patients.[38] Furthermore, the alleged benefits of TV repair in this select group of patients include a decreased rate of congestive heart failure or TR progression; however, the benefits in terms of hard end points have not been evident.[13] Thus, our finding of an increased SSS development without additional benefits, especially after adjustment, suggested that the "routine" RA MP was not helpful in patients with mild or no TR. This finding is in line with the results of a recent randomized trial in which an additional RA MP failed to show a better rhythm control rate (66% in the biatrial maze group versus 61% in the LA maze group).[4] In a recent meta-analysis of 10 randomized and observational studies, the rhythm control rate up to 1 year

Table 6. Predictors of Recurrent AF After MVS and MP

	Univariable Analysis			Multivariable Analysis		
Variable	HR	95% CI	*P* Value	HR	95% CI	*P* Value
Age, per 10 y	1.29	1.14–1.46	<0.001	1.22	1.08–1.39	0.002
Men	0.70	0.52–0.95	0.023	0.77	0.56–1.05	0.102
Hypertension	1.33	0.98–1.82	0.069	. . .	. . .	. . .
Diabetes mellitus	1.48	0.94–2.31	0.087	. . .	. . .	. . .
Left atrial area, per mm^2	1.01	1.01–1.02	0.001	1.01	1.00–1.02	0.008
Right atrial area, per mm^2	1.02	1.01–1.04	<0.001	1.01	1.00–1.03	0.114
Moderate-to-severe tricuspid regurgitation	1.88	1.41–2.51	<0.001	1.37	0.98–1.92	0.070
Lesion extent (biatrial vs left atrial maze)	1.71	1.21–2.40	0.002	. . .	. . .	. . .

AF indicates atrial fibrillation; CI, confidence interval; HR, hazard ratio; MP, maze procedure; MVS, mitral valve surgery.

was superior in the biatrial maze group, but was inconclusive after that period, whereas the PPM rate representing SSS development was definitely higher in the biatrial maze group than in the LA maze group (7.0% versus 5.5%; HR, 1.75; 95% CI, 1.16–2.66; P=0.008).[39]

Limitations

Because this was a retrospective observational study conducted at a single center, selection bias was possible. Technical revolutions in MPs during the study period of >10 years and the nonrandomization of MPs and TV repair are inherent limitations of this study. However, because clinical events, such as hospital admission or mortality, could be assessed and baseline and follow-up clinical data, such as echocardiographic, electrocardiographic, and Holter recordings of all patients, were available for analysis, we believe that our main findings are valid despite these limitations. There was continuous technical advancement in the details of the MP, such as posterior box lesion for pulmonary valve isolation, simplified RA lines, and more attempts for LA-confined procedure. The impact of such advancement cannot be fully assessed in this retrospective analysis. However, we believe the impact of lesion extent would be constant on the basis of the result of supplementary sensitivity analysis. In this analysis, when the year of surgery was put into the final propensity model, the resultant risk of SSS (HR, 4.18; 95% CI, 1.40–12.55; P=0.011) and AF recurrence (HR, 1.29; 95% CI, 0.85–1.96; P=0.240) were consistent with the main analysis. The decisions about extent of surgical procedure were largely based on the surgeon's experience and cannot be exactly assessed, despite meticulous review of medical records and surgical findings. This could be another inherent limitation of a retrospective study.

Conclusions

Patients who underwent MVS and a concomitant MP have an ongoing cumulative risk of SSS development, with a higher risk of adverse clinical events, and this should be considered an important complication of MPs. Minimizing lesion extent is warranted considering higher risk of SSS development with no clinical benefit of additive biatrial MP during MVS.

Disclosures

None.

