A prospective randomized trial of the cut-and-sew Maze procedure in patients undergoing surgery for rheumatic mitral valve disease

Huishan Wang, MD,^a Jinsong Han, MD,^a Zengwei Wang, MD,^a Zongtao Yin, PhD,^a Zhigang Liu, MD,^b Yan Jin, MD,^a and Hongguang Han, MD^a

ABSTRACT

Objective: To evaluate the safety and efficacy of the addition of the cut-and-sew Maze III procedure (CSM) for mitral valve replacement (MVR) in patients with atrial fibrillation (AF) associated with rheumatic mitral valve disease (RMVD).

Methods: A total of 130 patients with persistent or long-standing persistent AF associated with RMVD were assigned at random to either the CSM plus MVR (Maze III) group or MVR alone (non-Maze) group. The primary endpoint was a composite of freedom from stroke and death at 1 year.

Results: There were no significant differences between the Maze III and non-Maze groups in terms of major complications and in-hospital mortality. One-year freedom from stroke or death was better in the Maze III group compared with the non-Maze group ($P = .0028$; hazard ratio, 0.2653; 95% confidence interval, 0.1122 to 0.6270). The risk of AF recurrence in the Maze III group was 0.002-fold that in non-Maze group ($P = .000$).

Conclusions: Addition of the CSM to an MVR procedure can decrease the risk of stroke or death and high sinus rhythm at 1 year without increasing the operative risk. CSM is a safe and effective approach to treating AF associated with RMVD. (J Thorac Cardiovasc Surg 2018;155:608-17)

Composite Kaplan-Meier curves of freedom from stroke and death for the Maze III group (dotted blue line) and non-Maze group (solid red line).

Central Message

CSM is a safe and effective approach to treating AF associated with RMVD.

Perspective

In this prospective, randomized trial, hospital mortality and complications showed no differences between the Maze III group and the non-Maze group, but 1-year freedom from stroke or death was better in the Maze III group.

See Editorial Commentary page 618.

Atrial fibrillation (AF) is present in 40% to 60% of patients with rheumatic mitral valve disease (RMVD), which remains a health threat in developing countries.^{1,2} If left untreated, AF is an independent predictor of morbidity and mortality and late stroke after mitral valve surgery.²⁻⁴ The modified Maze IV procedure by surgical ablation with an alternative source of energy, such as radiofrequency and cryoablation, have emerged to surgically treat AF. The latest The American Association

for Thoracic Surgery guidelines include recommendations for these surgical devices.⁵ However, only approximately 40% of patients with AF undergo a modified Maze procedure with concomitant mitral valve surgery.^{6,7} The reason for this may be related to the debate regarding the efficacy of the alternative energy sources, with the creation of continuous linear transmural atrial lesions, which act as an electrophysiological conduction block, considered doubtful. A retrospective study from our center reported a 1-year and 5-year freedom from AF of 76% and 67%, respectively.⁸

From the ^aDepartment of Cardiovascular Surgery, General Hospital of Shenyang Military Area Command, Shenyang; and ^bTEDA International Cardiovascular Hospital, Tianjin, China.

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Address for reprints: Huishan Wang, MD, Department of Cardiovascular Surgery, Shenyang Northern Hospital, 83 Wenhua Rd, Shenhe District, Shenyang, Liaoning 110016, China (E-mail: huishanwang@hotmail.com).

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Abbreviations and Acronyms

AF	= atrial fibrillation
CSM	= cut-and-sew Maze III
ECG	= electrocardiogram
INR	= International Normalized Ratio
LAA	= left atrial appendage
LAD	= left atrial dimension
LVEF	= left ventricular ejection fraction
LVEDD	= left ventricular diastolic dimension
LVESD	= left ventricular systolic dimension
MVR	= mitral valve replacement
RMVD	= rheumatic mitral valve disease
SR	= sinus rhythm

In general, the cut-and-sew Maze III procedure (CSM) is considered the gold standard for surgical management of AF because of the ensured transmurality, especially for those cases involving mitral valve disease and a thick left atrial wall.⁹⁻¹² Unfortunately, CSM is still viewed as a complex and high-risk procedure, and most surgeons are reluctant to perform it during cardiac operations. A possible source of this reluctance may be related to the limited available evidence, with the majority of studies related to the impact of the CSM on operative risk observational studies instead of prospective randomized controlled trials.¹³⁻¹⁵

Therefore, we designed this prospective, randomized trial to reevaluate the safety, efficacy, and cost-effectiveness of standard CSM combined with mitral valve replacement (MVR) for patients with AF associated with RMVD, and to compare the operative results between this group and a group of patients who underwent MVR alone during the same time period.

