

# The Cox-Maze Procedure III for Atrial Fibrillation in Adults with Congenital Heart Disease

Akihisa Furuta MD, Masaaki Koide MD, Yoshifumi Kunii MD

Department of Cardiovascular Surgery, Seirei Hamamatsu General Hospital, Hamamatsu, Japan

\*Corresponding Author: Akihisa Furuta, Seirei Hamamatsu General Hospital

# ABSTRACT

Objective: To evaluate results of the Cox-maze procedure III in adults with congenital heart disease

Methods: Retrospective study was performed on 17 adults with congenital heart disease who underwent elective open heart surgery with the Cox-maze procedure III from 2003 to 2014.

**Results:** Mean age was  $54.3\pm16.1$  years. There were no early and late deaths. Early complications were cardiac tamponade (n = 1) and cerebral infarction (n = 1). Mean follow-up time was  $55.6\pm31.3$  months. Late arrhythmias were detected in 3 patients. The 5-year freedom from arrhythmia was  $81.6\pm18.4$  %.

**Conclusions:** The Cox-maze procedure IV was effective and safe for atrial fibrillation of adult patients with congenital heart disease.

**Keywords:** The Cox-maze procedure, supraventricular arrhythmia, atrial fibrillation, adult congenital heart disease

# **INTRODUCTION**

Over 85% of children with congenital heart disease (CHD) can now be expected to reach adulthood, and the number of adults with CHD will therefore inevitably increase in the near future [1]. Adult patients with CHD may have particular problems, such as abnormal anatomy, increased atrial wall thickness, and sequelae of previous surgical procedures [2]. These combinations could produce a high lifetime risk for developing atrial arrhythmias [3, 4]. Atrial tachyarrhythmias including atrial fibrillation (AF) are major causes of morbidity and mortality in these patients due to thromboembolic events and hemodynamic compromise.

Since its introduction by Dr. James Cox in 1987, the Cox-maze procedure has proven to be an effective treatment for AF and has improved with the advances in interventional technology [5]. The Cox-maze procedure IV also has proven to be highly effective treatment for AF in adult patients with coronary or valvular disease [6]. However, it is not clear whether this procedure is a preferable method for the treatment of arrhythmia in adults with CHD. Therefore, we presented the results of the Coxmaze procedure III concomitantly with primary repair for adults with CHD at our institution, and discussed the effectiveness and the safety of this procedure.

# **MATERIALS AND METHODS**

## Patient

A retrospective study was performed on 17 patients aged 15 or older with CHD who underwent elective open heart surgery concomitantly with the Cox-maze procedure IV at Seirei Hamamatsu General Hospital, Shizuoka, Japan from September 2003 through December 2014. The demographic and other patient related data were obtained from medical records and clinical databases in our hospital. AF was divided into two types according to the Heart Rhythm Society [7] as follows: paroxysmal AF was defined by recurrent ( $\geq 2$ ) episodes of AF that were selfterminating and persistent AF was defined by a continuous episode of AF that was present for >7 days or <7 days but required medical or electrical conversion. Operative mortality is defined as (1) all deaths, regardless of cause, occurring during the hospitalization in which the operation was performed, even if after 30 days (including patients transferred to other acute care facilities); and (2) all deaths, regardless of cause, occurring after discharge from the hospital, but before the end of the 30th postoperative day (POD). Operative morbidity is defined as (1) all complications occurring during the hospitalization in which the operation was performed, even if after 30 days: and (2) all complications occurring after discharge from the hospital, but

before the end of the 30th POD. Follow-up information was obtained from subsequent hospital visits. The rhythm was evaluated using an electrocardiogram obtained  $\geq 1$  month after surgery at subsequent hospital visits. The study was approved by the ethics committee, and written consents were obtained from all the patients.

# **Operative procedure**

We performed the modified the Cox-maze procedure III procedure using cryoablation (CA) (Frigitronics CCS-200, AtriCure, Inc., Cincinnati, Ohio, USA) with or without radio-frequency ablation (RFA) to the primary repair. RFA was introduced on March 2010 and has been used in combination with CA from that time. After cardiopulmonary bypass was established with aortic and bicaval cannulation, the right atrium was opened, and the right-sided maze procedure was performed with the heart beating except for cases with an intracardiac shunt (Figure1). CA was applied on the tricuspid annulus and interatrial septum between the lateral wall and the coronary sinus. RFA or CA was applied on a line from the incision to the superior vena cava. inferior vena cava, right atrial appendage, and tricuspid annulus. After the right-sided maze procedure, the left-sided maze procedure was performed with cardiac arrest (Figure2). RFA or CA was applied on a line encircling the pulmonary veins, on a line from the incision to the mitral annulus and the left atrial appendage, and between the left atrial appendage and the left upper pulmonary vein. The left atrial appendage was closed internally and excluded. Cryolesions were created with the cryoprobe for 1-2 minutes at -60 °C RFA, which gave feedback when the lesion was transmural, was performed using either the Isolater Synergy Ablation System (AtriCure, Inc., Cincinnati, Ohio, USA) or the Cardioblate (Surgical Ablation System, Medtronic, Inc., Minneapolis, Minn., USA).

