

## Outcome of Concomitant Cox Maze Procedure with Narrow Mazes and Left Atrial Volume Reduction

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**Background:** To improve sinus rhythm conversion, the Cox maze III procedure with narrow mazes (width:  $\leq 3.0$  cm) was performed in combination with left atrial volume reduction. **Methods:** From October 2007 to April 2013, 87 patients with atrial fibrillation (paroxysmal in 3, persistent in 14, and permanent in 70) underwent the Cox maze procedure concomitant with another cardiac procedure. They were followed-up with serial electrocardiographic and echocardiographic studies. We used 24-hour Holter monitoring tests to evaluate postoperatively symptomatic patients. **Results:** At the mean follow-up time of 36.4 months, 81 patients (94.2%) had sinus rhythm and two were on anti-arrhythmic medication (one on a beta-blocker and the other on amiodarone). Five patients (5.8%) with postoperative recurrent and persistent atrial fibrillation never experienced sinus rhythm conversion; however, they did not require any medication for rate control. On postoperative echocardiography, the left atrial A waves were more frequently observed after concomitant mitral valve repair than after concomitant mitral valve replacement (82.4% vs. 40.4%, respectively;  $p < 0.001$ ). **Conclusion:** For the Cox maze procedure, narrow mazes and atrial volume reduction resulted in excellent sinus rhythm conversion without the preventive use of anti-arrhythmic drugs, and they did not affect the presence of the left atrial A waves on echocardiography.

Key words: 1. Arrhythmia surgery  
2. Technique  
3. Outcome assessment

### INTRODUCTION

Atrial fibrillation (AF) is present in up to 50% of the patients undergoing mitral valve surgery and in 1% to 6% of the patients undergoing coronary artery bypass grafting or aortic valve surgery [1-3]. Since the introduction of the maze procedure for the treatment of AF in 1987 [4], it has been simplified by replacing the maze incisions with cryoablation and radiofrequency ablation [5]. Although some randomized trials have demonstrated an excellent conversion rate of sinus

rhythm with radiofrequency ablation [6], 20% to 30% of the patients undergoing the maze procedure have exhibited recurrent AF during the follow-up period [7].

Among the maze procedures that were performed in the same fashion, the dimensions of the mazes differ widely in accordance with the left atrial sizes. However, maze dimensions are an important factor for successful sinus rhythm conversion, interrupting reentrant circuits in the left atrium (LA). We set the maze dimension at  $\leq 3.0$  cm in all patients requiring the maze procedure. The enlarged LA was reduced

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**Table 1.** Patient characteristics (n=87)

Characteristic	Value
Age (yr)	59.5±10.0 (34–78)
Male gender	34 (39.1)
Hypertension	52 (59.8)
Diabetes mellitus	13 (14.9)
Congestive heart failure	39 (44.8)
Duration AF (mo)	58.1±89.2
Duration AF (mo)	30 (2–500)
Left atrial dimension (mm)	55.8±9.7 (31–85)
Giant left atrium <sup>a)</sup>	24 (27.6)
Paroxysmal/persistent/permanent AF	3/14/70 (3.4/16.1/80.5)
Left ventricular ejection fraction (%)	55.8±6.7
Previous cerebro-vascular accident	5 (5.7)
Redo-valve surgery	3 (3.4)
Mitral valve lesion	78 (89.5)
MS dominant	44 (56.4)
MR dominant	34 (43.6)
Double- and triple-valve disease	25 (28.7)
Non-valve lesion	3 (3.4)

Values are presented as mean±standard deviation, number (%), or median (range).

AF, atrial fibrillation; MS, mitral stenosis; MR, mitral regurgitation.

<sup>a)</sup>Left atrial dimension > 60 mm.

by the resection of the redundant inferior wall of the LA with and without plication of the posterior walls, left lateral wall, or superior walls of the LA. The aim of this study is to evaluate the efficacy of narrow mazes and left atrial reduction in the Cox maze procedure.

## METHODS

This study was approved by Chonbuk National University Hospital institutional review board. Each patient included in these analyses provided informed consent.

