



## Evaluation of Early and Intermediate Outcomes of Cryo-Maze Procedure for Atrial Fibrillation

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### ABSTRACT

**Introduction:** Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in patients with mitral valve disease affecting 50% of patients undergoing mitral valve surgery, contributing to increased risks of systemic embolization, anticoagulant-related hemorrhage and mortality. The maze procedure is an effective way to treat AF. Over the last several years, cryoablation was substituted for atrial incision in many reports to simplify the maze procedure. However, few studies have been carried out to evaluate the results of cryoablation surgery. In the present study we evaluated the results of this procedure.

**Methods:** In this cross sectional study, 47 AF patients were treated with Cryo-Maze surgery method. Rhythm assessment using electrocardiographic and echocardiographic survey was performed in all patients before surgery, during the patients' hospital stay, on discharge and after six months.

**Results:** Survival rate of the studied patients at six months was 93.6%. Sinus rhythm restoration rate in Cryo-Maze patients was 72.1% on discharge and 76.7% six months after their operation.

**Conclusion:** The present study revealed that Cryo-Maze procedure is an effective and safe therapeutic modality in AF while normal sinus rhythm can be achieved in patients following this intervention.

### Introduction

Atrial fibrillation (AF) is one of the most common cardiac dysrhythmias with an overall incidence of about 1 percent of the general population (25% in people aged 40 and older and 10% in people aged over 80 years).<sup>1-3</sup>

Tachycardias such as AF can lead to very hazardous complications including hemodynamic instability, vascular thrombosis, heart failure, increased incidence of peripheral embolism and individual functional limitations such as dyspnea and tiredness during activity. For this reason, several medical and surgical therapeutic strategies have been proposed and investigated for management of AF.<sup>4-6</sup>

Anti-arrhythmic medications and surgical incisions using a special catheter are employed in patients with proper performance and in diverse conditions.<sup>7</sup> Unfortunately, medical treatments have many limitations and in recurrence has been reported in more than 60% of AF cases.<sup>8</sup> Surgical treatment of AF using Cox-Maze procedure has been very effective with long-term cure rate of about 90%.<sup>9</sup> Five major goals of AF treatment include: AF Elimination,

sinus rhythm restoration, synchronization between atrial and ventricular contractions (atrioventricular synchrony), reconstruction of atrial contractile function and reduction of thromboembolic events risk.<sup>10,11</sup> Despite the long-term benefits of the Cox-Maze surgical method, incising and suturing techniques are difficult tasks for cardiac surgeons and they hardly acknowledge it as a routine procedure.<sup>12</sup> Recently in the light of technology advances in the field of biomedical engineering an appropriate tool for abolishing AF has been provided which in fact is a modified kind of Cox-Maze surgical procedure replacing old incising techniques for abolishing AF.<sup>12,13</sup>

### Materials and methods

Between 2006 and 2009, 47 patients who were scheduled to undergo elective coronary artery bypass surgery (CABG) in Madani educational heart hospital, Tabriz, Iran were selected and participated in the study.

Patients were selected among patients with valvular heart disease, ischemic heart disease and other valvular disorders which caused cardiac dysrhythmias as tachyarrhythmias (AF) who were referred to our center for cardiovascular

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surgery. Method of samplings was simple sampling and all patients with atrial fibrillation rhythm who underwent CABG or valve surgery were enrolled in this study. Inclusion criteria were patients with AF disorder and continuous participation in the follow-up. After obtaining and recording medical history, initial clinical examination, electrocardiography and echocardiography were performed before surgery. These patients were classified into four classes according to the American Heart Association functional classification. All patients admitted electively were visited by an anesthesiology expert team. Drug history was investigated. In patients who were taking warfarin, it was discontinued then heparin was started for patients every six hour following study.

Operation time, cardiopulmonary bypass (CPB) and long-term clamp time and any complications during and immediately after surgery in all patients were monitored and recorded. In all patients double-wire pacemaker was implanted.

In the presence of AF or artificial valve, antiarrhythmic and anticoagulant therapy was applied.