METHODS

This study was designed as a prospective, randomized trial comparing the outcomes of CSM plus MVR with MVR alone. Patients with persistent or long-standing persistent AF associated with RMVD were included. RMVD was diagnosed based on a history of rheumatic fever or mitral valve defects or on a morphological evaluation of the excised mitral valve. Patients with degenerative or ischemic mitral valve lesions or paroxysmal AF were excluded, as were patients who underwent concomitant MVR and aortic valve replacement.

Eligible patients were assigned at random at a 1:1 ratio to either the CSM plus MVR (Maze III) group or the MVR alone (non-Maze) group using a random number method. The Ethics Committee of the General Hospital of Shenyang Military Area Command approved this study, and all patients provided signed informed consent. This study has been registered in the Chinese Clinical Trial Register (no. ChiCTR18007269).

According to the 2014 American College of Cardiology/American Heart Association/Heart Rhythm Society guidelines, persistent AF is defined as continuous AF sustained for >7 days, and long-standing persistent AF was defined as the duration of >12 months.¹⁶ The duration of AF was defined as the time between the day when AF was documented

by 12-lead electrocardiogram (ECG) or 24-hour Holter ECG and the day of surgery. Early death was defined as death occurring less than 30 days after surgery. Stroke, including ischemic and hemorrhagic stroke, was confirmed by computed tomography scan; a transient ischemic attack was not considered a stroke in this study. Stroke occurring within 30 days was defined as early stroke. The primary endpoint was a composite of freedom from stroke or death at 1 year. The secondary endpoint was the risk of AF recurrence. Other outcomes included hospital costs and serious adverse events during hospitalization, such as bleeding and heart failure.

Operative Approach

All of the CSM procedures were performed by a single senior surgeon (Huishan Wang) (Video 1). The CSM technique has been described in detail previously.¹⁷ In brief, a median sternotomy approach was used in all patients. Cardiopulmonary bypass was set up using conventional ascending aorta and bicaval cannulation. Myocardial protection was achieved with moderate hypothermia, and antegrade perfusion was ensured with blood cardioplegia. Right-side incisions were done on a beating heart after initiation of moderate hypothermia and cardiopulmonary bypass. Left-side incisions were performed along with MVR after aortic cross-clamping (Video 2). The right-side incisions included atrial appendage incision, anterior atrial incision, posterior incision to the tricuspid valve annulus, lateral incision between the superior vena cava and inferior vena cava, and inferior incision to the tricuspid valve annulus. Major left-side incisions included an incision encircling the pulmonary veins, incision to the mitral valve annulus, and excision of the left atrial appendage. Four 3-mm cryolesions (-60°C for 2 minutes) were added, 1 from the mitral annulus to the coronary sinus, 1 on the bridge region between the left superior and inferior pulmonary vein orifice and the base of the left atrial appendage (LAA) (Figure 1 and Video 3), and 2 at the level of the tricuspid annulus (Figure 2). After cardioplegic arrest and aortic cross-clamping, the MVR was performed routinely. Double-continuous full-layer inverting mattress sutures with 4-0 polypropylene were used for all left-side incisions to prevent bleeding (Figure 3 and Video 4).

In the Maze III group, the LAA was managed with excision and closure with 4-0 polypropylene (Video 5). In the non-Maze group, the LAA was excluded either by ligation if the orifice diameter was <3 cm or by closure with 4-0 polypropylene from the inside if orifice diameter was >3 cm. The LAA was excised if a thrombus was found inside the left atrium or LAA. Tricuspid annuloplasty was performed using a Carpentier-Edwards Physio tricuspid annuloplasty ring if more than moderate tricuspid regurgitation was diagnosed by echocardiography.

