

## Predictive Factors of Sustained Sinus Rhythm and Recurrent Atrial Fibrillation after the Maze Procedure

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**Background:** We examined perioperative predictors of sustained sinus rhythm (SR) in patients undergoing the Cox maze operation and concomitant cardiac surgery for structural heart disease. **Materials and Methods:** From October 1999 to December 2008, 90 patients with atrial fibrillation (AF) underwent the Cox maze operation and other concomitant cardiac surgery. Eighty-nine patients, all except for one postoperative death, were followed-up with serial electrocardiographic studies, 24-hour Holter monitoring tests, and regular echocardiographic studies. **Results:** Eighty-nine patients undergoing the maze operation were divided into two groups according to the presence of SR. At the time of last follow-up (mean follow-up period, 51.0±30.8 months), 79 patients (88.8%) showed SR (SR group) and 10 patients (11.2%) had recurrent AF (AF group). Factors predictive of sustained SR were the immediate postoperative conversion to SR (odds ratio, 97.2; p=0.001) and the presence of SR at the 6th month postoperatively (odds ratio, 155.7; p=0.002). Duration of AF, mitral valve surgery, number of valves undergoing surgery, left atrial dimension, and perioperative left ventricular dimensions and ejection fractions were not predictors of postoperative maintenance of SR. **Conclusion:** Immediate postoperative SR conversion and the presence of SR at the 6th postoperative month were independent predictors of sustained SR after the maze operation.

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

### INTRODUCTION

Atrial fibrillation (AF) is present in up to 50% of patients undergoing mitral valve surgery and in 1% to 6% of patients undergoing coronary artery bypass grafting or aortic valve surgery [1-3]. Since the maze operation for the treatment of AF was introduced in 1987 [4], it has been simplified by replacing most incisions for making the mazes with cryoablation or radiofrequency (RF) ablation [5]. Some randomized

trials have demonstrated an excellent conversion rate of the sinus rhythm (SR) with RF ablation [6], but, 20% to 30% of those undergoing the maze operation showed recurrent AF during the follow-up period [7]. An enlarged left atrium (LA) was a major factor in the initiation and maintenance of AF [8] and LA volume reduction was helpful for the elimination of AF in patients undergoing mitral valve surgery [9]. We identified perioperative factors predictive of maintenance of SR without recurrent AF during the follow-up period in the

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† A part of this article was presented at the 41st Autumn Academic Meeting of the Korean Society for Thoracic and Cardiovascular Surgery. Received: July 30, 2012, Revised: October 9, 2012, Accepted: October 17, 2012

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**Table 1.** Patient characteristics (n=89)

Characteristic	Value
Age (yr)	57.1±9.8 (25-75)
Male gender	38/89 (42.7)
Duration AF (mo)	41.8±37.7
Duration AF (median, range, mo)	36 (6-240)
Left atrial dimension (mm)	55.4±9.4 (32-86)
Giant left atrium <sup>a)</sup>	4/89 (4.5)
Persistent/permanent AF (%)	11/78 (12.4/87.6)
Mitral valve lesion	82/89 (92.1)
MS dominant	51/89 (57.3)
MR dominant	31/89 (34.8)
Single mitral valve disease	54/89 (60.7)
Single aortic valve disease	2/89 (2.2)
Double and triple valve disease	28/89 (31.5)
Non-valve lesion	5/89 (5.5)

Values are presented as mean±standard deviation or number (%). AF, atrial fibrillation; MS, mitral stenosis; MR, mitral regurgitation.

<sup>a)</sup>Left atrial dimension > 65 mm.

patients undergoing the Cox maze operation and concomitant cardiac surgery.

