

## **Efficacy of non-cardioplegic radiofrequency ablation Maze-III procedure (RFA Maze-III) for the treatment of atrial fibrillation (AF) during the valve replacement surgery.**

**Yang Yan<sup>1</sup>, Lu-Qin Yan<sup>1</sup>, Xiao-Jiang Yu<sup>2</sup>, Wei-Jin Zang<sup>2\*</sup>**

<sup>1</sup>Department of Cardiovascular Surgery, First Affiliated Hospital, Xi'an Jiaotong University, Xi'an, PR China

<sup>2</sup>Department of Pharmacology, College of Medicine, Xi'an Jiaotong University, Xi'an, PR China

### **Abstract**

**Background:** The non-cardioplegic surgery has a better myocardial protection compared to cardioplegic surgery. Combination of valve replacement surgery with RFA Maze-III procedure can achieve better clinical efficacy. The goal of this study was to evaluate the efficacy of RFA Maze-III under the non-cardioplegic and mild hypothermic Cardiopulmonary Bypass (CPB) condition for the treatment of chronic Atrial Fibrillation (AF) during the valve replacement surgery.

**Hypothesis:** The non-cardioplegic RFA Maze-III is a safety and efficacy procedure for the treatment of AF during valve replacement surgery.

**Methods:** From 2007 to 2013, 84 consecutive patients with rheumatic heart disease and chronic AF underwent RFA Maze-III and heart valve replacement surgery in our hospital, 46 of which had non-cardioplegic procedure. Continuous electrogram monitoring was performed to observe the cardio-electrical activities of patients during RFA Maze-III and valve replacement surgery. All the patients were follow-up with 24 h Holter and echocardiography in the perioperation and at 12 months after the operation.

**Results:** Sinus rhythm was recovered and maintained perioperatively in 73.7% (28/38) of cases in the cardioplegic group, which was significantly lower than that (91.3%, 42/46) in the non-cardioplegic group. One year after operation, sinus rhythm was maintained in 78.9% (30/38) of cases with cardioplegic surgery, which was significantly lower than that (89.1%, 41/46), in the group with non-cardioplegic surgery.

**Conclusion:** Mild hypothermic non-cardioplegic surgery is feasible, safe and efficient in the treatment of AF by RFA Maze-III. In addition, non-cardioplegic operation simplifies the surgical procedure and makes the process more clearly.

**Keywords:** Atrial fibrillation, Non-cardioplegic operation, Valve replacement, Modified radiofrequency ablation Maze-III procedure (RFA Maze-III).

*Accepted on December 26, 2016*

### **Introduction**

Atrial Fibrillation (AF) is the most prevalent arrhythmia in human affecting approximately 1.5-2% of the general population. Under the age of 60, the prevalence is less than 1%, but it is up to 6% in the population above 80 [1-5], and up to 70% in the patients with valvular heart disease [6]. When valvular disease is complicated with AF, cardiac output can be reduced by 15%-20%. With a substantial higher risk of stroke and systemic thromboembolism, AF is associated with an increase in mortality and morbidity [7].

The mechanisms of AF are not well understood despite intense investigations over the past decade [8]. The triggers for initiation and an anatomic substrate for maintenance are both principle elements for the development of AF [9]. Several

other hypotheses (like multiple wavelet re-entry, rotors, or spiral wave) have been proposed to elucidate the electrophysiological mechanisms that initiate and maintain AF [10]. The atrial maze procedure and ablation lines designed to interrupt multiple wavelets and spiral re-entry are developed. Combination of valve replacement surgery with RFA Maze-III procedure can achieve better clinical efficacy for the patients with AF and valvular heart disease [11,12].