VIDEO 1. Surgical procedure. Video available at: [http://www.jtcvsonline.com/article/S0022-5223\(17\)31787-7/fulltext](http://www.jtcvsonline.com/article/S0022-5223(17)31787-7/fulltext).

VIDEO 2. Incisions of the posterior free wall of the left atrium. Video available at: [http://www.jtcvsonline.org/article/S0022-5223\(17\)31787-7/fulltext](http://www.jtcvsonline.org/article/S0022-5223(17)31787-7/fulltext).

Postoperative Protocols

In the Maze III group, amiodarone was selectively used in patients who experienced atrial or ventricular arrhythmias during hospitalization and was continued for 3 months if no contraindications existed. Electrical cardioversion was performed as needed within the first 6 months after surgery.

In the non-Maze group, amiodarone was used when sinus rhythm (SR) was restored after electrical cardioversion was performed during surgery. However, if SR failed to restore, external electrical cardioversion was not provided, and rate control strategy was obliged to perform because of the negligible success rate (external electrical cardioversion was not used if SR failed to restore after 3 months). Digoxin or beta-blockers was used to control heart rate in all patients without bradycardia for at least 3 months postoperatively.

After surgery, heart rhythm was monitored continuously throughout the hospital stay, and temporary epicardial wires were used for atrial and/or ventricular pacing as needed. For patients who received a mechanical prosthesis, warfarin was continued. For patients who received a bioprosthetic implant, if stable SR was achieved, warfarin was administered for 3 months, but if AF or atrial flutter persisted, warfarin was continued beyond this time point. The target range for prothrombin time/International Normalized Ratio (INR) was 2.0 to 2.5.

FIGURE 1. Incision of left lesions and cryoablation. (A) The left appendage is inverted and amputated, and a 1.5-cm cryoprobe is used to freeze the intervening tissue, effectively joining these incisions. (B) Cryolesions are placed on the coronary sinus and mitral annulus.

VIDEO 3. Cryolesions at the left Maze lesions. Video available at: [http://www.jtcvsonline.org/article/S0022-5223\(17\)31787-7/fulltext](http://www.jtcvsonline.org/article/S0022-5223(17)31787-7/fulltext).

Follow-up

All patients were prospectively followed up at our outpatient clinic at 1, 3, 6, and 12 months postsurgery and then yearly thereafter. Heart rhythm was defined mainly on the basis of 24-hour Holter ECG and in part by 12-lead ECG. Left atrial dimension (LAD), left ventricular diastolic dimension (LVEDD), left ventricular systolic dimension (LVESD), left ventricular ejection fraction (LVEF), and A-waves were evaluated by 2-dimensional echocardiographic analysis and Doppler color flow imaging (Philips iE33 ultrasound machine; Philips Healthcare, Andover, Mass). INR values were recorded at regular intervals.

Statistical Analysis

In the literature, the incidence of a composite of stroke or death is approximately 20% in patients with undergoing MVR without the Maze III procedure, and the highest reported incidence in patients undergoing

FIGURE 2. Incision of the right lesion and cryoablation. The right appendage is inverted, and this incision is taken to the tricuspid annulus, again dissecting from within the atrium, and a cryolesion is placed at the annulus. *The 2 sites and lines of cryoablation.

FIGURE 3. Double full-layer inverting mattress sutures. The left atrial incisions are closed to the right-sided pulmonary veins.

