The impact of mitral valve surgery combined with maze procedure
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Abstract

Objective: Recent studies indicated that successful maze procedure for atrial fibrillation (AF) adjunct to mitral valve surgery provided a lower incidence of stroke and recurrence of AF. The purpose of this study is to review the 13-year experience of these combined procedures and to identify the risk factors and late outcomes of successful maze procedures compared to failed maze procedures. Methods: At a single institution, 521 consecutive patients underwent combined maze procedures with mitral valve replacements or valvuloplasties. Three kinds of maze techniques were primarily used: Cox—maze III, Kosakai maze, and cryo-maze procedure. Three months after the operation, 394 patients were in sinus rhythm (Group S) while the remaining 116 patients were in continuous or intermittent AF (Group F), excluding 11 early death patients. Risk factors for Group F were determined by the analysis of all patient demographics. Survival, freedom from stroke, cardiac events, and AF recurrence were analyzed. Results: The proportion of the patients without any other simultaneous procedures was greater in Group S (41% vs 29%, \( P < 0.02 \)). The distributions of mitral valve surgery and maze procedure techniques were similar in these two groups. A left atrium larger than 70 mm [hazard ratio (HR) = 2.6; 95% confidence interval range 1.04—6.3, \( P = 0.043 \)], preoperative AF history longer than 10 years (HR = 8.2; 4.5—15.1, \( P < 0.001 \)) and f-wave voltage in V1 smaller than 0.1 mV (HR = 6.2; 5.0—15.2, \( P < 0.001 \)) were determined to be risk factors for unsuccessful maze procedures. All the results of Cox proportional hazards models showed superiority in Group S; actuarial survival rates (HR = 2.7; 1.04—7.0, \( P = 0.035 \)), freedoms from stroke (HR = 3.0; 1.1—8.1, \( P = 0.003 \)) and cardiac events (HR = 4.3; 2.9—6.1, \( P < 0.001 \)). Freedom from AF recurrence rate was 98.4% at 5 years and 81.0% at 12 years in Group S, and 73.0% and 60.1% in overall patients. Conclusions: Patients with successful maze procedures resulted in higher survival rate, greater freedom from stroke and cardiac events. The large left atrium, small f-wave, and long AF duration were significant risk factors for failed maze procedures, suggesting that earlier surgical interventions would result in superior results in mitral valve surgery combined with maze procedure.

Keywords: Atrial fibrillation; Mitral valve; Maze procedure

1. Introduction

Atrial fibrillation (AF) is the most common sustained arrhythmia. It induces a certain morbidity and mortality [1], and is associated with 40—60% of those patients who undergo surgical treatments for mitral valve disease [2,3]. Recent studies have shown achievements of sinus rhythms by maze procedures even when done in combination with mitral valve or other cardiac operations [4,5], and with results comparable to lone maze procedures [6,7]. Several researchers have reported that combining maze procedure with mitral valve surgery has advantages with regard to survival [8], cardiac function [9,10], and stroke incidence [11,12]. At the same time, various modifications over the past decade have improved and refined the maze procedure [6,12—21]. This has enabled surgeons to perform maze procedures rapidly and safely. However, there are few reports of intermediate or long-term results of these series [22]. The purpose of this study is to review the 13-year experience of mitral valve surgery combined with maze procedure at a single institution, and to identify risk factors and late outcomes of successful maze procedures compared to failed maze procedures.

2. Patients and methods

2.1. Patients

We reviewed 521 consecutive patients (253 males, the median age was 60 years, ranging 23—82 years) who underwent mitral valve replacements (MVR) or valvuloplasties (MVP) combined with maze procedures at our National Cardiovascular Center between April 1992 and December
2004. The patients were assigned to two groups; successful maze (Group S, \(n = 394\)) and failed maze (Group F, \(n = 116\)), according to the documented rhythm at 3-month follow-up. Eleven early death patients were excluded. Preoperative and perioperative data sets were collected from operative records, anesthesia charts, clinical histories, and laboratory investigations including electrocardiograms (ECGs) and echocardiograms.