The most accepted therapy was valve replacement surgery combined with RFA Maze-III under the Cardiopulmonary Bypass (CPB) and cardioplegic condition. In previous studies, we performed valve replacement surgery combined with RFA Maze-III for 51 patients under the CPB and cardioplegic condition. Under the cardioplegic condition, the RFA Maze-III surgery needed to observe the surgery complications and

whether the block occurred after heart resuscitation. From 2010 to 2013, we performed the same surgery for 58 patients under the CPB and non-cardioplegic condition. Beating heart surgery has the better myocardial protection compared to cardiac arrest surgery [13,14]. In addition, beating heart surgery can facilitate the observation of ECG changes to the RFA Maze-III during surgery. After 12 months, we conducted follow-up examinations, in order to assess the cardio-electrical activities outcomes of two operation methods.

## Methods

### Participants

A total of 84 cases (Cardioplegic group: 38; Non-Cardioplegic group: 46) from First Affiliated Hospital of Xi'an Jiaotong University were included in this study. This research was approved by First Affiliated Hospital of Xi'an Jiaotong University.

**Case selection and exclusion criteria:** All cases had rheumatic heart disease with an AF history of more than 1 year. All cases required open heart surgery. Patients and their families agreed to perform RFA Maze-III. All patients consent to conduct follow-up examinations after 6-12 months of surgery. Patients with sick sinus syndrome or emergency surgery, or those patients who could not come to the hospital for follow-up examinations were excluded.

In the cardioplegic group, regular CPB was established and the nasopharyngeal temperature was maintained at 28~30°C. The inferior vena cava and the ascending aorta were clamped and St. Thomas solution was perfused to stop the heart beating. After heart beating stopped, valve was replaced and RFA Maze-III was performed.

In the non-cardioplegic group, the nasopharyngeal temperature was maintained at 31~34°C during the period of CPB. During the surgery, only the inferior vena cava was clamped, while the ascending aorta was not clamped. For those patients who need aortic valve replacement, coronary sinus was inversely

perfused with warm blood during the aorta clamping period, which allows the heart in an empty beating state. Valve replacement and formation and RFA Maze-III were performed. During the surgery period, perfusion pressure of systemic circulation was maintained between 50 and 60 mmHg. Conversion of the heart rhythm was analysed for patients in both groups [15].

The variable tested in this research is successful case number of ablation during the surgery, AF recurrence case number 7 days after ablation, number of cases maintaining sinus rhythm after 1 year, Cardiothoracic Ratio (CTR), Left Atrial Diameter (LAD), Left Ventricular End-Systolic Diameter (LVESD), Left Ventricular End-Systolic Diameter (LVEDD) and Left Ventricular Ejection Fraction (LVEF).

### Statistical analysis

All data are reported as mean  $\pm$  SD for continuous variables and number of subjects (%) for categorical variables. Comparisons of CTR, LAD, LVESD, LVEDD and LVEF in cardioplegic and non-cardioplegic group were conducted by a paired Wilcoxon signed rank test or chi square analysis. SPSS 13.0 software (SPSS, Chicago, IL) was used to perform data analysis.  $P < 0.05$  was considered statistical significance.

## Results

All patients had rheumatic heart disease combined with AF. 71 cases mainly presented mitral stenosis, while 13 cases mainly presented mitral regurgitation. Complication with tricuspid regurgitation occurred in 64 cases, while complication with aortic valve stenosis and (or) regurgitation occurred in 22 cases. Preoperative classification showed that 28 cases had a heart function of grade I-II, 50 cases had a heart function of grade III and 6 cases had a heart function of grade IV. ECG examination indicated that all patients had AF. Comparison of the general information between the cases in the non-cardioplegic and those in the cardioplegic groups was shown in Table 1.