MVR with the Maze III procedure is approximately 3%. In this study, at $\alpha = 0.05$, we calculated that enrollment of 65 cases would give this study 95.26% power. SPSS version 17.0 (SPSS, Chicago, Ill) and GraphPad Prism 5 (GraphPad Software, La Jolla, Calif) were used for statistical analysis. The Kolmogorov–Smirnov χ^2 test was applied to determine normality. Continuous data were reported as mean $\pm$ standard deviation, and the difference between the 2 groups were evaluated using the Student *t* test for mean values of normally distributed continuous variables. Continuous data are expressed as median and range, and outcomes were compared using the Mann–Whitney *U* test for non-normally distributed data. Categorical outcomes are presented as percentages and were compared using either the Pearson χ^2 test or Fisher exact test. A generalized linear model was used for comprehensive assessment of heart rhythm at different times in the 2 groups. Between-group differences in echocardiography measures and INR from baseline to 12 months postsurgery were evaluated by repeated-measures analysis of variance. Survival and stroke curves were calculated using the Kaplan–Meier method and compared using the log-rank test. $P < .05$ was considered to indicate statistical significance.

VIDEO 4. Closure of the encircling incision. Video available at: [http://www.jtcvsonline.org/article/S0022-5223\(17\)31787-7/fulltext](http://www.jtcvsonline.org/article/S0022-5223(17)31787-7/fulltext).

VIDEO 5. Incision and closure of the left atrial appendage. Video available at: [http://www.jtcvsonline.org/article/S0022-5223\(17\)31787-7/fulltext](http://www.jtcvsonline.org/article/S0022-5223(17)31787-7/fulltext).

RESULTS

Patients

Between October 2013 and January 2015, a total of 130 patients were enrolled in this study. Of these, 65 patients (19 males and 46 females) were assigned at random to the CSM Maze III group (Maze III group), and 65 (29 males and 36 females) were assigned to the MVR-alone group (non-Maze group). The trial design and patient profiles are shown in Figure 4. There was no significant between-group difference in age, sex, LVEF, AF status (persistent or permanent), New York Heart Association function class, left atrial and left ventricular dimension (LAD, LVEDD, LVESD), types of mitral valve pathology, drug history (anticoagulants and antiarrhythmics), and history of stroke, hypertension, or diabetes. Preoperative patient characteristics are summarized in Table 1.

Perioperative Results

As shown in Table 2, the mean aortic cross-clamp time was approximately 30 minutes longer in the Maze III group than in the non-Maze group ($P < .001$), and the mean cardiopulmonary bypass time was approximately 60 minutes longer in the Maze III group ($P < .001$). The distribution of concomitant surgical procedures was similar in the 2 groups.

Early mortality did not differ between the 2 groups; 1 patient (1.5%) died in each group ($P = 1.000$). In the Maze III group, 1 patient died of multiple organ failure due to left ventricular rupture at 4 days after repair. The cause of early death in the patient in the non-Maze group was heart failure.

FIGURE 4. Trial design and profile.

The rate of in-hospital major complications, including low cardiac output syndrome, heart failure, early stroke, renal failure, reexploration for bleeding, and pneumonia, did not differ significantly between the 2 groups (Table 2). However, there was a significant difference in the need for temporary pacemaker implantation (75.4% in the Maze III group vs 7.7% in the non-Maze group; $P < .001$). Use of an intra-aortic balloon pump (IABP) and electrical cardioversion were not statistically significantly different between the 2 groups ($P = 1.000$ and 0.244 , respectively).

The median length of intensive care unit (ICU) stay was not significantly different between groups (25 hours in

the Maze III group vs 24 hours in the non-Maze group; $P = .832$). The mean length of hospital stay was approximately 15 days for the Maze III group and 14 days in the non-Maze group, a statistically significant difference ($P = .031$). In addition, amiodarone use also differed significantly between the 2 groups ($P < .001$).

The mean cost of hospitalization was higher in the Maze III group ($\$17,053.59 \pm \2763.21 vs $\$15,548.80 \pm \4505.18 ; $P = .023$), as a result of the greater need for temporary pacemaker implantation and longer hospital stays.