### 1) Patients and combined surgery

From October 2007 to April 2013, 87 patients (34 men and 53 women; mean age, 59.5±10.0 years) with paroxysmal (n=3.4%), persistent (n=14, 16.1%), or permanent AF (n=70, 80.5%) underwent the Cox maze procedure concomitant with another cardiac operation (Table 1). The primary surgical indication was structural heart disease in all patients. Mitral valve disease was observed in 78 patients (89.5%); 41

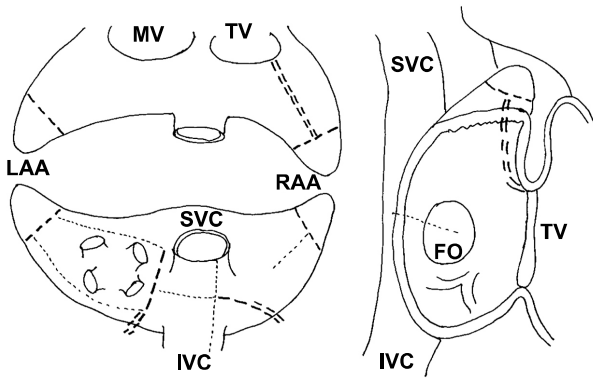
**Table 2.** Surgical procedures

Variable	Value
Concomitant procedures	
Mitral valve replacement	41 (47.1)
Mitral valve repair	37 (42.5)
Tricuspid valve repair	69 (79.3)
Isolated tricuspid valve repair	3 (3.4)
Coronary artery bypass graft	3 (3.4)
Ascending aortic aneurysm	3 (3.4)
Aortic root reimplantation	1 (1.1)
Myxoma	1 (1.1)
Atrial septal defect	1 (1.1)
Ventricular septal defect	1 (1.1)
No. of procedures	
2	11 (12.6)
3	48 (55.5)
4	25 (28.7)
5	3 (3.4)
Left atrial reduction plasty	
Left atrial appendage excision	87 (100.0)
Isthmus resection	34 (39.1)
Left atrial lateral wall plication	9 (10.3)

Values are presented as number (%).

(47.5%) underwent mitral valve replacement, and 37 (42.5%) underwent mitral valve repair. Non-valve cardiac disease was present in three patients (3.4%); one each with myxoma, a huge left atrial thrombus, and an ascending aortic aneurysm. Twenty-five patients (28.7%) underwent multi-valve surgery. The mean duration of AF was 58.1±89.2 months (range, 2 to 500 months).

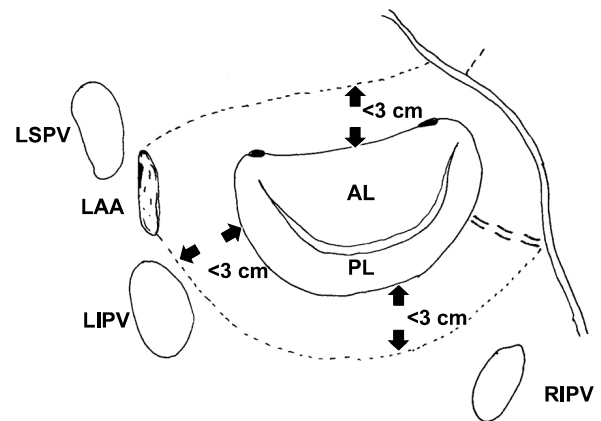
The mean atrial dimension was 55.8±9.7 mm (range, 31 to 85 mm) in the two-dimensional parasternal long-axis view. Left atrial reduction plasty by an isthmus excision was performed in 34 patients (39.1%); nine (10.3%) required additional plication of the posterior wall, the left lateral wall, and the superior wall of the enlarged LA (Table 2). Sixty-nine patients (79.3%) underwent tricuspid valve repair. Of these, three (3.4%) underwent isolated tricuspid valve repair and right atrial reduction plasty. All data were retrospectively analyzed from the medical records, including the operative records, standard 12-lead electrocardiograms, and transthoracic and transesophageal echocardiograms.