### 2.2. Surgical procedures

Detailed surgical techniques of Kosakai maze and cryo-maze have been reported previously [18,20]. In brief, PV isolation is performed by cut and sew technique in Kosakai maze, and by cryoablation in cryo-maze. Cryoablation is also used in right side and the rest in the left side, from PV isolation line to mitral annulus and left atrial appendage in both procedures. The Cox—maze III [21], Kosakai maze and cryo-maze were mostly performed in this series (Table 1). The full lesion set of both left and right maze procedures were performed in all cases. Small populations of maze procedures were performed with radio-frequent devices, including both monopolar and bipolar generations. The surgical procedures used in the present series for mitral valves were MVR in 336 patients (66%) and MVP in 174 patients (34%). All patients who underwent maze procedures without mitral valve operations were excluded. Over 97% of MVR patients received mechanical valves and postoperative anticoagulant medications. MVP patients underwent valvuloplasties in various techniques according to preoperative and intraoperative transeosophageal echocardiograms and anatomical findings. Other simultaneous operations were summarized in Table 1.

### 2.3. Follow-up

Patient data were determined by reference to medical records and correspondence with the primary physician.

#### Table 1 Surgical procedures

<table>
<thead>
<tr>
<th>Operative procedures</th>
<th>Group S, (n = 394) (%)</th>
<th>Group F, (n = 116) (%)</th>
<th>(P)-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maze procedures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cox—maze III</td>
<td>36 (9.1)</td>
<td>11 (9.5)</td>
<td>0.91</td>
</tr>
<tr>
<td>Kosakai maze</td>
<td>174 (44)</td>
<td>59 (51)</td>
<td>0.19</td>
</tr>
<tr>
<td>Cryo-maze</td>
<td>177 (45)</td>
<td>44 (38)</td>
<td>0.18</td>
</tr>
<tr>
<td>Radiofrequency</td>
<td>7 (1.8)</td>
<td>2 (1.7)</td>
<td>0.97</td>
</tr>
<tr>
<td>Mitral valve procedures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MVR</td>
<td>259 (66)</td>
<td>77 (66)</td>
<td>0.90</td>
</tr>
<tr>
<td>MVP</td>
<td>135 (34)</td>
<td>39 (34)</td>
<td>0.90</td>
</tr>
<tr>
<td>Simultaneous operations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MV only</td>
<td>162 (41)</td>
<td>34 (29)</td>
<td>0.02</td>
</tr>
<tr>
<td>MW + AVR</td>
<td>72 (18)</td>
<td>16 (14)</td>
<td>0.26</td>
</tr>
<tr>
<td>MW + TAP</td>
<td>81 (21)</td>
<td>43 (37)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MW + CABG</td>
<td>14 (3.5)</td>
<td>2 (1.7)</td>
<td>0.32</td>
</tr>
<tr>
<td>MV + ASD closure</td>
<td>18 (4.5)</td>
<td>3 (2.5)</td>
<td>0.34</td>
</tr>
<tr>
<td>MW + others</td>
<td>12 (3.0)</td>
<td>5 (4.3)</td>
<td>0.50</td>
</tr>
</tbody>
</table>


Sinus rhythm was defined on the basis of 12-lead ECG analysis. Warfarin was administered to all patients soon after starting oral intake, and was continued long-term in patients with sustained AFs or mechanical valves in mitral and/or aortic positions with the target range of prothrombin time international normalized ratio between 1.8 and 2.8. In MVP patients with sinus rhythm, warfarin was discontinued in 3 months. When the AF was sustained even after the administrations of class la or lc antiarrhythmic drugs, cardioversion was considered during hospitalization or at the first or second monthly outpatient visit. Heart rates were controlled by digoxin, verapamil, or beta-blockers in all patients without bradycardia. These antiarrhythmic drugs continued until 3 months postoperatively and tapered off over the next several months. A stroke was defined as a neurological deficit concomitant with ischemic image findings on a computed tomography or a magnetic resonance imaging. All cardiac and non-cardiac events were recorded. Cardiac events were defined by strokes, early (within 30 days) and late pacemaker implantations, hospital admissions for congestive heart failure or arrhythmia, anticoagulant related events and following cardiac operations. Follow-up data were complete at 5.2 ± 3.6 years in Group S and 5.8 ± 3.6 years in Group F (\(P = 0.11\), range 0.5—13.1 years).