TABLE 1. Preoperative data

Variable	Maze III (n = 65)	Non-Maze (n = 65)	t/ χ^2 value	P value
Female sex, n (%)	46 (70.8)	36 (59.0)	3.303	.069
Age, y, mean $\pm$ SD	55.92 $\pm$ 7.17	55.37 $\pm$ 7.67	0.426	.671
Type of AF, n (%)				
Persistent	12 (18.51)	13 (20)	0.050	.824
Long-standing persistent	53 (81.5)	52 (80)	0.050	.824
Lesion set, n (%)				
Stenosis	14 (21.5)	13 (20)	0.047	.829
Regurgitation	3 (4.6)	4 (6.2)	0.151	.698
Combined	48 (73.8)	48 (73.8)	0.000	1.000
With TR	22 (33.8)	21 (32.3)	0.035	.852
LAD, mm, mean $\pm$ SD	51.75 $\pm$ 8.02	51.43 $\pm$ 8.43	0.224	.823
LVEF, mm, mean $\pm$ SD	0.55 $\pm$ 0.04	0.54 $\pm$ 0.03	1.569	.119
LVEDD, mm, mean $\pm$ SD	48.68 $\pm$ 7.18	50.07 $\pm$ 6.88	-1.310	.192
LVESD, mm, mean $\pm$ SD	35.32 $\pm$ 5.61	35.62 $\pm$ 5.43	-0.302	.764
NYHA functional class, n (%)				
III	64 (98.5)	63 (96.9)	0.341	.559
IV	1 (1.5)	2 (3.1)	0.341	.559
Cardiothoracic ratio, mean $\pm$ SD	0.55 $\pm$ 0.04	0.55 $\pm$ 0.03	1.171	.244
History of stroke, n (%)	5 (7.7)	8 (12.3)	0.769	.380
Left atrial thrombus, n (%)	15 (23.1)	11 (16.9)	0.769	.380
Oral anticoagulants, n (%)	10 (15.4)	9 (13.8)	0.062	.804
Hypertension, n (%)	12 (18.5)	14 (21.5)	0.192	.661
Diabetes mellitus, n (%)	7 (10.8)	10 (15.4)	0.609	.435
Antiarrhythmic drug use, n (%)	5 (7.7)	8 (12.3)	0.769	.380

SD, Standard deviation; AF, atrial fibrillation; TR, tricuspid regurgitation; LAD, left atrial dimension; LVEF, left ventricular ejection fraction; LVEDD, left ventricular diastolic dimension; LVESD, left ventricular systolic dimension; NYHA, New York Heart Association.

Follow-up Results

Among the 128 early survivors, 8 patients (6.25%) were lost to follow-up after the initial hospitalization. Three patients in the Maze III group were lost, at 1 month, 4 months, and 5 months. The 5 patients lost to follow-up in the non-Maze group included 3 within 3 months (2 at 2 months and 1 at 1 month) and 2 within 6 months (1 at 4 months and 1 at 5 months). During the follow-up period, there were no deaths in the Maze III group, but 3 deaths in the non-Maze group, due to anticoagulation-related cerebral bleeding in 2 patients at 8 months and 10 months after discharge and to embolic stroke in 1 patient at 5 months after discharge.

No patients in the Maze III group but 8 patients in the non-Maze group experienced stroke after discharge, even though all of these patients' INR values were within the target range (2.0 to 2.5). Among these 8 patients, 3 died of cerebral bleeding, 1 died of embolic stroke, and 5 survived after embolic stroke. One-year freedom from stroke or death was better in the Maze III group compared with the non-Maze group, as shown in the Kaplan-Meier plot in Figure 5 (hazard ratio, 0.2653; 95% confidence

interval, 0.1122 to 0.6270; $P = .0028$). The survival rate at 1 year postsurgery was 93.84% in the Maze III group and 86.15% in the non-Maze group. Actuarial survival curves did not differ significantly between the 2 groups (hazard ratio, 0.4501; 95% confidence interval, 0.1511 to 1.341; $P = .1517$) (Figure 6).

The risk of AF recurrence was 0.002-fold greater ($P = .000$) in the Maze III group compared with the non-Maze group. At 1 year, 92.9% (52 of 56) of patients in the non-Maze group continued to receive β -blockers or amiodarone for heart rate control, compared with only 8.2% (5 of 61) of the patients in the Maze III group ($\chi^2 = 83.760$; $P < .001$).