**Fig. 1.** The Cox maze procedure. Epicardial view of the atria and endocardial view of the right atrium. Both atrial appendages were amputated and narrow mazes (maze width  $<3.0$  cm) were made in both atria. Thick single-dotted lines represent 'cut-and-sew' lesions; thick double-dotted lines represent cryoablation lines; and fine single-dotted lines represent ablation lines that were made using a bipolar radiofrequency electrode. MV, mitral valve; TV, tricuspid valve; LAA, left atrial appendage; RAA, right atrial appendage; SVC, superior vena cava; IVC, inferior vena cava; FO, foramen ovale.

## 2) Surgical procedures

**(1) Maze procedure:** We performed the Cox maze procedure for all the study patients by using a combination of radiofrequency and cryoablation lesions. To make precise ablation lesions, a bipolar radiofrequency electrode (Medtronic Inc., Minneapolis, MN, USA) was applied for an additional 40 seconds after each lesion did not conduct electricity. A cryoprobe (Cooper Surgical, Trumbull, CT, USA) was applied for 90 seconds per lesion (Fig. 1) [8]. A left atriotomy incision was made through Sondergaard's groove, and a vertical right atriotomy was made at the bottom 1/3 of the right atrium. After both atrial appendages were amputated, a box lesion circumscribing four pulmonary veins was made through the left atriotomy and the left atrial appendage opening, using a bipolar radiofrequency electrode, and four more radiofrequency lesions were made in the right atrial wall, the posterior septal wall, and the superior and inferior sinuses. Two cryoablation lesions were made on the right atrial wall: one between the right atriotomy and the tricuspid annulus, and the other between the right atrial appendage opening and the tricuspid annulus. Two additional cryoablation lesions were



**Fig. 2.** A narrow maze in the left atrium. The ablation lines circumscribing the pulmonary veins were made  $\le 3.0$  cm away from the mitral valve annulus in all directions. LSPV, left superior pulmonary vein; LAA, left atrial appendage; LIPV, left inferior pulmonary vein; AL, anterior leaflet; PL, posterior leaflet; RIPV, right inferior pulmonary vein.

made on the inner and the outer LA walls between the inferior end of the left atriotomy and the mitral annulus, including the coronary sinus. The left atrial appendage opening was externally closed with a continuous 4-0 polypropylene suture and reinforced with 3 to 4 interrupted pledgeted 4-0 polypropylene sutures.

The radiofrequency box lesions circumscribing four pulmonary veins were made within 3.0 cm of the mitral annulus in all directions (Fig. 2). In the right atrial wall and the interatrial septum, the distances between the ablation lines were also  $\le 3.0$  cm.

**(2) Atrial reduction plasty:** The redundant inferior wall of the enlarged LA (LA dimensions:  $>50$ - $55$  mm) was excised just above the coronary sinus and then re-sutured using continuous 4-0 polypropylene sutures. For a markedly enlarged LA with a redundant thin atrial wall in all directions, plication of the left lateral wall, the superior wall, and the posterior walls of the LA was performed if necessary, as well as the excision of the redundant inferior wall. The left atrial plication was performed using two rows of continuous 4-0 polypropylene sutures [9].

**Table 3.** Perioperative and late postoperative characteristics

Variable	Value
Bypass time (min)	228±43
Cross clamp time (min)	187±41
Postoperative temporary pacing	22 (25.6)
In-hospital postoperative atrial fibrillation	22 (25.6)
Pneumonia	2 (2.3)
Permanent pacemaker for sinus node dysfunction	2 (2.3)
Recovery to sinus rhythm	
Immediately after surgery	87/87 (100.0)
At postoperative month 6	80/86 (93.0)
At the last follow-up	81/86 (94.2)
Mean clinical follow-up period (mo)	36.4±17.4
Mean echocardiographic follow-up period (mo)	17.8±17.2

Values are presented as mean±standard deviation or number (%).

### 3) Echocardiography

Transthoracic echocardiographic images were obtained with commercially available echocardiography machines (Vivid 7 system; GE Healthcare, Milwaukee, WI, USA) equipped with 2.5-MHz transducers. LA dimensions were measured on an M-mode tracing taken from a parasternal long-axis view. At discharge from the hospital and after more than 6 postoperative months, left atrial 'A' waves, suggesting the mechanical contraction of LA, were assessed in four-chamber views and the E/A ratios were measured.