References

1. Cox JL, Jaquiss RD, Schuessler RB, Boineau JP. Modification of the maze procedure for atrial flutter and atrial fibrillation, II: surgical technique of the maze III procedure. *J Thorac Cardiovasc Surg*. 1995;110:485–495.
2. Ad N, Suri RM, Gammie JS, Sheng S, O'Brien SM, Henry L. Surgical ablation of atrial fibrillation trends and outcomes in North America. *J Thorac Cardiovasc Surg*. 2012;144:1051–1060.
3. Doukas G, Samani NJ, Alexiou C, Oc M, Chin DT, Stafford PG, Spyt TJ. Left atrial radiofrequency ablation during mitral valve surgery for continuous atrial fibrillation: a randomized controlled trial. *JAMA*. 2005;294:2323–2329.
4. Gillinov AM, Gelijns AC, Parides MK, DeRose JJ Jr, Moskowitz AJ, Voisine P, Ailawadi G, Bouchard D, Smith PK, Mack MJ, Acker MA, Mullen JC, Rose EA, Chang HL, Puskas JD, Couderc JP, Gardner TJ, Varghese R, Horvath KA, Bolling SF, Michler RE, Geller NL, Ascheim DD, Miller MA, Baqiella E, Moquete EG, Williams P, Taddei-Peters WC, O'Gara PT, Blackstone EH, Argenziano M; CTSN Investigators. Surgical ablation of atrial fibrillation during mitral-valve surgery. *N Engl J Med*. 2015;372:1399–1409.
5. Kim JB, Moon JS, Yun SC, Kim KW, Jung SH, Choo SJ, Song H, Chung CH, Lee JW. Long-term outcomes of mechanical valve replacement in patients with atrial fibrillation: impact of the maze procedure. *Circulation*. 2012;125:2071–2080.
6. Blomström-Lundqvist C, Johansson B, Berglin E, Nilsson L, Jensen SM, Thelin S, Holmgren A, Edvardsson N, Biomstrom P. A randomized double-blind study of epicardial left atrial cryoablation for permanent atrial fibrillation in patients undergoing mitral valve surgery: the SWEdish Multicentre Atrial Fibrillation study (SWEDMAF). *Eur Heart J*. 2007;28:2902–2908.
7. Abreu Filho CA, Lisboa LA, Dallan LA, Spina GS, Grinberg M, Scanavacca M, Sosa EA, Ramires JA, Oliveira SA. Effectiveness of the maze procedure using cooled-tip radiofrequency ablation in patients with permanent atrial fibrillation and rheumatic mitral valve disease. *Circulation*. 2005;112:I20–I25.
8. Robertson JO, Cuculich PS, Saint LL, Schuessler RB, Moon MR, Lawton J, Damiano RJ, Maniar HS. Predictors and risk of pacemaker implantation after the Cox-maze IV procedure. *Ann Thorac Surg*. 2013;95:2015–2021.
9. Worku B, Pak SW, Cheema F, Russo M, Housman B, Van Patten D, Harris J, Argenziano M. Incidence and predictors of pacemaker placement after surgical ablation for atrial fibrillation. *Ann Thorac Surg*. 2011;92:2085–2089.
10. Soni LK, Cedola SR, Cogan J, Jiang J, Yang J, Takayama H, Argenziano M. Right atrial lesions do not improve the efficacy of a complete left atrial lesion set in the surgical treatment of atrial fibrillation, but they do increase procedural morbidity. *J Thorac Cardiovasc Surg*. 2013;145:356–363.