In this study, both groups showed significant reductions in LAD, LVEDD, and LVESD and significant improvement in LVEF compared with preoperative findings (Table 3). Meanwhile, at 1 year postsurgery, patients in the Maze III group had significantly greater LVEF and significantly smaller LAD than those in the non-Maze group ($P < .001$ and $.002$, respectively), but there were no significant between-group differences in LVEDD and LVESD ($P = .928$ and 0.240 , respectively). At the last follow-up,

TABLE 2. Perioperative results

Variable	Maze III (n = 65)	Non-Maze (n = 65)	t/χ^2 /Mann-Whitney <i>U</i> test value	<i>P</i> value
Cardiopulmonary bypass time, min, mean $\pm$ SD	164.82 $\pm$ 30.57	107.03 $\pm$ 18.96	12.949	.000
Cross-clamp time, min, mean $\pm$ SD	88.06 $\pm$ 13.46	54.20 $\pm$ 8.49	17.399	.000
Concomitant procedures, n (%)				
Tricuspid valve plasty	22 (33.8)	21 (32.3)	0.035	.852
CABG	6 (9.2)	5 (7.7)	0.099	.753
Left atrium thrombectomy	8 (12.3)	9 (13.8)	0.068	.795
Type of prosthesis, n (%)				
Mechanical prosthesis	61 (93.8)	60 (92.3)	0.119	.730
Bioprosthesis	4 (6.2)	5 (7.7)	0.119	.730
Serious adverse events, n (%)				
Low cardiac output syndrome	4 (6.2)	5 (7.7)	0.119	.730
Heart failure	1 (1.5)	1 (1.5)	0.000	1.000
Early stroke <30 d, n (%)				
Ischemic	1 (1.5)	3 (4.6)	1.032	.301
Hemorrhagic	0	0		
Peacemaker implantation, n (%)				
Temporary pacemaker	49 (75.4)	5 (7.7)	61.326	.000
Permanent pacemaker	0	0		
Renal failure, %	0	0		
Reexploration, n (%)	1 (1.5)	3 (4.6)	1.032	.301
Pneumonia, n (%)	8 (12.3)	9 (13.8)	0.068	.795
Early death, n (%)	1 (1.5)	1 (1.5)	0.000	1.000
Intra-aortic balloon pump, n (%)	1 (1.5)	1 (1.5)	0.000	1.000
ICU stay, h, median (range)	25 (16-94)	24 (22-56)	2067.500	.832
Hospital stay, d, median (range)	15 (11-25)	14 (12-18)	1658.000	.031
Electrical cardioversion, n (%)	5 (7.7)	2 (3.1)	1.359	.244
Amiodarone use, n (%)	33 (50.8)	11 (16.9)	16.628	.000
Hospital cost, US\$, mean $\pm$ SD	17,053.59 $\pm$ 2763.21	15,548.80 $\pm$ 4505.18	2.296	.023

SD, Standard deviation; CABG, coronary artery bypass grafting; ICU, intensive care unit.

the number of patients with an A-wave differed significantly between the 2 groups: mitral A-wave: 86.9% (53 of 61) in the Maze III group versus 0 in the non-Maze

group; $\chi^2 = 88.949$; $P < .001$; tricuspid A-wave: 96.7% (59 of 61) in the Maze III group versus 8.9% (5 of 56) in the non-Maze group; $\chi^2 = 90.817$; $P < .001$.

FIGURE 5. Composite Kaplan-Meier curves of freedom from stroke and death for the Maze III group (dotted blue line) and non-Maze group (solid red line). Tick marks represent censored data; error bars represent 95% confidence limits.

FIGURE 6. Actuarial survival curves. Freedom from composite of stroke or death curves for the Maze III group (solid red line). Tick marks represent censored data; error bars represent 95% confidence limits.