### 4) Postoperative follow-up

Patients who experienced postoperative sinus rhythm conversion were temporarily prescribed anticoagulation therapy and either digoxin or a beta-blocker. Class I or III antiarrhythmic agents were not used. In cases of recurrent or persistent AF after surgery, a class III antiarrhythmic drug (amiodarone) was held for three months until the sinus rhythm was restored; electrical cardioversion was not performed. Anticoagulation therapy was discontinued at 3 postoperative months for patients without mechanical valve replacement and another indication for anticoagulation medication. Continuous treatment of warfarin was employed for one patient with a huge left atrial thrombus and another with a questionable left ventricular thrombus. All other patients received continuous aspirin (100 mg per a day).

Echocardiography was performed before surgery, during postoperative admission, at discharge, at 6 months, and then annually. Patients who had paroxysmal palpitation were asked to undergo 24-hour Holter monitoring to assess their sinus rhythm.

### 5) Statistical analysis

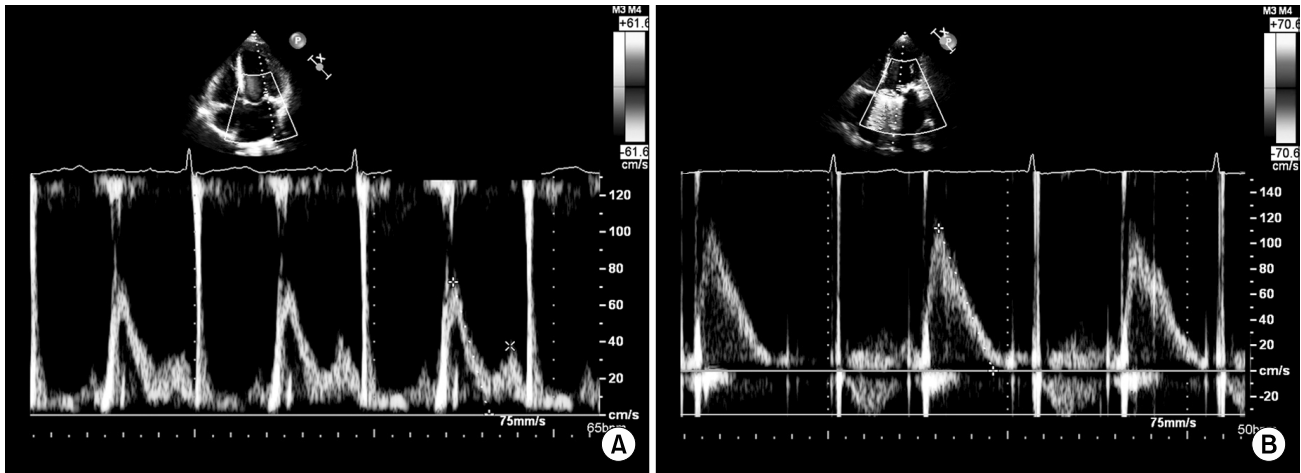
All data were expressed as mean and standard deviation. Categorical variables were compared using the chi-square or Fisher's exact tests. The Mann-Whitney U-test was used to compare the nonparametric samples. A logistic regression analysis was performed to determine predictive factors regarding the maintenance of the sinus rhythm, and a stratified analysis using the Mantel-Haenszel chi-square test was performed to assess the impacts of rheumatic valve disease and mitral valve surgery on the presence of the left atrial A waves. The PASW SPSS ver. 18.0 (SPSS Inc., Chicago, IL, USA) program was used for all the statistical calculations. A confidence level of 95% was considered statistically significant.

## RESULTS

### 1) Postoperative data

In the operating room after surgery, 22 patients (25.6%) required temporary ventricular pacing due to bradycardia: the remaining 64 (74.4%) showed sinus rhythm (Table 3). Twenty-two patients (26.5%) experienced an AF relapse during their hospital stay: 17 of them experienced return to sinus rhythm before discharge.