**Table 1.** Comparison of basic characteristics of patients between cardioplegic and non-cardioplegic groups.

Groups	Case no	M/F	Age (y)	History of AR (y)	CTR	LAD (mm)	LVESD (mm)	LVEDD (mm)	LVEF
Cardioplegic	38	17/21	41.1 $\pm$ 7.3	5.7 $\pm$ 3.5	0.58 $\pm$ 0.10	53.1 $\pm$ 11.5	42.1 $\pm$ 4.6	64.8 $\pm$ 5.2	46.7 $\pm$ 9.3
Non-Cardioplegic	46	20/26	42.1 $\pm$ 9.5	6.3 $\pm$ 2.2	0.59 $\pm$ 0.08	51.6 $\pm$ 13.2	44.1 $\pm$ 2.0	66.7 $\pm$ 3.2	45.2 $\pm$ 8.7

There was no significant difference between the two groups ( $P > 0.05$ ); CTR: Cardiothoracic ratio; LAD: Left Atrial Diameter; LVESD: Left Ventricular End-Systolic Diameter; LVEDD: Left Ventricular End-Systolic Diameter; LVEF: Left Ventricular Ejection Fraction.

In the non-cardioplegic group, 40 cases converted to sinus rhythm during the process of left atrial ablation. Among these 40 cases, 27 cases had heart rhythm conversions during the time of ablation for the left pulmonary vein, 11 cases had heart rhythm conversions during the time of ablation for the right pulmonary vein and 2 cases had heart rhythm conversions

during the time of ablation for the pulmonary vein to the mitral valve. Alternating AF and sinus rhythms occurred in 4 cases and arrhythmia disappeared after using amiodarone during the period of CPB. Two cases converted to sinus rhythms during the process of right atrial ablation. The rhythms of both cases

## Efficacy of non-cardioplegic radiofrequency ablation Maze-III procedure (RFA Maze-III) for the treatment of atrial fibrillation

changed during the time of ablation for the right atrium to the tricuspid valve (Table 2).

**Table 2.** The ablation site of the patients with changes of heart rhythm during the process of ablation.

Group	Case no	Conversion no	Ablation site when rhythm changed during the process of non-cardioplegic operation			
			Left pulmonary vein	Right pulmonary vein	Left, right lung vein ablation connection	Ablation for the right atrium
Non-cardioplegic	46	42	27 (64.3%)	11 (26.2%)	2 (4.8%)	2 (4.8%)

In the non-cardioplegic group, five cases had AF within 7 days after surgery and 4 cases converted to sinus rhythm after using amiodarone. The remaining 1 case still had AF. Two cases had atrial flutter and converted to sinus rhythm after electrical Cardioversion. 3 cases still had AF after the maze procedure and sinus rhythm was not recovered after treatment with amiodarone. Among the 46 cases in the non-cardioplegic group, 42 cases maintained sinus rhythm within 7 days after the surgery. All these patients were routinely given amiodarone at a dosage of 150 mg/day for 6 months and 41 cases (89.1%) maintained sinus rhythm with detectable P wave 12 months after the surgery. Five cases had AF.

In the cardioplegic group, after cardiac resuscitation, 28 patients converted to sinus rhythm, 2 patients had nodal rhythm, while the remaining 8 cases still had AF rhythm. Among the patients who converted to sinus rhythm after

resuscitation, 7 cases had alternating AF and sinus rhythm. After using amiodarone, arrhythmias disappeared. 2 patients had atrial flutter and sinus rhythm was recovered after the synchronous electrical Cardioversion. 4 cases had AF within 7 days after surgery and amiodarone treatment was ineffective. 8 cases still had AF rhythm after cardiac resuscitation and after amiodarone treatment sinus rhythm were recovered in 3 patients. Among 38 patients in the cardioplegic group, 27 cases maintained sinus rhythm after 7 days of the surgery. Regular dosage of amiodarone (150 mg) was used for 6 months after the surgery. Follow-up examination was performed after 12 months of surgery. ECG examination showed that 30 cases presented sinus rhythm (78.9%) with detectable P wave, 2 cases presented nodal rhythm, and 6 cases presented AF. Comparison of the surgical cardioversion between the two groups was shown in Table 3.