TABLE 3. Comparison of echo measurements between the 2 groups

Variable	Maze III				Non-Maze			
	Preoperative	1 mo	3 mo	1 y	Preoperative	1 mo	3 mo	1 y
LAD, mm	51.92 ± 8.01	43.02 ± 5.07	43.79 ± 6.99	42.36 ± 5.69	51.45 ± 8.50	43.80 ± 6.66	44.11 ± 5.76	45.61 ± 5.26
LVEDD, mm	48.69 ± 7.32	43.89 ± 6.06	45.08 ± 4.53	44.28 ± 3.42	49.79 ± 6.23	45.61 ± 5.85	45.46 ± 4.50	44.34 ± 3.82
LVESD, mm	35.38 ± 5.74	32.44 ± 5.01	32.69 ± 3.35	32.11 ± 3.34	35.43 ± 5.40	32.75 ± 4.59	33.59 ± 3.22	32.84 ± 3.28
LVEF	0.55 ± 0.03	0.59 ± 0.03	0.58 ± 0.04	0.60 ± 0.03	0.54 ± 0.03	0.59 ± 0.03	0.57 ± 0.03	0.55 ± 0.04

Data are mean ± standard deviation. LAD, Left atrial dimension; LVEDD, left ventricular diastolic dimension; LVESD, left ventricular systolic dimension; LVEF, left ventricular ejection fraction.

Echocardiography showed no significant tricuspid insufficiency in either group at the last follow-up. There were no significant differences in INR values between the 2 groups at any time point (baseline, $P = .979$; 1 month, $P = .521$; 3 months, $P = .093$; 12 months, $P = .215$) (Table 4).

DISCUSSION

The CSM is still not universally accepted as standard practice in the surgical treatment of AF even though it has been repeatedly demonstrated to be the most effective approach to curing AF. The complexity of the procedure and concerns about bleeding are considered the major drawbacks of CSM. Consequently, surgical ablation with alternative sources of energy, such as radiofrequency and cryoablation, has become the predominant surgical technique for AF. Nonetheless, in a previous report from our center, 1-year freedom from AF was only 76% and 5-year freedom from AF was only 67% after surgical ablation using bipolar radiofrequency to treat AF associated with RMVD.⁸ Moreover, surgical ablation is associated with significantly higher hospital costs compared with the CSM, and thus is less cost-effective. For these reasons, we made a procedural switch from surgical ablation to CSM to improve the long-term outcomes of this patient population.

Our results in the present study demonstrate that the addition of CSM is not associated with a significant increase in early mortality compared with MVR alone. Our results are in agreement with other reported series.^{10,18,19} Furthermore, the incidence of postoperative complications did not differ significantly between our 2 groups despite the longer cardiopulmonary bypass and aortic cross-clamp times in the Maze III group. More importantly, we found that the addition of CSM is associated with a significant decrease in the incidence of stroke or death at 1 year. In

this study, 86.0% of the Maze III patients showed restoration of left atrial transport function. This restored left atrial transport function after CSM may contribute to the prevention of thrombus formation in the left atrium, and hence a lower incidence of embolic stroke. Buber and colleagues²⁰ reported similar findings that showed a significantly greater risk of thrombus embolization in patients in whom atrial transport function was not restored even if SR conversion had been achieved.²⁰

Some surgeons are reluctant to perform additional CSM because of the belief that patients with a mechanical prosthesis must receive warfarin therapy. However, Bando and colleagues²¹ have reported that restoration of SR nearly eliminated the incidence of stroke after the Maze procedure plus MVR, whereas therapeutic anticoagulation could not prevent the risk of late stroke if AF was left untreated.²¹ In the present study, there were 3 late deaths in the non-Maze group due to anticoagulation-related cerebral complications, even though these patients' INR values were within the target range of 2.0 to 2.5.

The main purpose of the Maze III procedure is to eliminate symptomatic tachycardia, hemodynamic impairment caused by the loss of atrial contraction, and thromboembolism. As expected, we found significant improvements in left ventricular size and function after additional CSM. We also found an A-wave in the majority of patients in the Maze III group. The improvements in left ventricular and left atrial function would definitely contribute to positive long-term outcomes in these patients.

