Surgical Treatment of Atrial Fibrillation with Concomitant Mitral Valve Disease: An Asian Review

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Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in patients with mitral valve disease and is present in up to 50% of patients undergoing mitral valve surgery, contributing to increased risks of systemic embolization, anticoagulant-related hemorrhage and mortality. The Cox maze III procedure, introduced in 1987 by Dr. James Cox, was the first effective operation for AF and is recognized as the gold standard therapy for AF associated with organic heart disease. However, few surgeons have adopted the Cox maze III procedure, as it is a lengthy operation with extensive cutting, suturing and blood loss. Several groups in Asia have successfully developed less invasive approaches using a number of different energy sources to create continuous lines of ablation to replace the surgical incisions. Because high-density real-time intraoperative mapping to define the mechanisms of AF is currently not available to guide AF ablation in most surgical groups, an anatomic approach to ablation based on our understanding of the pathophysiology and empiric results is reasonable. The preoperative left atrial size and duration of AF are primary predictors of sinus conversion after the maze procedure for patients with persistent and permanent AF and mitral valve disease. The maze procedure combined with an atrial volume reduction technique may increase the sinus conversion rate. Future progress will require a better understanding of the mechanisms of AF, and minimally invasive cardiac surgery with endoscopic AF ablation needs to be explored in the Asian region. (Chang Gung Med J 2008;31:538-45)

Key words: atrial fibrillation, maze procedure, mitral valve disease

In the Framingham Heart Study, the lifetime risks for development of atrial fibrillation (AF) were 1 in 4 for men and women 40 years of age and older, underscoring the major public health burden posed by AF and the need for further investigation into predisposing conditions, preventive strategies, and more effective therapies.⁹ Atrial fibrillation is the most common sustained cardiac arrhythmia in patients with mitral valve disease and present in up to 50% of patients undergoing mitral valve surgery, contributing to increased risks of systemic embolization, anticoagulant-related hemorrhage and mortality.⁵,⁶ In patients undergoing mitral valve surgery, persistence of postoperative AF is both a marker and a risk fac-
Antiarrhythmic drugs currently available for treating AF suffer from limited efficacy and the potential for life-threatening ventricular proarrhythmia. For these reasons, a definitive therapeutic strategy for AF should be incorporated into the operative strategy for patients with mitral valve disease and AF undergoing mitral valve surgery.

The first effective operation for AF was introduced in 1987 by Dr. James Cox. The Cox maze III procedure involves creating a myriad of incisions on both the right and the left atria (Fig. 1). The operation is based on the belief that AF is produced by multiple macroreentry circuits in the atria. The Cox maze III procedure was highly successful in restoration of sinus rhythm and atrial transport function in patients with lone AF. Later, the Cox maze III procedure was extended to patients with AF associated with organic heart disease and more than 90% of patients with chronic AF associated with mitral valve disease resumed sinus rhythm after the Cox maze III procedure. Few surgeons have adopted the Cox maze III procedure, as it is a lengthy operation with extensive cutting, suturing and blood loss. Moreover, the procedure had significant morbidities. In one report, pacemakers were required in 23.3% of patients who underwent Cox maze III operations as concomitant procedures due to bradycardia and 12.8% of patients without the preoperative diagnosis of sick sinus syndrome required postoperative pacemaker implantation. The shortcomings of the Cox maze III procedure led to interest in developing less invasive surgical approaches to AF, either simplification of the lesion set or replacement of the surgical incisions with continuous lines of ablation using a variety of different energy sources.

Modification of the Cox maze procedure in patients with mitral valve disease: lesion set

Electrophysiological findings in human AF have shown that repetitive activations arising from the pulmonary veins are one of the fundamental mechanisms triggering, and perhaps perpetuating AF. Indeed, Sueda et al. simply isolated the posterior left atrium including the four pulmonary veins without any incisions on the right atrium in patients with permanent AF associated with mitral valve disease, and found that 74% of the patients were cured of AF in a

![Fig. 1](image-url) The Cox maze III procedure. Left, epicardial view of the atria. Right, endocardial view of the atria. Solid line with cross bars, incision and suturing. FO: fossa ovalis; IVC: inferior vena cava; LAA: left atrial appendage; MV: mitral valve; PV: pulmonary vein; RAA: right atrial appendage; SVC: superior vena cava; TV: tricuspid valve.
follow-up period of up to 3 years.\(^{(18)}\) Harada et al. were the first to utilize intraoperative mapping in determining the optimal surgical procedure to cure AF and to apply cryothermy to the left atrial appendage where regular and repetitive electrical discharges originated, and successfully terminated AF.\(^{(19)}\) They further examined the usefulness of intraoperative mapping in 12 patients and demonstrated that regular and repetitive activation originated in the left atria while activation in the right atria was extremely complex and chaotic in the majority of the patients with permanent AF and mitral valve disease.\(^{(20)}\) From these findings, they concluded that the left atrium acts as an electrical driving chamber for permanent AF. However, sinus rhythm was not restored in more than 20% of patients with permanent AF associated with mitral valve disease following simple left atrial isolation without any incisions on the right atrium\(^{(19)}\). Thus, with some patients who have reentrant activations in the right atrium, bilateral incisions in addition to pulmonary vein isolation are necessary and inevitable.\(^{(21,22)}\) Nitta et al. used a 256-channel mapping system with custom-made epicardial patch electrodes to examine atrial activation during AF and to determine the optimal procedure intraoperatively.\(^{(23)}\) A simple left atrial procedure, consisting of pulmonary vein isolation and left atrial incisions without any right atrial incisions, was performed in patients in whom the right atrial activation was passive, and all were cured of AF. In the remaining patients who had reentrant activations in the right atria, bilateral incisions in addition to pulmonary vein isolation were done and 89% of the patients were cured from AF.

