Surgical Outcomes of Cox-maze IV Procedure Using Bipolar Irrigated Radiofrequency Ablation and Cryotherapy in Valvular Heart Disease

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**Background:** We evaluated the efficacy of Cox-maze IV procedure using bipolar irrigated radiofrequency ablation and cryotherapy in chronic atrial fibrillation associated with valvular heart disease. **Material and Methods:** From November 2005 to June 2009, ninety four patients have undergone valvular heart surgery with Cox-maze IV procedure. Preoperative duration of atrial fibrillation was 7.6±6.5 years and follow-up duration was 22.7±12.3 months. **Results:** There were two (2.1%) postoperative deaths not related to maze procedure. Two cerebrovascular accidents, five low cardiac output syndromes and two permanent pacemaker implantations have occurred after surgery. Preoperative ejection fraction on echocardiography was 55.3±8.1% and ejection fraction of postoperative six month was 54.7±6.5%. Left atrial size of preoperative and postoperative were 61.5±11.6 mm and 53.1±8.4 mm at each. Freedom from atrial fibrillation rate at postoperative six-month was 80.7% and the cases of recurrence of atrial fibrillation after six months were three (3.3%). Risk factors for failure or recurrence of maze procedure were old age (p=.010) and preoperative moderate or severe tricuspid regurgitation (p=.033). **Conclusion:** The Cox-maze IV procedure using RFBP2 and cryotherapy is quite safe and freedom from atrial fibrillation at postoperative 6 month was 82.5%. Risk factors for failure or recurrence of atrial fibrillation after Cox-maze IV were old age and preoperative moderate tricuspid regurgitation.

**Key words:** 1. Arrhythmia surgery 2. Valve disease 3. Arrhythmia 4. Ablation

**INTRODUCTION**

Atrial fibrillation (Afib) is the most frequent continuous cardiac arrhythmia and it could be present under abnormal organic cardiac disease or not. When it occurs under any situation, it causes the reduction of cardiac output and in-tra-atrial thrombus formation which could be an origin of systemic embolism because there is no mechanical activity in both atrial chambers.

As provided in American College of Cardiology and American Heart Association, the treatment of Afib is composed of several anti-arrhythmic or rate control agents, ele-
tric sinus conversion and anticoagulant agents [1,2]. Among these modalities, surgical Cox-maze procedure has been known as the best tool for confident sinus conversion. Since Cox-maze procedure was first performed at 1987, it has been modified twice to Cox-maze III procedure. After late 1990’s, by means of various energy sources such as cryoablation, unipolar or bipolar radiofrequency ultrasound and microwave it has been modified to be Cox-maze IV procedure which is less invasive and costs lesser procedure time [3]. The lesion sets of Cox-maze IV procedure can be matched with that of Cox-maze III procedure. However, the durability of Cox-maze IV procedure is not guaranteed compared to original cut and sew technique in terms of transmurality formation in some papers [4,5].

In addition, because it could cause considerable aortic cross clamp time, frequent bleeding episodes from incision line and operative complexity, original cut and sew technique was abandoned in these days.

So, in this paper, we tried to provide appropriate treatment for Afib associated with valvular heart disease by analyzing the results of Cox-maze IV procedure using bipolar radiofrequency and cryoablation.

A retrospective analysis was made of ninety four consecutive patients who underwent Cox-maze IV procedure associated with valvular heart disease between November 2005 and June 2009 in our institution (Seoul National University Hospital). The operation was performed by single surgeon (K-H Kim).

Since the year 2000, we have performed Cox-maze III procedure using cryoablation (Frigitronics®, cardiovascular cryosurgical system-200, Atricure Inc, Chester, OH), and after early 2005, we adopted bipolar radiofrequency (RFBP2, bipolar irrigated radiofrequency, Cardioblate®BP2, Medtronic Inc, Minneapolis, MN) in Afib surgery. All patients had valvular heart disease which was candidate for open valvular heart surgery and there was no patient who had lone Afib.

The causes of valvular heart disease were sixty-two rheumatic diseases (66.0%), twenty-two degenerative diseases (23.4%) and ten cases (10.6%) of the other etiologies such as mixed form or congenital cause. Among them, six cases (6.4%) were redo-sternotomy.