### 2.4. Statistical analysis

Survival, freedom from cardiac events, stroke, and AF recurrence were estimated by the Kaplan—Meier method, and those curves were compared with log-rank tests. The risk factors for Group F (failed maze) were determined by a logistic regression model. Both groups were analyzed by univariate and multivariate analysis with a Cox proportional hazards model for late results. The differences were considered statistically significant at \(P < 0.05\).}

### 3. Results

#### 3.1. Patient demographics

Preoperative demographics of these groups are in Table 2. The distribution of prevalence for the differing types of mitral valve pathology was similar. Among these patients, 31 (8.1%) in Group S and 3 (2.7%) in Group F had intermittent AFs preoperatively which showed no significant differences (\(P = 0.07\)), and the rest of them had chronic histories of sustained AF with the average durations of 4.6 ± 4.1 years (±SD) and 11.1 ± 6.1 years (\(P < 0.001\)). Patients with previous operations were in high risk of failed maze procedures by univariate analysis, but not by multivariate analysis. A left atrium larger than 70 mm [hazard ratio (HR) = 2.6; 95% confidence interval range 1.04—6.3, \(P = 0.043\)], preoperative AF history longer than 10 years (HR = 8.2; 4.5—15.1, \(P < 0.001\)) and f-wave voltage in V1 smaller than 0.1 mV (HR = 6.2; 5.0—15.1, \(P < 0.001\)) were recognized as significant risk factors by a logistic regression model (Table 3).

These two groups had similar distributions of surgical procedures for mitral valve and maze procedure techniques (Table 1). Those patients with only mitral valve procedures were significantly less in Group F (\(P = 0.02\)). More than 40% of
patients in Group F (n = 56) patients underwent simultaneous tricuspid annuloplasties with or without aortic valve replacements (P < 0.0001).

3.2. Early results

Of all the 521 patients, 11 (2.1%) patients died during hospitalization. Causes of death included low output syndromes with multiple organ failure (n = 5), stroke (n = 2), respiratory distress syndrome (n = 1), mediastinitis (n = 1), aortic dissection during the operation (n = 1), and a sudden death of unknown cause in the 8th postoperative day (n = 1). Postoperative complications included required pacemaker implantations for 9 patients (1.7%) with a diagnosis of sick sinus syndrome within 30 days after the operation who were counted in Group F. No significant difference was found between the two groups with regard to re-exploration (n = 15 in Group S, n = 9 in Group F), stroke (n = 1, n = 2), respiratory distress (n = 6, n = 2), or valve related complications (n = 4, n = 3).

3.3. Survival and late outcome

The overall survival was 88.5% at 13 years follow-up after the operation. Survival at 5 and 10 years was 98.4% and 94.6%, respectively, in Group S compared with 94.8% and 89.8% in Group F. Actuarial survival curves demonstrated significant differences between these two groups (P = 0.035, Fig. 1). The causes of late mortality were non-cardiac deaths (a liver cancer and a suicide in Group S), congestive heart failure (n = 1 in Group S, n = 2 in Group F), stroke (n = 1, n = 2), intracranial hemorrhage (n = 1, n = 2), unknown cause (n = 3, n = 3), and arrhythmia (n = 1 in Group F). Late pacemaker implantations were undertaken in 32 patients (n = 16, n = 16, P = 0.005). The total number of pacemaker implantations was 41 (8.0%) in overall follow-up period, including nine early cases, which underwent within 30 days after operation.