During a mean follow-up of 38.4±17.4 months (range, 6 to 69 months), 86 patients were completely followed-up, while one died of pneumonia at postoperative day 82. At discharge, 80 (93.0%) of the patients exhibited sinus rhythm, and the remaining 6 (7.0%) were prescribed amiodarone. Of the 80 patients who obtained sinus rhythm conversion, 73 (84.9%) had no anti-arrhythmic medication at discharge and seven (8.1%) were prescribed a beta-blocker or diltiazem for rate control due to sinus tachycardia. At 6 months, 80 patients (93.0%) had sinus rhythm recovery without antiarrhythmic medication, while one patient returned to sinus rhythm and another to recurrent AF. At the last follow-up, 81 patients (94.2%) had si-



**Fig. 3.** Sample echocardiographic examinations of two patients after the Cox maze procedure. Examples of echocardiograms from a patient (A) with and (B) without the left atrial A waves, suggesting mechanically active and inactive atria, respectively.

nanus rhythm (Table 3) and two (2.3%) were taking amiodarone due to the intermittent recurrence of AF. Two patients (2.3%) had permanent pacemaker insertion for sinus node dysfunction at 4 and 6 months, respectively.

A postoperative left atrial thrombus developed after the discontinuation of warfarin in one woman with an LA 60 mm in size that would not be diminished due to the LA wall calcification. It disappeared quickly with warfarin re-medication.

### 2) Factors predicting sinus rhythm conversion after the maze procedure

The presence of sinus rhythm at postoperative month 6 was the only factor predicting the sinus rhythm at the last follow-up (odds ratio, 158.0; 95% confidence interval, 11.7 to 2,131;  $p < 0.001$ ). Sex, age, underlying cardiac lesions, number of procedures, duration of AF, presence and type of mitral valve disease, preoperative and postoperative left atrial dimensions, and left ventricular ejection fraction were not risk factors for the failure of the sinus rhythm conversion.

### 3) Left atrial dimensions and left atrial reduction plasty

Although preoperative LA dimensions were greater in the patients (35 patients, 40.2%) with LA reduction plasty than in those (52 patients, 59.8%) without ( $59.5 \pm 11.6$  cm vs.  $53.4 \pm 7.3$  cm;  $p = 0.008$ ), postoperative LA dimensions did not

differ between the two groups ( $49.9 \pm 7.0$  cm vs.  $49.2 \pm 6.7$  cm;  $p = 0.652$ ).

Even without reduction plasty, the 52 patients experienced a significant decrease in the LA dimensions with the removal of the left atrial appendage and mitral valve surgery or other concomitant cardiac surgery ( $53.4 \pm 7.3$  cm preoperatively vs.  $49.2 \pm 6.7$  cm postoperatively;  $p < 0.0001$ ). Thirty-five patients who underwent reduction plasty also showed marked reduction in the LA dimensions (preoperatively vs. postoperatively,  $59.5 \pm 11.6$  cm vs.  $49.9 \pm 7.0$  cm;  $p < 0.0001$ ). A giant LA ( $> 6.0$  cm) was observed in 24 patients (27.6%) preoperatively and in four (4.6%) postoperatively. All three patients who had isolated tricuspid valve repair underwent concomitant right atrial reduction plasty due to the marked dilatation of the right atrium.

### 4) Impact of mitral valve surgery and rheumatic valve disease on left atrial A wave

Of the 78 patients undergoing mitral valve surgery, 73 ( $n = 34$ , mitral valve repair;  $n = 39$ , mitral valve replacement) revealed sinus rhythm conversion at a mean echocardiographic follow-up time of  $17.8 \pm 17.2$  months. Of the 73 patients with sinus rhythm conversion, 44 (60.3%) showed left atrial A waves (Fig. 3), suggesting mechanically active atria. A larger number of rheumatic valve patients with sinus conversion (total  $n = 44$ ) underwent mitral valve replacement than

**Table 4.** Left atrial A waves on echocardiograms of 34 rheumatic and 39 non-rheumatic patients with sinus conversion who underwent mitral valve repair and replacement combined with the maze procedure

Variable	Presence of left atrial A waves	Absence of left atrial A waves	p-value <sup>a)</sup>
Mitral valve repair (n=34)	28 (82.4)	6 (18.6)	0.001
Mitral valve replacement (n=39)	16 (40)	23 (60)	
Non-rheumatic (n=29)	24 (82.8)	5 (17.2)	0.004
Rheumatic (n=44)	20 (45.5)	24 (54.5)	

Values are presented as number (%).