All patients had chronic continuous Afib preoperatively and we excluded the patients who had paroxysmal Afib. The mean period of Afib was 7.6±6.5 years.

There were eleven patients (11.7%) who had an episode of
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**Fig. 1.** Lesion sets of Cox-maze IV procedure. RA=Right atrium; TV=Tricuspid valve; LPA=Left pulmonary artery; RPA=Right pulmonary artery; LA=Left atrium; MV=Mitral valve; LAA=Left atrial auricle.

cerebrovascular accident and ten (10.6%) who had been prescribed anti-arrhythmic agent and no patient who had been performed direct current electric cardioversion preoperatively (Table 1).

Table 2 shows combined valvular operations and associated cardiac diseases. Mitral procedures requiring repair or replacement were most frequent combined procedure (87 cases, 92.6%). Tricuspid interventions were next frequency (84 cases, 89.4%). Aortic valvular operations were 32 cases (34.0%). Coronary artery bypass grafting with valvular surgery were 5 cases (5.3%) and ascending aorta procedures requiring reduction plasty or replacement were 7 cases (7.4%). We performed only three cases of left atrial reduction plasty. In tricuspid position, we performed annuloplasty using MC3 ring (Edwards LifeScience, Irvine, CA, USA) whenever there was annular dilatation more two-finger breadth on intraoperative finding in spite of preoperative mild tricuspid regurgitation.

Operative procedure was in progress as usual open heart surgery; Under general anesthesia, Swan-Ganz catheter was inserted via internal jugular vein to pulmonary artery. After median sternotomy, we put the arterial cannula on ascending aorta usually and dual venous cannula on separate vena cava.

According to combined surgery, we generally performed right atrial ablation on beating heart before aorta cross clamping to minimize the myocardial ischemic time. Ablation procedure for left atrium was performed during aorta cross clamp time with main combined procedure.

All ablation procedures obtained transmural lesion by instrumental guidelines; we applied a cryothermy using N2O for more two minute under −60°C and bipolar radio-frequency twice using 25−30 watt energy.

Fig. 1 shows our Cox-maze IV lesion sets. After right atriotomy (horizontal line), a lesion set extended to tricuspid annulus via internal right atrial wall toward two o'clock by cryoablation. Then, small incision was made on right atrial auricle and bipolar radio frequency was applied to right atrial oblique line via free wall, and cryoablation was attempted to internal right atrial wall lesion to the annulus toward ten o'clock. With bipolar radio frequency, right atrial para-septal lines were made to both vena caval directions. In addition, septal line to foramen ovale was constructed by bipolar radio frequency, too.

Regarding left atrial lesion sets, separate both pulmonary artery box lesions were made by bipolar radio frequency with extended left atriotomy incision. Then, the lines between both box lesions were constructed by cryoablation or radio-frequency superiorly and inferiorly. Whenever there was Marshall ligament around left pulmonary artery, we cut it down. There were seventeen cases (18.1%) in which Marshall ligament existed. Before mitral prosthesis insertion, cryoablation was applied on mitral isthmus to mitral annulus. At last, we ablated the lesion between left pulmonary artery box line and left atrial auricle with cryothermy and obliterated the left atrial auricle externally with simple double tie ligation or
Outcomes of Cox-maze IV Procedure

We reviewed the preoperative risk factors and several echocardiographic parameters such as left atrial size and left ventricular ejection fraction at preoperative, before discharge, postoperative 6 months and 12 to 18 months. We also performed 12-lead electrocardiography (ECG) daily during perioperative period and checked it bi-monthly for two years after operation, and performed Holter monitoring in occasion as needed.

In this study, we defined “free from Afib” as ECG showed normal sinus rhythm, junctional rhythm, atrial pacing rhythm or other regular ventricular beat. We also defined a failure of maze procedure as case of Afib at postoperative 6 months and regarded recurrence of Afib after 6 months as a recurrence of Afib.

Data were analyzed with SPSS 12.0 software (SPSS, Inc., Chicago, IL). Ten preoperative and postoperative variables were evaluated in a univariate analysis to identify potential predictors of maze failure or Afib recurrence. Univariate analyses were performed for all parameters by means of $\chi^2$ analysis and Student’s t test for continuous variables. A multivariable analysis (logistic regression model) was used to identify factors for Afib recurrence or maze failure. A value of $p$ less than 0.05 was considered statistically significant.