Freedom from stroke after 5 and 10 years was 97.9% and 92.4% in Group S, respectively, compared with 84.4% and 76.6% in Group F (P = 0.003, Fig. 2). Freedom from cardiac events after 5 and 10 years was 85.9% and 73.0% in Group S, and 51.2% and 34.1% in Group F, respectively (P < 0.001). All results from multivariate analyses revealed improved freedom from adverse events in Group S (Table 4).

Table 2
Patient demographics

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group S, n = 394 (%)</th>
<th>Group F, n = 116 (%)</th>
<th>Univariate analysis P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>192 (48)</td>
<td>58 (50)</td>
<td>0.81</td>
</tr>
<tr>
<td>Age &gt; 70 years old</td>
<td>41 (10)</td>
<td>15 (13)</td>
<td>0.55</td>
</tr>
<tr>
<td>Intermitent AF</td>
<td>31 (8.1)</td>
<td>3 (2.7)</td>
<td>0.07</td>
</tr>
<tr>
<td>Reoperation</td>
<td>55 (14)</td>
<td>27 (23)</td>
<td>0.03</td>
</tr>
<tr>
<td>Voltage of f-wave in V1 &lt; 0.1 mV</td>
<td>19 (5.1)</td>
<td>61 (52)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AF history &gt; 10 years</td>
<td>33 (8.6)</td>
<td>59 (52)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Left atrial diameter &gt; 70 mm</td>
<td>20 (5.1)</td>
<td>22 (19)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 3
Risk factor for Group F (failed maze, logistic regression model)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Hazard ratio</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left atrial diameter &gt; 70 mm</td>
<td>2.6</td>
<td>1.04—6.3</td>
<td>0.043</td>
</tr>
<tr>
<td>AF history &gt; 10 years</td>
<td>8.2</td>
<td>4.5—15.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Voltage of f-wave in V1 &lt; 0.1 mV</td>
<td>6.2</td>
<td>5.0—15.2</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 4
Impact of successful maze procedure (Cox proportional hazards model)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Hazard ratio</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survival</td>
<td>2.7</td>
<td>1.04—7.0</td>
<td>0.035</td>
</tr>
<tr>
<td>Freedom from cardiac death</td>
<td>3.0</td>
<td>1.1—8.1</td>
<td>0.003</td>
</tr>
<tr>
<td>Freedom from stroke</td>
<td>4.2</td>
<td>2.1—8.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Freedom from cardiac events</td>
<td>4.3</td>
<td>2.9—6.1</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
3.4. Recurrence of AF

In Group S, there were 36 (9.1%) late recurrences of AF during the follow-up. In Group F, there was one (0.8%) spontaneous return to sinus rhythm at 8 months after the operation. In this series, actuarial freedom from AF recurrence in Group S was 98.4% at 5 years and 81.0% at 12 years. Overall results for the combined groups (Group S + Group F) were 73.0% at 5 years and 60.1% at 12 years (Fig. 3).

Those patients with a preoperative AF history of less than 5 years had a 79% AF recurrence free rate at 10 years, while those patients with AF history longer than 15 years had only a 23% recurrence free rate (Fig. 4A, \( P < 0.001 \)). Larger atrial dimensions were associated with lower AF recurrence free rates. Only 52% of patients with over 70 mm left atrial diameters were in sinus rhythm at 10 years, compared to 74% of those patients with left atrial diameters of less than 50 mm (Fig. 4B, \( P < 0.001 \)).