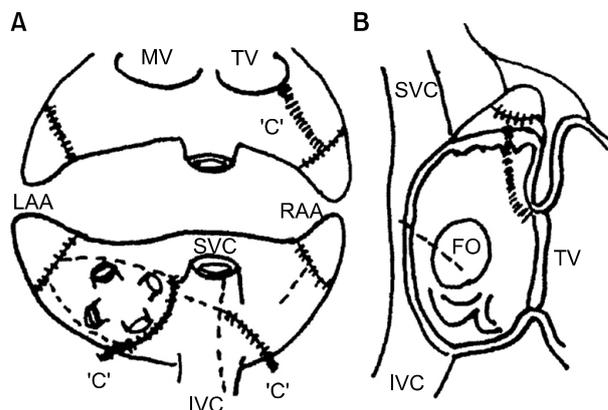
## MATERIALS AND METHODS

### 1) Study population

From October 1999 to December 2008, 90 patients with permanent or persistent AF underwent the Cox maze operation and concomitant cardiac surgery. Eighty-nine patients (38 men and 51 women; mean age, 57.1±9.8 years), that is, all except one who experienced surgical death, were included in the study (Table 1).

They had structural heart disease, which was the primary surgical indication. Mitral valve disease was found in 82 patients (92.1%) and non-left heart valve disease in 5 patients (5.5%), which included two with myxoma, two with an atrial septal defect, and one with coronary artery disease. Twenty-eight patients (31.5%) underwent multi-valve surgery. Seventy-eight patients (87.6%) had permanent AF and 11 patients (12.4%) had persistent AF. The mean atrial dimension was 55.4±9.5 mm (range, 32 to 86 mm) in a two-dimensional parasternal long-axis view.

All of the data were retrospectively analyzed from the



**Fig. 1.** The Cox-maze procedure. (A) Epicardial view of the atria. (B) Endocardial view of the right atrium. 'C': cryoablation at coronary sinus (inner and outer atrial walls), two junctions of tricuspid annulus and ablation lines, and one junction of mitral annulus and ablation line; excision of both atrial appendages. Dotted lines: cut-and-suture lines or bipolar radiofrequency ablation lines. MV, mitral valve; TV, tricuspid valve; LAA, left atrial appendage; RAA, right atrial appendage; SVC, superior vena cava; IVC, inferior vena cava; FO, fossa ovalis.

medical records, including the surgical records, standard 12-lead electrocardiograms, and transthoracic and transesophageal echocardiograms. "Recurrent AF" was defined as the presence of AF at the last follow-up. "Immediate post-operative SR conversion" was defined as the conversion to SR that occurred immediately after the patient was weaned from cardiopulmonary bypass and that remained present at discharge. "Early SR conversion" was defined as SR that was present at the postoperative 6th month. "Sustained SR" was defined as SR that had been maintained by the final follow-up visit.

### 2) Surgical procedure

We performed the Cox maze operation with the cut-and-sew (CS) technique in 36 patients and with the RF ablation technique in 53 patients, as previously described (Fig. 1) [10,11]. In both techniques, a left atriotomy was made through Sondergaard's groove, a vertical right atriotomy was made in the lower 1/3 of the right atrium, and both atrial appendages were amputated. In the CS technique, the mazes were made with incisions and sutures and cryoablation was applied to two incision ends in the tricuspid annulus and on

one incision end in the mitral annulus. Cryoablation was performed with a cryoprobe (Cooper Surgical Inc., Trumbull, CT, USA). In the RF technique, the mazes were made with a bipolar RF electrode (Medtronic Inc., Minneapolis, MN, USA), which was applied for 40 seconds more even after the cryoablation was finished for each lesion, and cryoablation was applied in the same annular portions of the mitral and tricuspid valves. The bases of both atrial appendages were closed with a continuous 4-0 or 5-0 Prolene suture.

### 3) Echocardiography

Transthoracic echocardiographic images were obtained by using commercially available echocardiography machines (Vivid 7 system; GE Medical Systems, 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. The left ventricular ejection fraction was calculated by using the modified Simpson's method.

### 4) Postoperative follow-up

Electrocardiography was performed in bed during admission, and at the first and the third week after discharge, and then every month or every 1.5 months for 1 year. Echocardiographic studies were performed before the operation, immediately after the operation, the postoperative second week, the postoperative sixth month, and then yearly. In patients with SR usually but suspicious paroxysmal palpitation, a 24-hour Holter monitoring test was performed to evaluate the paroxysmal AF waves. Neither cardioversion nor class I or III antiarrhythmic drugs were used during the follow-up period. A low dose of beta-blockers was used for rate control in patients with early postoperative tachyarrhythmia. Angiotensin receptor blocker was used to maintain the systolic blood pressure within 110 to 120 mmHg and to re-model the LA. Anticoagulation therapy was given for at least 3 months and discontinued in patients who had postoperative SR conversion and underwent valve repair or tissue valve replacement. The patients with recurrent AF continued or re-started anticoagulation.