RESULTS

There were two operative mortalities (2.1%). One patient was expired because of sudden rupture of left ventricle after mitral valve replacement and the other was death from postoperative low cardiac output syndrome.

Postoperative morbidities were two cerebrovascular accidents (2.1%), two reoperations due to bleeding (2.1%), two superficial wound infections (2.1%), one case of permanent pacemaker insertion (1.1%) and thromboembolism (1.1%). In addition, low cardiac output syndrome which needed use of inotropics for over five days was 5 cases (5.3%) and bradycardia which sustained for over three days was 25 cases (26.6%). And there was no postoperative renal failure.

The mean period for cardiopulmonary bypass time was 225±47.1 (136~343) minutes and that of aortic cross clamp time was 152.2±40.8 (43~249) minutes. Five patients (5.3%) needed total circulatory arrest period which is mean 13.2±2.3 (10~16) minutes.

Except two mortalities and two follow up loss, ninety patients have been followed up in outpatient department and mean follow up period was 22.7±12.3 (0.7~43.5) months.

1) Transthoracic echocardiographic (TTE) findings

Preoperative echocardiography revealed that left ventricular ejection fraction was mean 55.3±8.1 (32~75)% and left atrial size was mean 61.5±11.6 (26~93) mm. More than moderate tricuspid regurgitation was present on 34 patients (36.2%). However, seventy five patients (79.8%) including them were revealed to have dilated annulus of tricuspid position and underwent tricuspid annuloplasty using MC3 ring.

At postoperative period, we compared preoperative TTE with postoperative 6 month and latest examination (postoperative mean 18.5±6.9 months). The left ventricular ejection fraction was slightly improved from preoperative 55.3±8.1% to postoperative 6 month 54.7±6.5%, latest 56.5±7.0%. And left atrial size showed significant reduction after operation (preoperative 61.5±11.6 mm, postoperative 6 month 53.1±8.4 mm) then increasing tendency on latest examination (54.7±9.8 mm). Numbers of postoperative more than moderate tricuspid regurgitation were significantly reduced to only four (preoperative 34 patients) after aggressive correction.

2) Electrocardiographic (ECG) findings

Just after operation, sixty seven patients (out of 94, 71.3%) showed normal sinus rhythm and sixteen (17.0%) showed consistent Afib. The others (eleven, 11.7%) showed junctional rhythm or pacing rhythm or undetermined rhythm. However, before discharge, proportion of Afib was increased to twenty seven (out of 92, 29.3%) and normal sinus rhythm was 49 (53.3%), the others 16 (17.4%). At postoperative 1 month, number of Afib was 27 (out of 92, 29.3%), normal sinus rhythm 57 (62.0%) and the others 8 (8.7%) as like as predischarge findings. However, at postoperative 6 months, Afib was decreased to 17 (out of 88, 19.3%), normal sinus rhythm 58 (65.9%), and the others 13 (14.8%). Then, this findings has been maintained to postoperative 12 months; Afib 18 (out of 90, 20.0%), normal sinus rhythm 58 (64.4%), the others 14 (15.6%).
Table 3. Risk factors analysis for maze failure or recurrence of atrial fibrillation

| Variables                      | No Afib (n=72) | Afib (n=20) | Univariate | Multivariate |
|--------------------------------|----------------|-------------|------------|--------------|
|                                |                |             | p-value    | p-value      | OR            |
| Age (yrs)                      | 54.2±10.4      | 62.2±7.1    | .000       | .010         | 1.093 (1.021 ~ 1.169) |
| Female sex                     | 45 (62.5%)     | 14 (70.0%)  | .536       | .106         |               |
| Rheumatic etiology             | 50 (69.4%)     | 10 (50.0%)  | .106       | .525         |               |
| Preop moderate or severe TR    | 21 (29.2%)     | 12 (60.0%)  | .011       | .033         | 3.597 (1.111 ~ 11.646) |
| Afib duration (yrs)            | 6.5±6.0        | 10.6±6.6    | .010       | .207         | 1.059 (.969 ~ 1.157) |
| Preop LA size (mm)             | 60.7±10.8      | 63.9±14.6   | .286       | .440         | .977 (.920 ~ 1.037) |
| LA reduction plasty            | 2 (2.8%)       | 1 (5.0%)    | .525       | .277         |               |
| CPB time (min)                 | 225.6±49.3     | 219.1±32.7  | .493       | .017         | 1.064 (.964 ~ 1.175) |
| ACC time (min)                 | 153.8±41.8     | 142.6±35.3  | .277       | .217         |               |
| Immediate postop LA size (mm)  | 52.1±7.8       | 56.9±7.7    | .017       | .217         |               |