4. Discussion

The Cox—maze procedure was innovated by Cox et al. [23,24] in 1987 as a surgical therapy for patients with chronic and paroxysmal AF. The basic concept has been widely received. Major modifications have supplanted the traditional ‘cut-and-sew’ with cryoablation [8,18,20], microwave [13] and radiofrequency [6,14], or mini-maze [16,17] and radial maze [15], with the continued goal of durable results in maintaining optimal cardiac function under sinus rhythm by rapid and safe surgical interventions. In this series of patients, we mainly used three kinds of maze procedures in 13 years; Cox—maze III, Kosakai maze and cryo-maze. As reported previously [12,18,20], cryo-maze is the modification of the Kosakai maze. The major difference in cryo-maze is the usage of cryoablation for PV isolation from the left atrium instead of ‘cut-and-sew’ technique in Kosakai maze. Nakajima et al. [20] described advantages of cryo-maze in cardiopulmonary bypass time \(( P = 0.001)\), aortic cross-clamp time \(( P = 0.03)\), early postoperative chest tube drainage \(( P = 0.02)\), and comparable result of freedom from AF recurrence at 3 years (cryo-maze: 97.7% vs Kosakai maze: 90.4%, \( P = 0.11 \)) in a case matched study. In this study, no significant difference was seen in AF recurrence free rate among these techniques as well, which may suggest that the cryo-maze is a trustworthy and less invasive procedure with equivalent results in AF recurrence free rates compared to the golden standard Cox—maze III or Kosakai maze procedure.

Several clinical studies have been reported on maze procedure outcomes in mixed patient populations. Khargi et al. [5] reviewed 48 clinical studies and reported that postoperative sinus rhythm recover rate was 78.3% in radiofrequency, microwave and cryoablation, and 84.9% in Cox—maze III. Gaynor et al. [22] and Cox et al. have reported outstanding results with their patients, including about 20% with simultaneous mitral valve procedures, who had a long-term AF recurrence free rate of 92.2% at 10 years. In our study, 98.1% (510/521) patients who underwent MVR or MVP combined with maze procedures survived the operations, and 394 (75.6%) of them reached successful maintenance of sinus rhythm at 3 months after the operation, and an overall AF recurrence rate of 73% at 5 years. Approximately 65% of patients underwent MVR, and most of them had rheumatic change in pathological findings. The differences of these results may be explained by patient backgrounds, which might exert an influence on the effectiveness of maze procedures.

In our series, we divided the patients into two groups according to ECG rhythm at 3 months follow-up after operations. Of the 116 patients (24.4%) with AF who were assigned to Group F, only one patient spontaneously converted to a sinus rhythm (8 months after operation). The others remained in AF. Those patients in Group S (who...
had sinus rhythms at 3 months after their operation) showed favorable AF recurrence free rates of 98.4% at 5 years and 81.0% at 12 years. However, when combined with Group F (who had no sinus rhythm at 3 months after their operation) the overall results were 73.0% at 5 years and 60.1% at 12 years. Late follow-up results also showed a significant difference between these groups with regard to survival, freedom from cardiac death, stroke, and cardiac events (Figs. 1–3). These data suggest that 3-month results are reasonable indicators of long-term prognoses for patients with mitral valve surgery combined with maze procedure.

The result of freedoms from AF in more than 70 mm LA group was 52% at 12 years. The majority of AF free patients in this category had more than 0.1 mV f-waves in the V1 lead (n = 19, 86%, P = 0.004). This result may suggest that there is a subgroup of patients with large LA and mitral pathology who could maintain sinus rhythm by the maze procedure with mitral valve surgery. In addition, the current study showed that longstanding AF, a large LA, and a low amplitude f-wave were significant risk factors for failed maze procedures (Table 3) and a high rate of AF recurrence (Fig. 4A and B). These are ‘traditional’ risk factors which have already been discussed in previous publications [6,19,25], but they are not mid or long-term results in large populations. Gaynor et al. [22] and Cox et al. reported the risk factors for late AF recurrence as (1) duration of preoperative AF and (2) Cox–maze procedure version—without any data on LA size or ECG findings. In this series, we were able to include all patient’s preoperative LA diameter by transthoracic echocardiography, 95% of ECG and 97% of recorded AF history with a follow-up period of 5.3 ± 3.5 years (range 0.5–13.1 years). These risk factors, measured out to significant mid to long-term follow-up data points, have a considerable meaning for our ability to predict outcomes in mitral valve surgery combined with maze procedure.