<sup>a)</sup>Chi-square test.

mitral valve repair (n=34 vs. n=10), and a larger number of non-rheumatic valve patients (n=29) underwent valve repair than valve replacement (n=24 vs. n=5;  $p < 0.001$ ). The left atrial A waves were observed more frequently in patients with mitral valve repair than in those with mitral valve replacement (82.4% vs. 40.0%;  $p < 0.001$ ) and in patients with non-rheumatic diseases than in those with rheumatic mitral diseases (82.8% vs. 45.5%;  $p = 0.004$ ) (Table 4). In the stratified analysis, mitral valve repair was a predictor of the presence of left atrial A waves ( $p = 0.015$ ; odds ratio, 0.28; 95% confidence interval, 0.06 to 0.74), but the rheumatic mitral lesion did not affect the rate at which the left atrial A waves were present ( $p = 0.213$ ; odds ratio, 0.47; 95% confidence interval, 0.13 to 1.63) (Table 5).

### 5) Postoperative course in patients with recurrent and persistent atrial fibrillation

Five patients with recurrent and persistent AF had mean heart rates of 64 to 82 beats per minute. Although they did not obtain sinus rhythm conversion with the use of a class III drug (amiodarone), they did not require medication for rate control.

## DISCUSSION

For our patients, the mazes were made in a narrow width ( $\leq 3.0$  cm) and the postoperative sinus rhythm conversion rate was quite excellent at 94.2%. Although some reports

**Table 5.** Stratified analysis of two predictive factors associated with the presence of left atrial A waves

Variable	Odds ratio	95% confidence interval	p-value <sup>a)</sup>
Mitral valve surgery (repair vs. replacement)	0.28	0.06–0.74	0.015
Rheumatic valve lesion (non-rheumatic vs. rheumatic)	0.47	0.13–1.63	0.213

<sup>a)</sup>Mantel-Haenszel chi-square test.

[8,10] described similarly excellent conversion rates of  $\geq 90\%$ , most reports [11-13] have posted conversion rates of 80% to 90%. All patients in our study achieved sinus rhythm conversion or regular ventricular rhythm immediately after surgery. Although 26.5% of the patients had an AF relapse during their postoperative hospital stay, most patients (except for six patients with persistent AF) returned to sinus rhythm at discharge without anti-arrhythmic medication. A beta-blocker, digoxin, and/or diltiazem were prescribed only for the patients who had rapid sinus rhythm; class I or III antiarrhythmic agents were never used. In a previous report [10], many patients were prescribed class I or III antiarrhythmic agents at discharge, and 17% of the surgical patients remained on antiarrhythmic medication at postoperative month 24. In the present study, we did not use preventive antiarrhythmic medications at discharge. Six patients who had persistent AF at discharge were prescribed amiodarone; however, sinus rhythm conversion was not obtained, and the medication was stopped at 3 months.

In dilated or diseased atria, AF is caused by two mechanisms: triggered activity and re-entry [14]. The main aim of making the mazes in the diseased atria is not only to interrupt the most common reentrant circuits but also to direct the sinus node impulse to the AV node along a specific route [15]. In atria with pathological derangements, the reentrant circuits have variable dimensions according to their different refractory periods [16]. In particular, when the circuits are relatively small due to short refractory periods, mazes that are made in the same pattern irrespective of the atrial size cannot effectively interrupt the reentrant circuits because the maze dimensions in the enlarged atria are frequently larger than those of the reentrant circuits. Narrow mazes might be more

effective in interrupting the reentrant circuits. We made narrow mazes ( $\leq 3.0$  cm) in all directions. However, the narrow mazes reduce the effective contractile area in the LA because the mechanically active atrial myocardium is excluded by the narrow mazes. In our study, without antiarrhythmic medication after surgery, sinus rhythm was maintained in  $\geq 90\%$  of the patients without a significant recurrence of AF. At the last follow-up, two of the patients with sinus rhythm conversion were on amiodarone and a beta-blocker medication, respectively. The narrow mazes surrounding the mitral annulus appeared to prevent the development of unstable sinus conversion.