OR=Odds ratio; Afib=Atrial fibrillation; TR=Tricuspid regurgitation; LA=Left atrium; CPB=Cardiopulmonary bypass; ACC=Aorta cross clamp; Postop=Postoperative.

Generally, in our definition of free from Afib, success rate of our Cox-maze IV procedure in valvular heart disease at postoperative 6 months was 80.7% (71 out of 88). After 6month, we could find three recurred Afib patients in our cohort which meant 3.3% (3 out of 90) of recurrence rate.

During follow up period after discharge, there was no newly developed cerebrovascular accident and no other morbidity associated with open heart surgery except one patient who underwent permanent pacemaker insertion due to sick sinus syndrome. All patients but four (two were early mortalities and two were follow up loss due to other hospital transfer) were regularly followed up in outpatient department. Among them, 53 patients (58.9%) have taken anti-arrhythmic agent such as amiodarone at postoperative 6 month.

3) Risk factors analysis for failure of maze procedure (Table 3)

We elucidated risk factors for failure of our Cox-maze IV procedure about seventeen patients of failure and three of recurrence. In univariate analysis, old age (p=.000), pre-operative longer duration of Afib (p=.010), preoperative more than moderate tricuspid regurgitation (p=.011) and pre-operative larger left atrial size (p=.017) were significant risk factors. However, in multivariate analysis, only old age (p=.010, odds ratio=1.093) and preoperative more than moderate tricuspid regurgitation (p=.033, odds ratio=3.597) were significant risk factors.

DISCUSSION

Maze procedure was introduced by L. Cox for the first time at 1980 and has been modified and developed to be a current procedure [6-8]. Although lesion sets of Cox-maze IV procedure are similar to those of Cox-maze III procedure, it is different that separate both pulmonary box lesion sets are made and connected each other, and other several energy sources such as cryoablation, radiofrequency or microwave are used [3]. This modification has been started with use of cryoablation instead of cut and sew technique since late 1990’s, and Haissaguerre et al suggested modification of separate pulmonary box lesion and connection [9]. So, we have performed Cox-maze IV procedure with established atriotomy lesion set, cryoablation and radio frequency as mentioned above column and made an addition of division of Marshall ligament [10,11].

Concerning bipolar radio frequency, it is inferior to construct transmural lesion than cut and sew technique but superior to avoid catastrophic bleeding from incision line and inevitable time of considerable myocardial ischemic period. So, it is very effective to apply both cryoablation and bipolar radio frequency to make the lesion sets with less time and less complication.

In this study population, although there were two early deaths, all mortalities were related to underlying cardiac disease and combined procedure not to maze procedure itself. In
addition, there were five patients complicated with low cardiac output syndrome who were taken longer operation time because of complexity of combined valve procedure. It goes without saying that such complications cannot be related to maze procedure completely, but minimal additional time to perform Cox-maze IV procedure causes little adverse effect to outcomes of the patients. The other complications were thought to be tolerable.

We report that results of Cox-maze IV procedure for treatment of chronic Afib associated with valvular heart disease is 80.7% of success rate at 6 months and 3.3% recurrence rate afterwards. Melby et al. reported that freedom from Afib rate (86%) of Cox-maze IV procedure using bipolar radio frequency was not inferior to that of original Cox-maze III with cut and sew technique even in small study population (8 patients) [12]. And Lee et al. also reported that there was no difference in conversion rate to sinus rhythm at 6 months in comparison with Cox-maze IV using bipolar radio frequency (40 patients) and classic cut and sew technique (35 patients); 95.0% vs. 97.1%, p=1.0 [13]. In addition, Khargi et al. commented that there was no difference (p=0.260) between classic cut and sew technique and other energy source use in 3832 patients of 45 studies after systematic review in Pubmed online research [4].