Although routine real-time intraoperative mapping is currently not available to guide AF ablation in cardiac surgery patients,\(^{(23)}\) an anatomic approach to ablation based on our understanding of the pathophysiology and empiric results is reasonable. We developed an anatomic sequential strategy for AF ablation.\(^{(24)}\) In the first phase, a modified left atrial maze operation was carried out with concomitant valvular surgery; the right side maze operation was subsequently carried out as a second phase of the sequential strategy only if AF reappeared following spontaneous restoration of heart beats during the operation. We found that comparing with the left atrial maze procedure, the application of simultaneous sequential strategy successfully restored sinus rhythm in an additional 22.2% of patients with persistent AF, and the overall sinus conversion rate of 88.9% was comparable with that of the standard biatrial maze procedure.\(^{(24)}\) In fact, such an anatomic (rather than map-guided) approach is rapidly becoming the foundation for catheter-based ablation of AF.\(^{(25-27)}\)

One of the shortcomings of the Cox maze III procedure is that pacemaker implantation is required in 23.3% of patients as a result of bradycardia.\(^{(25)}\) In an animal model, McLoughlin et al. showed that the maze procedure produced significant acute sinus node dysfunction and a trend toward sinus node dysfunction developing in the chronic phase of the maze procedure.\(^{(28)}\) Boineau et al. demonstrated that human physiological pacemaker tissue extended across a significantly larger area of atrial tissue than that had been previously recognized.\(^{(29)}\) Based on this concept, we introduced another atrial pacemaker complex preserved radiofrequency maze procedure, effectively restoring sinus rhythm and atrial transport function in the majority of patients with permanent AF and mitral valve disease and only 2.8% of patients developed late sinus node dysfunction postoperatively.\(^{(30)}\)

**Modification of the Cox maze procedure in patients with mitral valve disease: replacement of surgical incisions with ablation using a variety of different energy sources**

Another shortcoming of the Cox maze III procedure is that it is a lengthy operation with extensive cutting, suturing and blood loss. This has led to interest in developing less invasive surgical approaches to ablate AF using a variety of different energy sources.

Kosakai et al. modified the Cox maze III procedure with cryoablation for patients with organic heart disease and 86% of patients were free from AF and atrial flutter after the operation.\(^{(11)}\) Lee et al. reported similar results.\(^{(31)}\)

Intraoperative radiofrequency ablation is a novel surgical principle for the treatment of AF in combination with a standard open heart operation. We introduced intraoperative radiofrequency catheter ablation and cryoablation to modify the maze procedures to obviate the need for extensive atrial incisions in patients undergoing simultaneous valvular surgery and 80% of patients had restored sinus rhythm after surgery in our initial experience.\(^{(32)}\) Our results represent the first report in humans that the
maze procedure, using unipolar radiofrequency energy and cryoablation with concomitant valvular surgery, has an acceptable success rate in restoring sinus rhythm and atrial transport function.\(^{33}\) In our early experience with 77 patients with permanent AF and mitral valve disease undergoing the radiofrequency maze procedure and concomitant mitral valve operations, 65 patients (84.4\%) had persistent sinus conversion and 12 patients (15.6\%) did not regain sinus rhythm at a mean follow-up of 38 months. In addition, left atrial transport function was observed in 56 patients (86\%) and right atrial transport function was observed in all 65 patients (100\%) with restoration of sinus rhythm after the radiofrequency maze procedure.\(^{34}\)