This study also demonstrates that adding the Maze III procedure effectively reduces the risk of AF recurrence. The majority of patients in the Maze III group were able to discontinue antiarrhythmic drugs, whereas the majority in the non-Maze group still required medication to control heart rate. The major drawbacks of the addition of CSM in our series were the significantly longer length of hospital

TABLE 4. Comparison of INR between the 2 groups

Variable	Maze III				Non-Maze			
	Preoperative	1 mo	3 mo	1 y	Preoperative	1 mo	3 mo	1 y
INR	1.145 ± 0.210	2.317 ± 0.171	2.297 ± 0.219	2.277 ± 0.182	1.146 ± 0.184	2.294 ± 0.201	2.322 ± 0.172	2.230 ± 0.207

Data are mean ± standard deviation. INR, International Normalized Ratio.

stay and duration of temporary pacemaker implantation compared with the non-Maze group, with accordingly higher average hospitalization costs. Nonetheless, this cost is still much lower than that associated with bipolar radiofrequency ablation, according to our unpublished study of the efficacy of radiofrequency ablation for treating AF. In our unpublished study, we found a significantly higher average hospital cost in the Maze IV group compared with Maze III group (\$18,773.40 $\pm$ \$2973.415 vs \$16,983.4 $\pm$ \$2704.3; $P = .005$). Most of the patients who underwent an additional Maze III procedure required implantation of a temporary pacemaker because of persistent bradycardia or nodal rhythm in the perioperative period. The “wait, watch, and see” period prolongs the length of hospital stay. However, no patients required permanent pacemaker implantation. Several factors contributed to this: first, the younger patient age at surgery, with a lower incidence of sick sinus syndrome, and second, the exclusion of patients with a prolonged R-R interval demonstrated on 24-hour Holter ECG, and those with heart rate <60 bpm after electric conversion during surgery from the Maze III procedure. More importantly, after discharge, most of the patients who underwent CSM had discontinued anti-arrhythmic drugs, and the incidence of stroke was significantly reduced, contributing to improved quality of life and long-term outcomes. Although alternate energy sources offer the advantages of quicker application and the possibility of minimally invasive applications, CSM arguably remains the reference standard for the surgical treatment of AF and should still be considered, especially for patients in whom AF ablation is of critical importance.²²

One major reason cited for surgeons' reluctance to perform CSM is the perceived increased risk of bleeding and prolonged cardiopulmonary bypass. We routinely used double-continuous full-layer inverting mattress sutures with 4-0 polypropylene for all left-side incisions, which have proven very effective in preventing bleeding. There was no significant bleeding related to the left or right atrial Maze III lesions in our series.

In conclusion, the addition of the CSM technique to MVR may be associated with decreased risk of stroke and death at 1 year postsurgery, as well as a high sinus conversion rate, with no increase in operative risk. CSM is a safe and effective treatment for AF associated with RMVD. AF is an independent disease and should be treated primarily instead of secondarily. It is time for surgeons to reassess their preconceptions and be more open to performing CSM concomitantly with MVR to treat AF.

Study Strengths and Limitations

First, we followed strict inclusion and exclusion criteria. Only patients with RMVD were enrolled, and those with degenerative or ischemic mitral valve lesions were

excluded; however, this design also reduced the impact of etiology bias on the results. Second, according to the study design, only patients with persistent or long-standing persistent AF were included; thus, our results might not be applicable to patients with paroxysmal AF associated with RMVD. Third, all patients were enrolled from a single center, and the results might not be generalizable for other centers. Fourth, in the non-Maze group, LAA was managed by either LAA exclusion or LAA ligation owing to ethical considerations, given evidence showing that routine LAA ligation during cardiac surgery may prevent postoperative AF-related cerebrovascular accident²³; however, LAA elimination is often incomplete and goes undetected.²⁴ In this study, the management of LAA was not unified, and the completeness of LAA elimination was not evaluated. Fifth, this study does not provide any guidance as to whether other forms of the Maze procedure are equivalent in this patient population. Finally, the number of patients was relatively small, and the 1-year follow-up period was short. Additional data are needed to evaluate the addition of CSM to MVR in a longitudinal study.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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Key Words: cut-and-sew Maze procedure, prospective randomized trial, atrial fibrillation, rheumatic valve disease

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