**Table 3.** Comparison of the heart rhythm conversion rate between the two groups.

Groups	Case no.	Successful case No. of ablation during the surgery	AF recurrence case no. 7 d after ablation <sup>§</sup>	No. of cases maintaining sinus rhythm after 1 y
Cardioplegic	38	28 (73.7%)	11 (7/4; 63.6%)	30 (78.9%)
Non-cardioplegic	46	42 (91.3%)*	9 (8/1; 88.9%)*	41 (89.1%)*

<sup>§</sup>Success conversion case No. after drug usage/failed, success percentage; \*P<0.05.

The general parameters for the patients in the two groups were shown in Table 4.

**Table 4.** General information of the patients after surgery.

Groups	CTR	LAD (mm)	LVESD (mm)	LVEDD (mm)	LVEF (%)
Cardioplegic	0.55 ± 0.12	47.8 ± 2.5	39.6 ± 2.6	62.8 ± 5.2	49.7 ± 11.3
Non-cardioplegic	0.53 ± 0.06	45.6 ± 2.7	40.4 ± 3.7	61.7 ± 3.2	50.2 ± 9.9

There was no significant difference between the two groups (P>0.05).

## Discussion

The main hazard of AF is the occurrence of subjective symptoms caused by arrhythmia, hemodynamic changes due to the loss of atrioventricular synchronous and thromboembolism. AF results in the loss of effective atrial contraction, leading to the reduction of cardiac output by 10%. Moreover, the occurrence of rapid AF accompanied by fast ventricular rate causes the reduction of cardiac output by 40%. In China, 80%

of the patients with rheumatic mitral valve diseases are complicated with chronic AF before the surgery. Without treatment, self-healing of AF occurs in a very small portion of the patients after valve replacement surgery [16]. With the advancement in electrophysiological studies of Cox et al. designed maze procedure based on the idea that returning circulation easily occurred in the left atrial appendage, superior vena cava and pulmonary veins [17]. The principle of the procedure is to create a normal conduction channel from sinus

node to the atrioventricular node, which drives the ventricle and forms multiple blind pathways in both atriums. Consequently, the electrical impulses can excite all the atrial muscles. The separated myocardial tissues can block potential re-entrant loop and maintain synchronous activity and transmission of both atriums. Studies have shown positive effect of maze procedure in the treatment of AF. Performing maze procedure during valve replacement surgery has great benefit in the improvement of cardiac function [18]. However, the maze procedure has the disadvantage of wide operative range, complex incision, complicated technique on the “cut and sew” of right and left atriums, damages on other tissues, long operation time (1-1.5 h) and the occurrence of complications, e.g., bleeding and damages on conduction system.

Recent studies show that the clinical efficacy of Maze-III in which RFA is used in the open heart surgery is almost identical to that of the classical maze procedure in the treatment of AF [19]. However, Maze-III has many advantages compared to classical maze procedure and thus has been performed by many hospitals to replace classical maze procedure. Most hospitals use hypothermic CPB and cardioplegic approach to perform open heart surgery. However, hypothermia, cardiac arrest and CPB have many adverse effects. Therefore, some scholars propose CPB surgery without clamping aorta [13,14]. This surgical procedure does not interrupt coronary blood flow and the beating heart has sufficient blood and oxygen in the absence of load, which avoids the myocardial ischemia and reperfusion injury caused by cardiac arrest [15]. This approach does not require perfusion device for cardiac arresting solution, shortens the CPB time, and reduces the destruction of the physical components in the blood, the interference of clotting mechanism and the blood loss in the surgery. Therefore, we applied mild hypothermic non-cardioplegic open heart surgery coupled with RFA Maze-III to treat AF.