**Clinical determinants of sinus conversion by the maze procedure in patients with mitral valve disease**

Kosakai demonstrated that in patients with mitral valve disease who underwent the surgical maze procedure for AF, the sinus conversion rates decreased as the preoperative left atrial dimensions increased.\(^{35}\) We had similar observations in patients with permanent AF and mitral valve disease who underwent the saline-irrigated unipolar radiofrequency maze procedure while undergoing concomitant valvular operations (Fig. 2).\(^{34,36}\) In addition, we showed that the preoperative duration of AF was also a primary predictor of sinus conversion after the radiofrequency maze procedure for patients with persistent AF and mitral valve disease. In our study of 99 consecutive patients with persistent AF and mitral valve disease undergoing radiofrequency maze procedure and concomitant mitral valve operations, we found that the sinus conversion rate was significantly lower in patients with preoperative left atrial diameters > 56.8 mm than in patients with preoperative left atrial diameters < 56.8 mm (OR 7.41, 95\% CI 2.29 - 23.98, \(p < 0.001\)). The incidence of AF at 3 and 5 years was significantly greater in patients with left atrial diameters > 56.8 mm than in those with left atrial diameters < 56.8 mm (16.4\% vs 2.9\% and 38.7\% vs 11.5\%, respectively, \(p < 0.001\)) (Fig. 3).\(^{36}\)

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**Fig. 2** The radiofrequency maze procedure. Left, epicardial view of the atria. Right, endocardial view of the atria. Circle, cryoablation; solid line with cross bars, incision and suturing; dotted line, radiofrequency ablation. FO: fossa ovalis; IVC: inferior vena cava; LAA: left atrial appendage; MV: mitral valve; PV: pulmonary vein; RAA: right atrial appendage; SVC: superior vena cava; TV: tricuspid valve. Reprinted with permission from Chen et al.\(^{36}\)
In addition, the sinus conversion rate was significantly lower in patients with an AF duration > 66 months than in patients with AF duration < 66 months (OR 9.45, 95% CI 2.74 to 32.60, \( p < 0.001 \)). The incidence of AF at 3 and 5 years was significantly greater in patients with AF duration > 66 months than in those with AF duration < 66 months (22.6% vs 0% and 37.9% vs 12.5%, respectively, \( p < 0.0001 \)) (Fig. 4).\(^{(36)}\) Furthermore, we showed that the postoperative left and right atrial dimensions of patients who had sinus conversion by the radiofrequency maze procedure were significantly smaller than those of patients who did not regain sinus rhythm.\(^{(37)}\) Based on our report, Marui et al. developed a novel atrial volume reduction technique combined with the Cox maze III procedure or left atrial maze procedure in patients with large left atrial diameters (≥60 mm) and they found that the sinus conversion rate in patients with the volume reduction technique was significantly better that in patients without this technique.\(^{(38)}\)

**Future directions**

Minimally invasive cardiac surgery with endoscopic AF ablation is possible in selected patients\(^{(39)}\) but this technique needs to be explored in the Asian region.

**Conclusions**

Atrial fibrillation is the most frequent sustained cardiac arrhythmia in patients with mitral valve disease. If left untreated, AF increases morbidity and jeopardizes survival. The shortcomings of the cut-and-sew Cox maze III procedure have led to replacement of the operations with alternative energy sources to rapidly create lines of conduction block with fewer morbidities. Continued progress in understanding the mechanisms of AF and minimally invasive AF ablation will facilitate tailored ablation approaches and improve the surgical outcomes as well as the quality of life for individual patients with atrial fibrillation and concomitant mitral valve disease.

**REFERENCES**

Surgical treatment of atrial fibrillation in Asia


僧帽瓣疾病併心房纖維顫動的外科治療方式：亞洲的綜合評論
陳勉成 張仁平 陳永隆

心房纖維顫動是僧帽瓣疾病病人最常見持續性的心律不整，而且可在百分之五十進行僧帽瓣手術的病人身上見到心房纖維顫動的存在，心房纖維顫動會增加全身性血栓的形成、抗凝血劑相關的出血及死亡。西元 1987 年由 James Cox 醫師所發明的 Cox maze III 手術是第一個針對心房纖維顫動有效的治療手術，而且被公認為器質性心臟病合併心房纖維顫動的標準治療方式。然而，極少數的外科心臟醫師採用 Cox maze III 手術方式，因為它需要較長的手術時間用於切割及縫合，及其造成較多的血液流失。幾個亞洲的研究團隊已經成功的發展出，利用不同的能量來源來產生連續的病灶，用以取代傳統的手術切割方式。由於，目前大多數的手術團隊並無法擁有高密度即時的電生理學定位儀器，來確定心房纖維顫動的機制而引導迷路手術。所以，根據我們所瞭解的病生理學知識及經驗性的累積，使用解剖學上固定路線來燒灼的處理方式是合理的。術前左心房的大小及心房纖維顫動已存在的時間，是主要預測持續性或永久性心房纖維顫動及僧帽瓣疾病病人，接受迷路手術後是否能回復成正常竇性心臟節律的決定因子。迷路手術合併心房容積減少手術可能會增加回復成正常竇性心臟節律的機率。未來的發展包括需要更瞭解心房纖維顫動的機制，另外使用內視鏡作為治療心房纖維顫動的微創迷路手術方式，也是未來需要進一步在亞洲區域進行發展的方向。(長庚醫誌 2008;31:538-45)

關鍵詞：心房纖維顫動，迷路手術，僧帽瓣疾病