Decisive points for success of maze procedure are not only surgical technique such as exact lesion set formation and guarantee for transmurality but also factors of patient itself such as etiology of Afib (rheumatic or non-rheumatic), Afib duration and atrial size. Because this study is not a comparative design, we cannot suggest that Cox-maze IV procedure using cryoaablation and bipolar radio frequency is superior to other type of maze procedure. However, considering relative high proportion of rheumatic valvular disease and lack of lone Afib in this study population, the success rate of 80.7% is comparable to other papers [4,12]. In addition, Cox-maze IV using cryoaablation and bipolar radio frequency is very efficacious and valuable as there has been no newly developed cerebrovascular accident during follow up period.

With respect to prescription of anti-arrhythmic agent in this study, 58.9% at postoperative 6 months is relatively higher than other reports. The reason is suggested that incidence of junctional rhythm and sinus tachycardia is relatively high. However, most patients could be discontinued to take anti-arrhythmic agent afterwards. And we think that direct comparison for anti-arrhythmic agent medication is not reasonable because each surgeon has different preference and indication for anti-arrhythmic agent.

It is widely known from lots of literatures that risk factors for failure of maze procedure were longer duration of Afib, larger left atrial size, and older age including rheumatic valvular heart disease and certain type of Afib [3]. This analysis also found that older age and preoperative more than moderate tricuspid regurgitation were statistically significant risk factors for failure of Cox-maze IV procedure. Old age means that the patient was supposed to have longer period of exposure to organic stress causing Afib and old age itself can be a cause of failure or recurrence for maze procedure because aging process lead a change of fibrosis and less elasticity in atrial wall. Longer duration of Afib was analyzed into significant risk factor in univariate analysis although not in multivariate. Like old age, it can be a cause of failure or recurrence for maze procedure in terms of organic change of atrial wall. However, because additional myocardial ischemic time is minimal in Cox-maze IV procedure; right side maze during pre-clamping period or cardioplegic infusion period and only about ten to fifteen minute to perform on left side maze, and maze procedure conduct rare complication, it is not reasonable that Cox-maze IV procedure should be avoided in old patients or complex cases.

Generally, preoperative more than moderate tricuspid regurgitation is related to left sided cardiac problem leading to right ventricular dilatation. In our cases, most patients who showed more than moderate tricuspid regurgitation were due to functional regurgitation except six patients who showed organic change causing replacement of tricuspid valve. In addition, it is well known that longer duration of Afib or pulmonary hypertension can lead considerable regurgitation in tricuspid valve.

It is debatable that correction of tricuspid regurgitation should be performed in left sided valvular operation. Especially in case of mild regurgitation, most surgeons recommended not to correct it, however, it would occur not infrequently during long term follow up period. And Dreyfus et al commented that tricuspid annuloplasty should be consid-
ered according to presence of annular dilatation not degree of regurgitation in functional tricuspid regurgitation [14]. Therefore, we performed constantly tricuspid annuloplasty using MC3 ring if there was evidence of annular dilatation on right atriotomy finding which showed over three finger breadth or over the size of Carpentier-Edwards ring 34 mm sizer and reported good results which showed low residual tricuspid regurgitation and no morbidity related to annuloplasty procedure [15].

Limitations of this study are; first, there is no comparative control group. Period of classic cut and sew technique in our institution was too long ago to compare current technique because of so many other variables. Besides, to strictly compare two techniques, only lone Afib patients should be studied for exclusion of operative bias. But, we had no such subject. Second, there was no data of both atrial mechanical activities. It is well known that no mechanical activity of atrium can lead evolution of thromboembolism even in normal sinus rhythm. We could not survey that of each patient in TTE data because this study was designed retrospectively. This should be mandatory to following research. Third, we should have surveyed more detail and in-depth manner such as Holter monitoring on analysis of ECG. However, many researchers would set up 12-lead ECG as a standard evaluation tools for Afib. Last, because this study includes many type of combined surgery, it is unreasonable to accept as results of maze procedure. Therefore, it is mandatory to survey on lone Afib.

**CONCLUSION**

The Cox-maze IV procedure using cryoablation and bipolar radio frequency is safe and comparable to other maze procedure with 80.7% of success rate at postoperative 6 months. And risk factors for failure or recurrence are old age and pre-operative more than moderate tricuspid regurgitation.

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