Our results showed that the success rate of ablation, the conversion rate of recurrent AF and the sinus rhythm maintenance rate after 12 months in the non-cardioplegic group was significantly higher than those in the cardioplegic group. There is currently no method to evaluate transmural activity and complete transmural activity is normally judged by empirical approach (radiofrequency ablation is performed until the appearance of yellow or gray colors), which increases the uncertainty of the surgery. When non-cardioplegic approach is used, we usually repeat one more time of ablation on the corresponding site where the central rhythm changed in order to ensure the efficiency of the ablation. If the cardiac rhythm does not convert to sinus rhythm after completion of ablation, RFA is repeated or the route of RFA is appropriately changed in order to achieve its efficacy. With the advancement of ablation technology, bipolar RFA can identify the transmural activity, which ensures complete transmural activity, but does not cause excessive myocardial damage. The advantage of visual observation in the cardioplegic surgery has instructive significance in the treatment of AF by bipolar RFA. In the surgical treatment of rheumatic mitral valve disease combined with AF, we found that ablation in the left atrium, especially in the left pulmonary vein openings, is particularly important. In

the non-cardioplegic group, most patients converted to sinus rhythm during the ablation of the left pulmonary vein openings. In contrast, very small portion of patients converted to sinus rhythm during the ablation of the right atrium. In addition, 6 months of amiodarone utilization is necessary for RFA Maze-III regardless of cardioplegic or non-cardioplegic surgery. This is because the ablation lines will be completely healed and scar formation occurs after 5 months of surgery, which produces a barrier to block the conduction of abnormal electrical activity. On the other hand, sustained AF causes atria remodeling. Utilization of amiodarone can relieve the instability of the rhythm caused by the reduced refractory period and the recurrence rate due to the anatomic structure caused by AF. However, the dosage of amiodarone should be adjusted. Some scholars propose that if the heart rate is slow and electrocardiogram Q-T interval is prolonged, use of amiodarone should be terminated. We used drugs that can increase sinus rhythm for those patients and achieved good efficacy. It is worthy to note that there are many factors, e.g., the length of disease history of AF, the size the atrium and the left atrial wall tension, that affect the success of ablation of AF [20-23].

In this study, we found that it is easier to avoid arrhythmia in the non-cardioplegic group than that in the cardioplegic group. In some patients, there are sinus bradycardia, sinus arrest and sinus-atrial blockage. We speculate that this is due to the existence of sinus node malfunction that has been masked by AF before surgery. Surgery affected the functional integrity and the blood supply of sinus node. Surgery may also affect the cardiac autonomic regulation leading to the occurrence of arrhythmias. Because of the heart rhythm monitoring during the whole process of ablation procedure, problems can be detected early and further injury can be avoided. However, the conclusion in this research was based on one research center from China. Whether it's appropriate for extension to other places still need further exploration.

## Conclusion

RFA Maze-III performed in the mild hypothermia non-cardioplegic surgery is a safe and feasible approach with better clinical efficacy for the treatment of AF. In addition, it simplifies the surgical procedure, makes the surgery more precise and has pronounced protective effect on the heart.

## References

1. Lip GYH, Merino J, Ezekowitz M. A prospective evaluation of edoxaban compared to warfarin in subjects undergoing cardioversion of atrial fibrillation: the EdoxabaN vs. warfarin in subjects undergoing cardioversion of atrial fibrillation (ENSURE-AF) study. *Am Heart J* 2015; 169: 597-604.
2. Rordorf R, Chieffo E, Savastano S. Anatomical mapping for atrial fibrillation ablation: a head-to-head comparison of ultrasound - assisted reconstruction versus fast anatomical mapping. *Pacing Clin Electrophysiol* 2015; 38: 187-195.

*Efficacy of non-cardioplegic radiofrequency ablation Maze-III procedure (RFA Maze-III) for the treatment of atrial fibrillation*