11. Maisch B, Lotze U, Schneider J, Kochsiek K. Antibodies to human sinus node in sick sinus syndrome. *Pacing Clin Electrophysiol*. 1986;9:1101–1109.
12. Tuinenburg AE, Van Gelder IC, Van Den Berg MP, Grandjean JG, Tielman RG, Smit AJ, Huet RC, Van Der Maaten JM, Volkers CP, Ebels T, Crijns HJ. Sinus node function after cardiac surgery: is impairment specific for the maze procedure? *Int J Cardiol*. 2004;95:101–108.
13. Kim JB, Bang JH, Jung SH, Choo SJ, Chung CH, Lee JW. Left atrial ablation versus biatrial ablation in the surgical treatment of atrial fibrillation. *Ann Thorac Surg*. 2011;92:1397–1405.
14. Gillinov AM, Argenziano M, Blackstone EH, Iribarne A, DeRose JJ Jr, Ailawadi G, Russo MJ, Ascheim DD, Parides MK, Rodriguez E, Bouchard D, Taddei-Peters WC, Geller NL, Acker MA, Gelijins AC. Designing comparative effectiveness trials of surgical ablation for atrial fibrillation: experience of the cardiothoracic surgical trials network. *J Thorac Cardiovasc Surg*. 2011;142:257–264.
15. Calkins H, Kuck KH, Cappato R, Brugada J, Camm AJ, Chen SA, Crijns HJ, Damiano RJ Jr, Davies DW, DiMarco J, Edgerton J, Ellenbogen K, Ezekowitz MD, Haines DE, Haissaquerre M, Hindricks G, Iesaka Y, Jackman W, Jalife J, Jais P, Kalman J, Keane D, Kim YH, Jirchhof P, Klein G, Kottkamp H, Kumagai K, Lindsay BD, Mansour M, Marchlinski FE, McCarthy PM, Mont JL, Morady F, Nademanee K, Nakagawa H, Natale A, Nattel S, Packer DL, Pappone C, Prystowsky E, Raviele A, Reddy V, Ruskin JN, Shemin RJ, Tsao HM, Wilber D. 2012 HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design. *Europace*. 2012;14:528–606.
16. Henn MC, Lancaster TS, Miller JR, Sinn LA, Schuessler RB, Moon MR, Melby SJ, Maniar HS, Damiano RJ Jr. Late outcomes after the Cox maze IV procedure for atrial fibrillation. *J Thorac Cardiovasc Surg*. 2015;150:1168–1178.
17. Gammie JS, Haddad M, Milford-Beland S, Welke KF, Ferguson TB Jr, O'Brien SM, Griffith BP, Peterson ED. Atrial fibrillation correction surgery: lessons from the Society of Thoracic Surgeons national cardiac database. *Ann Thorac Surg*. 2008;85:909–914.
18. Kulikov AA, Bokeria LA. Assessment of sinoatrial node function in patients with persistent and long-standing persistent forms of atrial fibrillation after maze III procedure combined with mitral valve operation. *J Atr Fibrillation*. 2016;9:1408.
19. Izumoto H, Kawazoe K, Eishi K, Kamata J. Medium-term results after the modified Cox/maze procedure combined with other cardiac surgery. *Eur J Cardiothorac Surg*. 2000;17:25–29.
20. Jessurun ER, van Hemel NM, Defauw JA, Stomeel MA, Kelder JC, de la Riviere AB, Ernst JM. Results of maze surgery for lone paroxysmal atrial fibrillation. *Circulation*. 2000;101:1559–1567.
21. Albåge A, Johansson B, Kennebäck G, Kallner G, Schersaten H, Jideus L; Swedish Arrhythmia Surgery Group. Long-term follow-up of cardiac rhythm in