The study has some limitations. This was neither a prospective study nor a case-controlled study, so the patient demographics and concomitant surgical procedures were not matched. We divided our patients into two groups according to a 12-lead ECG at 3 months after the operation in outpatient clinic, not 24-h Holter tests or continuous monitoring, which means both groups might have included inappropriate patients.

In conclusion, preoperative AF history longer than 10 years, left atrial dimensions larger than 70 mm, and f-wave voltage in V1 lead smaller than 0.1mV were independent determinants of unsuccessful maze procedures. Furthermore, patients with persistent AF 3 months after a combined mitral valve/maze procedure were associated with a lower rate of survival, freedom from stroke, and future cardiac events.

References


Appendix A. Conference discussion

Dr U. Mehlhorn (Cologne, Germany): Actually, it shows what others have also shown and it supports that patients with mitral regurgitation should be operated early on and we shouldn’t wait too long. But couldn’t it be that you compared sicker patients versus healthier patients and are showing these different results? And did the results change the practice in your department? Thus, do you attempt a maze in all patients or don’t you attempt the patients with those risk factors?

Dr Itoh: Actually in 1995 we had reviewed the results of 2-year experience of maze procedures and analyzed the risk factors for unsuccessful maze procedures, and we already had almost the same results 10 years ago. Since
then, we have been trying to do maze procedures for limited patients according to those results. But sometimes we had to do maze procedures in some cases like a large, 80-mm left atrium, or a 15-year history of atrial fibrillation.

Dr Mehlhorn: What is your anticoagulation strategy? I saw that the group with failed maze procedure had much higher rates of stroke.

Dr Itoh: Usually Coumadin is used in all patients with atrial fibrillation. So almost all of the failed maze patients had got Coumadins. In this series we have 65% of mitral valve replacements and over 90% of them were replaced by mechanical valves. Even the patients with successful maze procedures had Coumadin if they had undergone mechanical valve operations.

Dr Mehlhorn: But I'm asking about the patients with a maze in sinus rhythm, how do you anticoagulate those patients?

Dr Itoh: In mitral valvuloplasty patients, we’ve got 77% success rate. And 70% of mitral valvuloplasty patients have no Coumadin, no anticoagulations basically.

Dr A. Hurle (Alicante, Spain): Have you ever tried left atrial reduction techniques? And if so, have you noticed any changes in your results from this respect?

Dr Itoh: Actually, it contains less than 10% of the left atrial plications, which had no inference on the results.

Dr H. Azar (Norfolk, VA, USA): There are two key factors that impact long-term survival: The left ventricular function and rhythm. Have you tried to separate as to how much your improvement related to the difference in the left ventricular function in the patients who had successful results from maze? Because that’s a key aspect of long-term survival.

Dr Itoh: In this series, we have no data for that.

Dr J. Kobayashi (Osaka, Japan): I’m a coauthor of this paper.

In answer to the first question, we resect the part of left atrium and reduce the left atrial size. We tried to avoid the occurrence of reentry circuit by reducing the size of the left atrium.

And in answer to the second question, in the Journal of Heart Valve Disease, we have published a paper about left ventricular function 2 or 3 years ago. Sinus rhythm recovery is good for the left ventricular function too. The left ventricular size and left ventricular ejection fractions are improved by sinus restoration after the maze procedure.

Dr J. Melo (Carnaxide, Portugal): In your study, the cutoff line for a high success rate predictor was a LA larger than 65 mm. In the registry, with 2000 patients we are running, that cutoff point was much smaller, which is 57 mm, so much smaller LA as a predictor for good success.

My question is, do you have mostly regurg patients or stenosis patients? And how many of your patients had concomitantly tricuspid surgery?

So the question is to try to understand the differences in sizes of the left atria as predictor for a good success rate, my question is, you have mostly stenosis patients or regurg patients? And if you have many patients with concomitant tricuspid surgery? What’s the proportion of your patients with mitral stenosis or mitral insufficiency?

Dr Itoh: As I showed in the slide, mitral stenosis and the stenosis with regurgitation patients were almost 50%, and patients with mitral regurgitation were 45%.