In our study, 60% of the patients who underwent mitral valve surgery had left atrial A waves on echocardiography, suggestive of mechanically active left atria. Eighty percent of our patients with mitral valve repair exhibited left atrial A waves, compared with 69% to 90% in previous reports [17,18]. The myocardium in the maze surrounding the mitral annulus can function as contractile tissue. Most patients with mitral valve repair had a flexible posterior annular strip. As the flexible strip does not fix the posterior annular motion and the anterior annulus and both commissures were free from the annular strip or ring, the annular motion after valve repair would be preserved and work together with the surrounding myocardium. Both maze (atrial) and annular contractions might result in the presence of the left atrial A waves on echocardiography. In contrast, valve replacement fixes the entire circumference of the mitral annulus, and the narrow maze around the annulus cannot actuate effective contraction because of the loss of annular contraction. Forty percent of the patients who underwent concomitant mitral valve replacement exhibited the left atrial A waves.

In a previous report [19], rheumatic mitral valve disease was a predictive factor of low atrial contraction recovery (absence of left atrial A waves) in patients who experienced sinus rhythm recovery after the maze procedure. There were more rheumatic valve patients than non-rheumatic valve patients in the present study, and the left atrial A waves were present less often in rheumatic valve patients; however, a rheumatic mitral lesion did not affect the presence of left atrial contraction in the stratified analysis, which was performed to evaluate the impacts of mitral valve surgical meth-

ods and rheumatic valve lesions in the presence of the left atrial A waves. Mitral valve repair was the only predictive factor that could affect the presence of the left atrial A waves, possibly because mitral valve replacement was preferred in rheumatic mitral valve patients.

In many studies, risk factors for the failure of sinus rhythm conversion after the maze operation were the LA size and volume, age, AF duration, limited ablation procedure, and others [20-23]. In our study, such results were not deduced because 97% of the patients had persistent and permanent AF and the recurrence rate of AF was very low. Sex, age, underlying cardiac lesions, number of procedures, duration of AF, presence and type of mitral valve disease, preoperative and postoperative left atrial dimensions, and left ventricular ejection fraction were not significant predictive factors of sinus rhythm conversion.

Although the preoperative LA size is an independent predictor of recurrent AF after the maze procedure, the postoperative recurrence rate of AF may decrease if the LA size is reduced effectively. For moderately dilated LA ( $\geq 50$  mm), the LA can be reduced by the removal of the left atrial appendage and mitral valve surgery only. However, more dilated LA (usually  $\geq 55$  mm) was sufficiently reduced by excising the redundant inferior LA wall as well as the left atrial appendage. To reduce an excessively large LA (usually  $\geq 60$  mm), plication of the redundant posterior wall between both-side pulmonary veins and the redundant left lateral wall should be added to achieve sufficient volume reduction [9]. Although the absence of a left atrial contraction after the maze procedure has been associated with a five-fold increase in the stroke risk, and the large LA volume (volume index  $> 33$  mL/m<sup>2</sup>) has been associated with a three-fold risk increase [17], our study did not deduce such evidence.

For patients who had sinus conversion but experienced palpitation, we performed 24-hour Holter monitoring to search for symptomatic paroxysmal AF. Although we did not find the arrhythmias, we were unable to rule out paroxysmal AF with the test alone.

We suggest that combining the Cox maze procedure with narrow mazes (maze width  $\leq 3.0$  cm) and volume reduction can result in an excellent sinus rhythm conversion without preventive anti-arrhythmic medication. Left atrial contraction

might be recovered more frequently after concomitant mitral valve repair than after concomitant mitral valve replacement.

In conclusion, for patients who undergo the Cox maze procedure, the recurrence of AF is common and the absence of the left atrial A waves is also frequent. With narrow mazes ( $\leq 3.0$  cm) and left atrial volume reduction, the conversion rate of the sinus rhythm was excellent and the sinus rhythm was well sustained without postoperative class I or III anti-arrhythmic medication. The left atrial A waves in patients with sinus rhythm conversion might be present more frequently after concomitant mitral valve repair than after mitral valve replacement.

### CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

### ACKNOWLEDGMENTS

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