### 5) Statistical analysis

All data were expressed as the mean and standard

deviation. Multivariable logistic regression analysis was performed to test independent associations between several perioperative variables and postoperative midterm maintenance of SR. Categorical variables were compared using the chi-squared test or Fisher's exact tests. The Mann-Whitney U-test was used for the comparison of nonparametric samples. For all statistical calculations, the SPSS ver. 12.0 program (SPSS Inc., Chicago, IL, USA) was used. A confidence level of 95% was considered statistically significant.

## RESULTS

### 1) Preoperative data

Eighty-nine patients undergoing the maze operation were separated into two groups according to the presence of SR at the last follow-up time (Table 2). Group SR consisted of 79 patients (88.8%) (mean age,  $56.5 \pm 9.7$  years) who had SR at the last follow-up, and group AF consisted of 10 patients (11.2%) (mean age,  $61.6 \pm 10.0$  years) who had AF at the last follow-up. Between the two groups, there were no differences in distribution of age and sex, follow-up period, type of AF, mitral valve lesions, or preoperative LA dimension and left ventricular ejection fraction. The mean duration of AF was longer in the AF group than the SR group ( $76.3 \pm 65.6$  months vs.  $38.2 \pm 32.2$  months;  $p=0.004$ ).

### 2) Operative data

Between the two groups, there were no differences in whether valve surgery was performed (aortic, mitral, or multi-valve surgery), the ablation technique, or the postoperative left ventricular dimension. The mean postoperative LA dimension was larger in the AF group than the SR group ( $56.4 \pm 13.6$  years vs.  $45.9 \pm 8.1$  mm;  $p=0.014$ ). The 'immediate' SR conversion had been present in 77 (97.5%) of 79 patients in the SR group but only in 3 (30%) of 10 patients in the AF group ( $p < 0.0001$ ). 'Early' SR conversion had been identified in 78 (98.7%) of 79 patients in the SR group, but only in 4 (40%) of 10 patients in the AF group ( $p < 0.0001$ ). Two patients (one for each group) had postoperative left atrial thrombi during the follow-up period. Two patients (one for each group) underwent permanent pacemaker implantation for sick sinus syndrome during the follow-up period.

**Table 2.** Preoperative characteristics of patients undergoing the maze procedure

Characteristic	SR group <sup>a)</sup> (n=79)	AF group <sup>b)</sup> (n=10)	p-value
Age (yr)	56.5±9.7	61.6±10.0	0.12
Male	34 (43.0)	4 (40)	
Duration of AF (mo)	38.2±32.2	76.3±65.6	0.004
Persistent/permanent AF	10/69 (12.7/87.3)	1/9 (10.0/90.0)	1.0
Mitral valve lesion			0.30
MS dominant	43 (54.4)	8 (80)	
MR dominant	29 (36.7)	2 (20)	
Other cardiac disease without mitral valve disease	7 (8.9)	0	1.0
Non-valve cardiac disease	5 (6.3)	0	1.0
Follow-up (mo)	49.7±29.5	61.0±40.4	0.28
Preoperative LA dimension (mm)	54.6±8.7	61.7±13.0	0.13
Preoperative giant LA	10 (12.7)	3 (30)	0.16
Preoperative LVEF (%)	57.5±9.8	54.0±7.1	0.81

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

SR, sinus rhythm; AF, atrial fibrillation; MS, mitral stenosis; MR, mitral regurgitation; LA, left atrium; LVEF, left ventricular ejection fraction.

<sup>a)</sup>SR at the last follow-up time.

<sup>b)</sup>Recurrent AF at the last follow-up time.