Antibiotics were continued until 24 hours after the patients' arterial and venous catheters were removed. Electrocardiography was performed daily until discharge day, six months after discharge and at 6-month interval follow-up to evaluate patients. Echocardiography was performed to assess cardiac contractile function, regularly during hospitalization and also at six-months after surgery. Based on previous studies, the left atrial size below 50 mm was classified as small and over 50 mm was considered as large. Finally, based on previous studies for determination of the AF rhythm change according to atrium size, the left atrium size was exactly measured before surgery and classified into four groups: 45 mm, 45 to 50 mm, 50 to 55 mm and more than 55 mm. To review the findings of echocardiography, results of the present survey were divided into four groups of ejection fraction; over 55% was considered good, 55 to 45% fair, and below 45% as poor.

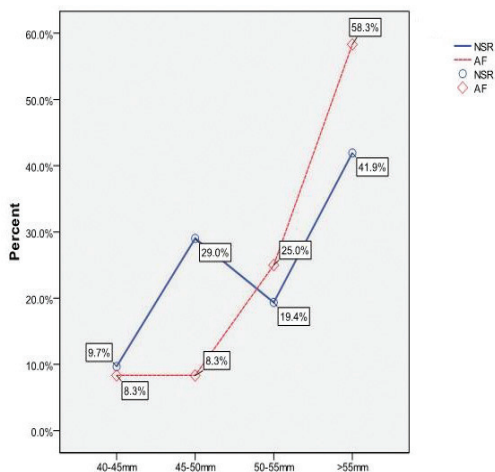
Cryo catheter surgical device using NO gas and C90-temperature for 2 to 3 minutes was used for patients. Following variables were studied: age, sex and ECG prior to discharge and follow-up period, cardiac contractile function through echocardiographic assessment of left atrial size, classification of individual performance (Function class), clamp time, CPB time and type of valvular disorders. SPSS version 17.0 (SPSS, Chicago, IL, USA) was used for statistical analysis and  $P < 0.05$  was considered statistically significant. Continuous variables with normal distribution were presented as mean  $\pm$  SD. Categorical variables were analyzed with *t*-test; finally, Chi-squared test was used for evaluation of qualitative variables. Paired *t*-test was used for evaluation of quantitative variables.

## Results

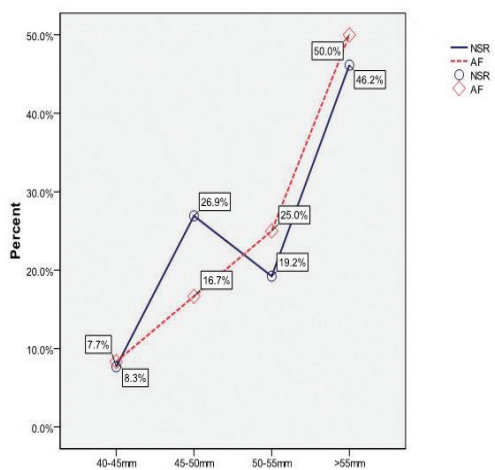
The study was performed on 47 surgical patients who

underwent Cryo-Maze procedure, including 10 men (21.3%) and 37 women (78.7%) with the mean age of  $49.4 \pm 10.1$  years (32-72). Total hospital mortality rate was 6.4% (in 3 cases) and no death was observed in patients after 6 months follow up. Electrocardiographic studies following surgery showed improvement in AF rhythm in 26 cases (4.68% with sinus rhythm) but 12 cases (6.31%) showed no improvement. AF rhythm improved on the discharge day in 31 cases and within six months in 33 cases. Eight patients had degenerative valvular disorders (17%) and 26 patients (3.55%) had rheumatic disorders. Mean pre- and postoperative atrial sizes were  $8.0 \pm 5.5$  cm and  $7.0 \pm 1.5$  cm respectively. Based on echocardiography, mean pre and post operation cardiac output was  $8.7 \pm 8.47\%$  and  $3.8 \pm 4.45\%$  respectively. Mean aortic clamping time was  $5.28 \pm 4.105$  minutes, and cardiopulmonary bypass time was  $8.34 \pm 5.147$  minutes during this surgery procedure respectively. The average grade of functional activity based on the American Heart Association Functional Class was class III.