3. Flegel KM, Shipley MJ, Rose G. Risk of stroke in non-rheumatic atrial fibrillation. *Lancet* 1987; 1: 526-529.
4. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. *Stroke* 1991; 22: 983-988.
5. Furberg CD, Psaty BM, Manolio TA. Prevalence of atrial fibrillation in elderly subjects (the Cardiovascular Health Study). *Am J Cardiol* 1994; 74: 236-241.
6. Cox JX, Schuessler RB, Agostino HJ. The surgical treatment of atrial fibrillation. Development of a definitive surgical procedure. *Thorac Cardiovasc Surg* 1991; 101: 569-589.
7. Nattel S, Opie LH. Controversies in atrial fibrillation. *Lancet* 2006; 367: 262-272.
8. Arle JE, Mei L, Carlson KW. High-frequency stimulation of dorsal column axons: potential underlying mechanism of paresthesia-free neuropathic pain relief. *Neuromodulation* 2016; 19: 385-397.
9. Chen SA, Hsieh MH, Tai CT. Initiation of atrial fibrillation by ectopic beats originating from the pulmonary veins: electro physiologic characteristics, pharmacologic response, and effects of radio-frequency ablation. *Circulation* 1999; 100: 1879-1886.
10. Moe GK, Abildskov JA. Experimental and laboratory reports. Atrial fibrillation as a self-sustained arrhythmia independent of focal discharge. *Am Heart J* 1959; 92: 1954-1968.
11. Aidietis A, Rucinskas K, Sirvydis V, Jurkuvenas P, Grebelis A. Radiofrequency modified maze procedure with mitral valve surgery: mid-term follow-up results. *Medicina (Kaunas)* 2004; 40: 1-6.
12. Tekumit H, Uzun K, Cenal AR. Midterm results of left atrial bipolar radiofrequency ablation combined with a mitral valve procedure in persistent atrial fibrillation: cardiovascular topics. *Cardiovasc J Afr* 2010; 21: 137-141.
13. Wei H, Hui L, Baoshi Z. Comparative study on beating heart and arrested heart under mild hypothermic cardiopulmonary bypass. *Chin J Thorac Cardiovasc Surg* 2001; 17: 96-98.
14. Ricci M, Macedo FI, Suarez MR, Brown M, Alba J. Multiple valve surgery with beating heart technique. *Ann Thorac Surg* 2009; 87: 527-531.
15. Preventza O, Coselli JS. Differential aspects of ascending thoracic aortic dissection and its treatment: the North American experience. *Ann Cardioth Surg* 2016; 5: 352.
16. Sims JB, Robes WC. Comparison of findings in patients with versus without atrial fibrillation just before isolated mitral valve replacement for rheumatic mitral stenosis (with or without associated mitral regurgitation). *Am J Cardiol* 2006; 97: 1035-1038.
17. Cox JL, Ad N, Palazzo T, Fitzpatrick S, Suyderhoud JP. Current status of the Maze procedure for the treatment of atrial fibrillation. *Semin Thorac Cardiovasc Surg* 2000; 12: 15-19.
18. Raanani E, Albage A, David TE. The efficacy of the Cox/maze procedure combined with mitral valve surgery: a matched control study. *Eur J Cardiothorac Surg* 2001; 19: 438-442.
19. Khargi K, Hutten BA, Lemke B, Deneke T. Surgical treatment of atrial fibrillation; a systematic review. *Eur J Cardiothorac Surg* 2005; 27: 258-265.
20. Geidel S, Ostermeyer J, Lass M. Three years' experience with monopolar and bipolar radiofrequency ablation surgery in patients with permanent atrial fibrillation. *Eur J Cardiothorac Surg* 2005; 27: 243-249.
21. Kim JB, Yun TJ, Chung CH. Long-term outcome of modified Maze procedure combined with mitral valve surgery: analysis of outcomes according to type of mitral valve surgery. *J Thorac Cardiovasc Surg* 2010; 139: 111-117.
22. Gaynor SL, Schuessler RB, Bailey MS, Ishii Y, Boineau JP. Surgical treatment of atrial fibrillation: predictors of late recurrence. *J Thorac Cardiovasc Surg* 2005; 129: 104-111.
23. Wang W, Buehler D, Martland AM. Left atrial wall tension directly affects the restoration of sinus rhythm after Maze procedure. *Eur J Cardiothorac Surg* 2011; 40: 77-82.

**\*Correspondence to**

Wei-Jin Zang

Department of Pharmacology

College of Medicine

Xi'an Jiaotong University

PR China