### 3) Postoperative data

During a mean follow-up of 51.0±30.8 months (median follow-up, 39.0 months; range, 18 to 134 months), 17 patients (18.9%) were lost during the followed-up period and their follow-up periods were at least 28 months. Neither primary cardiac surgery, presence of mitral valve surgery, type of AF, or duration of AF was predictive of recurrent AF. SR, atrial rhythm, or an atrial-based paced rhythm was present in 80 patients (89.9%) at discharge, in 82 patients (92.1%) at 6 months, and in 79 patients (88.8%) at the last follow-up visit (Fig. 1). At the last follow-up, 10 patients (11.2 %) had AF (group AF) (Table 3). All of the 7 patients (7.9%) with non-mitral valve surgery as a concomitant surgery had SR conversion and all of the 5 patients (5.5%) with non-valve surgery as a concomitant surgery also had SR conversion by the last follow-up time; the difference between the groups with the two types of surgery was not statistically significant.

### 4) Predictive factors of sinus rhythm after the maze operation

Factors predictive of ‘sustained SR’ (SR at the last follow-up visit) were ‘immediate postoperative SR conversion’

(odds ratio, 97.2; 95% confidence interval, 6.0 to 1,570.3; p=0.001) and ‘early SR conversion’ (odds ratio, 155.7; 95% confidence interval, 6.0 to 4,016.4; p=0.002) (Table 4). ‘Early SR conversion’ was associated with a high incidence of sustained SR at the time of the final follow-up. Factors predictive of ‘early SR conversion’ were young age (odds ratio, 0.77; 95% confidence interval, 0.66 to 0.99; p=0.031) and ‘immediate SR conversion’ (odds ratio, 15.3; 95% confidence interval, 1.4 to 168.7; p=0.026) (Table 5).

## DISCUSSION

In the study of 89 patients undergoing follow-up after a maze operation and concomitant cardiac surgery, ‘immediate postoperative SR conversion’ and ‘early SR conversion’ were independent predictors of ‘sustained SR’ after the maze operation. Underlying cardiac lesion, duration of AF, type of mitral valve disease, LA dimension, and preoperative and postoperative left ventricular dimensions and ejection fractions were not factors significantly predictive of ‘sustained SR’.

In many studies, risk factors for the failure of SR conversion after the maze operation have been found to be the LA size and volume, age, AF duration, limited ablation pro-

**Table 3.** Operative procedures and perioperative findings of SR group and AF group

Variable	SR group <sup>a)</sup> (n=79)	AF group <sup>b)</sup> (n=10)	p-value
Valve surgery	74 (93.7)	10 (100)	0.83
Mitral valve	47	7	
Mitral and aortic valve	25	3	
Aortic valve	2	0	
Tricuspid annuloplasty	46 (58.2)	6 (60)	1.0
Cut-sew/radiofrequency	48/31	5/5	0.52
Postoperative LA dimension (mm)	45.9±8.1	56.4±13.6	0.01
Postoperative giant LA	2 (2.5)	2 (20)	0.06
Postoperative LV dimension (mm)	51.3±7.3	51.8±5.8	0.77
Postoperative LA thrombus	1	1	
Permanent pacemaker	1	1	
'Immediate' SR conversion <sup>c)</sup>	77 (97.5)	3 (30)	<0.0001
'Early' SR conversion <sup>d)</sup> (SR at postoperative 6th mo)	78 (98.7)	4 (40)	<0.0001

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

SR, sinus rhythm; AF, atrial fibrillation; LA, left atrium; LV, left ventricle.

<sup>a)</sup>SR at the last follow-up time.

<sup>b)</sup>Recurrent AF at the last follow-up time.

<sup>c)</sup>SR conversion immediately after maze operation and the presence of SR at discharge.

<sup>d)</sup>The presence of SR at the postoperative 6th month.

**Table 4.** Independent factors for mid-term sustained sinus rhythm conversion after the maze procedure

Variable	Odds ratio	p-value	95% confidence interval
Immediate SR conversion	97.2	0.001	6.0–1,570.3
SR at postoperative 6th month	155.7	0.002	6.0–4,016.4
Left atrial dimension	6.7	0.174	0.4–105.6

SR, sinus rhythm.

cedure, and others [12-16]. The duration of AF is associated with perpetuation of arrhythmia, and spontaneous or electrical conversion of AF to SR is inversely related to duration of LA size. Duration of AF is also an independent predictor of LA size. In a clinical setting, LA size and AF duration are significantly and mutually related to each other. Many clinical investigations have recognized LA dilatation as a cause of AF [8,9]. LA dilatation, on the other hand, may also be a consequence of AF [16]. In our study, however, we did not find that the LA size or AF duration were independent predictors of sustained SR and recurrent AF during the midterm follow-up period after the maze operation. We suggest two possible reasons the LA size and the AF duration were not