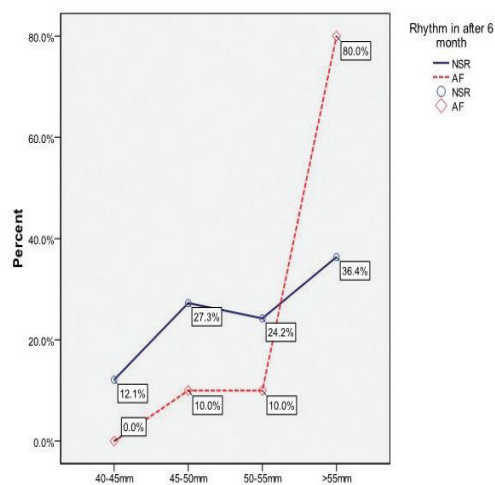
Patients with preoperative atrial size below 50 mm had sinus rhythm in 9 cases (75%) just following surgery, 12 cases (7.85%) on discharge and 13 cases (9.92%) six months later. Patients with preoperative atrial size above 50 mm had sinus rhythm in 9 cases (75%) following surgery, 19 cases (5.65%) on discharge and 20 cases (69%) six months later. Patients with preoperative atrial size, under 50 mm had sinus rhythm in 12 cases (70.6%) just following the operation, 16 (80%) on discharge and in 18 cases (90%) six months later. Change in sinus rhythm and AF rhythm classification based on the exact size of the atrium are shown in Figure 1, on discharge time in Figure 2 and six months after surgery in Figure 3. As observed in Figures 1-3, AF rhythm and treatment failure is increased by the increment of atrium size. Comparison of the atrial size before and after cryo surgical treatment indicated a significant difference between before and after the treatment using this method ( $P=0.002$ ). EF above 55% with sinus rhythm after surgery was seen in 7 cases (58.3%), in discharge time in 10 cases (66.7%) and six months after surgery in 7 cases (77.8%). EF between 55 to 45% with sinus rhythm after surgery was seen in 12 cases (70.6%), in discharge time in 14 cases (73.7%) and six months after surgery in 15 cases (78.9%). The EF under 45% with sinus rhythm improved after surgery was seen in 7 cases (77.8%), in discharge time and also in six months after surgery. Classification of cardiac output in patients after surgery based on echocardiography showed that, in cardiac output above 55%, sinus rhythm after surgery was seen in 4 cases (80%), in discharge time and six months after surgery in 6 cases each (85.7%). The cardiac output between 55 to 45% with sinus rhythm after surgery was seen in 14 cases (63.6%), in discharge time in 17 cases (68%) and six months after surgery in 19 cases (76%). The cardiac output less than 45% with sinus rhythm after surgery, in discharge time and also six months after



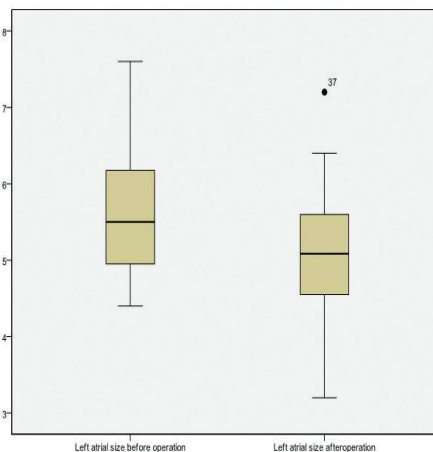
**Figure 1.** The frequency of sinus rhythm and AF rhythm according to the Left atrial size before operation



**Figure 2.** The frequency of sinus rhythm and AF rhythm according to the Left atrial size in discharge



**Figure 3.** The frequency of sinus rhythm and AF rhythm according to the Left atrial size in 6 months after treatment



**Figure 4.** Comparison of changes in atrial size before and after treatment

surgery was seen in 8 cases (72.4%),

### Discussion

Cox-Maze procedure is one of the most successful surgical treatments for atrial fibrillation and arrhythmias are appreciated in more than 90%; however, due to its complexity and invasiveness, this procedure is not popular.<sup>14</sup> In recent years many measures have been taken to simplify the surgical technique. The first attempt in 1992 was to use bipolar radiofrequency produced energy for removing the affected tissues. It, however, was not associated with desired success and several studies reported moderate effort of unipolar radiofrequency waves for treatments of AF.<sup>8</sup>

Causing high tissue temperatures during surgery and severe damage of tissues around the surgical site are some of limitations of the application of unipolar radiofrequency waves.<sup>8</sup> Therefore, cryo-maze procedure has drawn the attention as one of the latest surgical methods.<sup>15</sup> Despite previous evidence about the effects and risks of traditional surgical correction of atrial arrhythmias, cryo-maze method has no significant risk. Cryotomy is one of the primary sources of energy for cardiac electrical conduction system surgery that could replace conventional surgical procedures in experimental and clinical models.<sup>16</sup> This procedure has several benefits such as little tissue damage at the surgical margins and carries the lowest risk of thrombosis as compared to radiofrequency waves.