320 patients after the Cox-maze III procedure for atrial fibrillation. *Ann Thorac Surg*. 2016;101:1443–1449.

22. Kaplan BM, Langendorf R, Lev M, Pick A. Tachycardia-bradycardia syndrome (so-called "sick sinus syndrome"): pathology, mechanisms and treatment. *Am J Cardiol*. 1973;31:497–508.
23. Thery C, Gosselin B, Lekieffre J, Warembourg H. Pathology of sinoatrial node: correlations with electrocardiographic findings in 111 patients. *Am Heart J*. 1977;93:735–740.
24. Pasic M, Musci M, Siniawski H, Edelmann B, Tedoriya T, Hetzer R. Transient sinus node dysfunction after the Cox-maze III procedure in patients with organic heart disease and chronic fixed atrial fibrillation. *J Am Coll Cardiol*. 1998;32:1040–1047.
25. Pasic M, Musci M, Siniawski H, Grauhan O, Edelmann B, Tedoriya T, Weng Y, Hetzer R. The Cox maze III procedure: parallel normalization of sinus node dysfunction, improvement of atrial function, and recovery of the cardiac autonomic nervous system. *J Thorac Cardiovasc Surg*. 1999;118:287–296.
26. Simon R, Oelert H, Borst H, Lichtlen P. Influence of mitral valve surgery on tricuspid incompetence concomitant with mitral valve disease. *Circulation*. 1980;62:I152–I157.
27. Cohen SR, Sell JE, McIntosh CL, Clark R. Tricuspid regurgitation in patients with acquired, chronic, pure mitral regurgitation, I: prevalence, diagnosis, and comparison of preoperative clinical and hemodynamic features in patients with and without tricuspid regurgitation. *J Thorac Cardiovasc Surg*. 1987;94:481–487.
28. King RM, Schaff HV, Danielson GK, Gersh BJ, Orszulak TA, Piehler JM, Puga FJ, Pluth JR. Surgery for tricuspid regurgitation late after mitral valve replacement. *Circulation*. 1984;70:I193–I197.
29. Groves PH, Ikram S, Ingold U, Hall RJC. Tricuspid regurgitation following mitral valve replacement: an echocardiographic study. *J Heart Valve Dis*. 1993;2:273–278.
30. Porter A, Shapira Y, Wurzel M, Sulkes J, Vaturi M, Adler Y, Sahar G, Sagie A. Tricuspid regurgitation late after mitral valve replacement: clinical and echocardiographic evaluation. *J Heart Valve Dis*. 1999;8:57–62.
31. Staab ME, Nishimura RA, Dearani JA. Isolated tricuspid valve surgery for severe tricuspid regurgitation following prior left heart valve surgery: analysis of outcome in 34 patients. *J Heart Valve Dis*. 1999;8:567–574.
32. Matsuyama K, Matsumoto M, Sugita T, Nishizawa Z, Tokuda Y, Matsuo T. Predictors of residual tricuspid regurgitation after mitral valve surgery. *Ann Thorac Surg*. 2003;75:1826–1828.
33. Izumi C, Iga K, Konishi T. Progression of isolated tricuspid regurgitation late after mitral valve surgery for rheumatic mitral valve disease. *J Heart Valve Dis*. 2002;11:353–356.
34. Kim YJ, Kwon DA, Kim HK, Park JS, Hahn S, Kim KH, Kim KB, Sohn DW, Ahn H, Ph BH, Park YB. Determinants of surgical outcomes in patients with isolated tricuspid regurgitation. *Circulation*. 2009;120:1672–1678.
35. Song H, Kim MJ, Chung CH, Choo SJ, Song MG, Song JM, Kang DH, Lee JW, Song JK. Factors associated with development of late significant tricuspid regurgitation after successful left-sided valve surgery. *Heart*. 2009;95:931–936.
36. Kim HK, Kim YJ, Kim KI, Jo SH, Kim KB, Ahn H, Sohn DW, Oh BH, Lee MM, Park YB, Choi YS. Impact of the maze operation combined with left sided valve surgery on the change in tricuspid regurgitation over time. *Circulation*. 2005;112:I14–I19.
37. Dreyfus GD, Corbi PJ, Chan KMJ, Bahrami T. Secondary tricuspid regurgitation or diatation: which should be the criteria for surgical repair? *Ann Thorac Surg*. 2005;79:127–132.
38. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP III, Guyton RA, O'Gara PT, Ruiz CE, Skubas NJ, Sorajja P, Sundt TM III, Thomas JD; American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;129:2440–2492.
39. Phan K, Xie A, Tsai Y-C, Kumar N, La Meir M, Yan TD. Biatrial ablation vs. left atrial concomitant surgical ablation for treatment of atrial fibrillation: a meta-analysis. *Europace*. 2015;17:38–47.