**Table 5.** Independent factors for the presence of sinus rhythm at the postoperative 6th month

Variable	Odds ratio	p-value	95% confidence interval
Immediate sinus rhythm conversion	15.3	0.026	1.4–168.7
Age	0.77	0.031	0.61–0.98
Duration of atrial fibrillation	1.0	0.827	0.97–1.03
Left atrial dimension	0.93	0.218	0.83–1.04

independent predictors of recurrent AF. One reason is the clinical characteristics of our patient sample; the patients with preoperative giant LA (>65 mm) comprised a small proportion of only 4 patients (4.5%) in our study and most of the patients in our study experienced long AF duration. Another reason might be our surgical technique, in which the maze around the mitral annulus was narrow enough to interrupt reentrant circuits rather than the usual lesions meant to isolate the four pulmonary veins. We created a maze narrower than 38.1 to 50.8 mm. The effective maze procedure could be more effective for sustained SR than reduction of LA volume if the enlarged LA was not a giant one.

This study was designed to search for predictors for the maintenance of SR rather than predictors of SR conversion after the maze operation. In several studies, about 20% to 30% of the patients undergoing the maze operation had recurrent AF during the follow-up periods [7,8]. The main risk factors of maze failure in previous reports were age, LA dimension, duration of AF, amplitude of AF waves, rheumatic valve disease, permanent AF, and type of lesion sets of the maze procedure [8,14,15]. In our study, age, duration of AF, and postoperative LA dimension were identified as risk factors for early conversion (at postoperative 6 months), but not for sustained SR during the mid-term follow-up period. The risk factors for early conversion (at postoperative 6 months) were also described in a previous report [17].

For the patients who had experienced postoperative palpitation, we performed a 24-hour Holter monitoring test to search for symptomatic paroxysmal arrhythmia, but we did not find such evidence. However, paroxysmal AF cannot be completely ruled out with this test.

Immediate postoperative SR conversion is an important factor predictive of mid-term sustained SR after the maze procedure. Seventy-seven (97.5%) of 79 patients with 'immediate' SR conversion sustained SR during a mean follow-up period of 49.7 months. The patients in which SR converted immediately after the maze operation did not always maintain SR and most of them experienced temporary recurrent AF postoperatively for several days until they achieved SR conversion again before discharge from the hospital. Only two (3.5%) of 79 patients with immediate SR conversion after the maze procedure had recurrent AF and did not achieve SR conversion with early use of an anti-arrhythmic drug. Although the LA dimension and age were not predictive factors of recurrent AF in the mid-term follow-up, they were significant predictors of early SR conversion. Previous reports [17,18] have demonstrated that age is an important factor for SR conversion after the maze operation in patients with giant LA and a more aggressive surgical approach is required in younger patients with giant LA for more favorable results. Many reports [17,19] readily ruled the maze procedure a success or failure at the postoperative 3rd month or 6th month, but many cases for which operative success had been determined then experienced delayed recurrence of AF [19]. We

evaluated what could affect maintenance of the recovered SR during the mid-term follow-up after the same modality of maze procedure. The 6-month outcome is not a definitive result of the maze operation, but it may be a predictor of sustained SR by the midterm follow-up time. In our cases, as the recurrence rate was very low after SR conversion, the time-related recurrence rate using the Kaplan-Meier method or Cox-regression analysis could not be calculated.

We suggest that the immediate postoperative SR conversion (with the presence of SR at discharge) and the presence of SR at the postoperative 6th month are important predictors of sustained SR during the mid-term follow-up period.

## CONCLUSION

In the patients undergoing the Cox maze operation and concomitant cardiac surgery, 88.8% of them showed conversion to sinus rhythm at the follow-up of  $51 \pm 30.8$  months, and the conversion to sinus rhythm immediately after surgery and the presence of sinus rhythm at the 6th postoperative month were important factors for maintenance of continuous sinus rhythm without recurrent atrial fibrillation.

## CONFLICT OF INTEREST

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

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