Also, it does not harm endothelial cells.<sup>17</sup> There is no risk (or very low risk) of damage to other organs such as esophagus. Few deaths during surgery and absence of side effects of non-cardiac organs damage such as esophagus and phrenic nerve are considered as other advantages of the technique.<sup>18-20</sup>

In Melby and *et al.* study, aortic clamp time in Cryo-Maze procedure was 104 minutes. The aorta clamping time was much less than the old method and in their study the recovery rate of patients was 85 to 94%.<sup>21</sup> In

Nakajima and *et al.* study, aortic clamping time was 134 minutes. In Kosaka-Maze procedure aortic clamping time of 144 minutes was reported. Significant difference was observed between the surgical aortic clamping times in two methods. Duration of cardiopulmonary bypass time compared to the previous methods of surgical correction of atrial fibrillation is less.<sup>10</sup> In the present study, the mean aortic clamping time was 105 minutes which is a similar to the previous studies.

Lower cardiopulmonary bypass time and aortic clamping time is very important, because it is associated with a reduced risk of complications and ischemia during surgery. One of the features of this method is the less time of intervention, which may be one of the reasons of lower side effects. The Cryo-Maze procedure was evaluated in Gammie *et al.* study in patients with mitral valve dysfunction who were followed up for three years. They reported about 80% hospital mortality and 85% and 60% postoperative recovery rate after three years.<sup>22</sup>

In previous studies, the ability to modify the short time and alternative AF rhythm was 36%, long term AF was expressed only in 47% of patients.<sup>14</sup>

Rahmanian and colleagues reported mortality rates by 8.2% and related stroke of 4.3% in patients with AF treated with cryo. The recovery rate in this study was 71%.<sup>23</sup> Moten and colleagues described 41 patients treated with Stand-alone Cryo-Maze procedure, in which no death and the lowest stroke rate associated with this method of treatment were reported. There was no mortality.

One-year follow-up of patients showed that 87% had sinus rhythm and AF had been treated in the majority of patients.<sup>24</sup> According to the results of the present study, Cryo-Maze procedure is of minimal risk of surgical complications.

No stroke occurred in this surgical procedure. Hospital mortality rate was low in the present study which is similar to previous studies having employed this method. Majority of the causes of hospital mortality contributed to non-cardiac causes, such as increased plasma creatinine level, decreased platelet count or coagulation disorders and complications of hemodialysis. In the present study, the rate of recovery of patients following surgery, on discharge day and at six months after surgery was: 4.68% 1.72%, and 7.76% respectively. This surgical approach embraces better results than other therapies such as radiofrequency waves. As of Gammie and *et al*<sup>22</sup>, recovery rate was high in six months after surgery.

In previous studies, based on multiple regression models, the size of the left atrium is one of the most important factors associated with poor response to surgical AF modification treatment and a cut off point of 50 mm was estimated while a relative risk of 2/4 was reported for atrial size greater than 50 mm according to the Schopka *et al.* study.<sup>25</sup> The present study also revealed that when the atrial size was less than 50 mm, more patients were recovered. The improvement was seen in 90% of these

patients in six-month follow-up. And if the size of atrium was less than 50 mm the recovery rate would be lower which was seen in 65.2% of the patients.

The exact distribution of normal sinus rhythm and AF percentage with atrial size is shown in Figures 1 to 2 which indicate an increasing atrial rhythm in AF in the high size of atrial. The similarity of recovery rate with atrial size also was noted in the Schopka *et al.* study<sup>25</sup> Based on the evidence from the study of Cryo-Maze procedure, AF improvement has been significant with fewer complications than other surgical procedures.

**Ethical issues:** Before the surgery, all of the patients were informed about the advantages and disadvantages of this research and written informed consents were obtained. Also, The study was approved by the ethics committee of the University.

**Competing interests:** The authors had no competing interests to declare in relation to this article.

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