#### **Statistical Analysis**

A normal or abnormal distribution of continuous variables was confirmed by Shapiro-Wilk test. Data pertaining to continuous variables are presented as mean  $\pm$  standard deviation with normally distribution and the median plus 25-75th percentile interval for skewed data. Categorical variables were presented as proportions and frequencies. Freedom from arrhythmia, and surgical or catheter intervention for arrhythmia were analysed by Kaplan-Meier test with logrank test. For all analyses, p < 0.05 was considered indicative of a statistically significant difference.

All statistical analyses were performed using JUMP pro version 12 software (SAS Institute Inc., Cary, North Carolina, USA).



Figure1. The line of Cox-maze procedure (View inside the right atrium). The straight line depicts the cryoablation line. Cryoablation was applied on the tricuspid annulus and the atrial septum lateral to the coronary sinus ostium. Cryoablation was applied on the coronary sinus from the outside. The dotted line depicts the radiofrequency ablation or cryoablation line. Radiofrequency ablation or cryoablation was applied on a line from the incision to the superior vena cava, inferior vena cava, right atrial appendage, and tricuspid annulus.

AO, aorta; CS, coronary sinus; FO, foramen ovale; IVC, inferior vena cava; MV, mitral valve; SVC, superior vena cava; TV, tricuspid valve



**Figure2.** The line of Cox-maze procedure (View inside the left atrium). The straight line depicts the cryoablation line. Cryoablation was applied on a pulmonary vein isolation line and the mitral annulus. The dotted line depicts the radiofrequency ablation or cryoablation line. Radiofrequency ablation or cryoablation was applied on a line encircling the pulmonary veins, on a line from the incision to the mitral annulus and the left atrial appendage, and between the left atrial appendage and the left upper pulmonary vein.

IVC, inferior vena cava; MV, mitral valve; SVC, superior vena cava

# RESULTS

#### Patients

The patient data are shown in Table 1. Seventeen patients (6 males and 11 females) underwent the Cox-maze procedure IV. The mean age at the operation was  $54.3 \pm 16.1$  years. The primary diseases were atrial septal defect (n = 8), ventricular septal defect (n = 2), atrioventricular septal defect (n = 3), tetralogy of Fallot (n = 2), congenital mitral valve regurgitation (n = 1), and pulmonary atresia with intact ventricular septum (n = 1). Of 17 patients, 9 patients had a history of previous cardiac surgery. AF was comprised of persistent AF in 9 patients and paroxysmal AF in 8 patients. The median duration of AF was 11.5 (4-59) months. Echocardiography demonstrated that mean diameter of the left atrium was  $45.4\pm10.2$  mm, and 15 patients (88%) had a dilated right atrium.

## **Surgical Results**

The mean cardiopulmonary bypass time and aortic cross-clamp time were  $168.3 \pm 44.7$  minutes and  $106.9\pm29.2$  minutes, respectively. The primary repairs included atrial septal defect closure (n = 8), mitral annuloplasty (n = 6), mitral valve replacement (n = 1), mitral valvuloplasty (n = 5), pulmonary valve replacement (n = 3), ventricular septal defect closure (n = 1), and tricuspid annuloplasty (n = 6). RFA was performed in addition to the cryoablation in 10 cases of the 17 total cases.

# **Postoperative Results**

There were no operative deaths; however, the early complications included cardiac tamponade (n = 1) and cerebral infarction (n = 1). A patient (No.6) was diagnosed with cardiac tamponade on the 14th POD and underwent pericardial drainage on the same day. A patient (No.9) was diagnosed with cerebral infarction on the 7th POD. Computed tomography demonstrated occlusion of the posterior cerebral artery. Edaravone and heparin were administered immediately. This patient recovered full neurological function and was discharged **Table1.** *Patient data* 

without any persistent neurological morbidity. Early atrial arrhythmias were AF (n = 3), atrial flutter (n = 1), and atrial tachycardia (n = 1), and these arrhythmias had converted to normal sinus rhythm by the time of the patients' discharge.

Post-discharge follow-up was available for 14 patients of the surviving 17. The mean followup time was  $55.6 \pm 31.3$  months. The 5-year freedom from arrhythmia recurrence, and secondary surgical or catheter intervention for arrhythmia was 81.6±18.4% (Figure3). Although a patient with TOF (No.14) had a recurrence of AF 6 months after the operation, which lasted for one month and converted to normal sinus rhythm without any additional therapy. A patient with partial atrioventricular septal defect (No.12) had a pacemaker implantation for sick sinus syndrome 12 months after the operation. A patient with TOF (No.15) who experienced atrial tachycardia in the hospitalization underwent catheter ablation for atrial tachycardia 17 months after the operation. The remaining patients with follow-up kept a normal sinus rhythm. There were no deaths in the follow-up patients.



**Figure3.** Freedom from arrhythmia recurrence and secondary surgical intervention for arrhythmia. Freedom from arrhythmia recurrence and secondary intervention at 5 years was  $81.6\pm18.4$  %.

Pt. No	Sex	Age	Primary disease	Redo	Type of AF	AF duration (months)	LA diameter (mm)	Procedure	RF	Operative complication	Post- discharge complication	Surgical intervention
1	F	56	ASD	no	Persistent	3	58	ASD patch closure	no			
2	F	73	ASD	no	Paroxysmal	Unknown	35	ASD patch closure	no			
3	F	70	ASD	no	Paroxysmal	132	44	ASD patch closure	yes	AF		
4	М	59	ASD, MR, TR	no	Paroxysmal	91	38	ASD patch closure, MVR, TAP	no	AF		
5	М	67	ASD, MR, TR	yes	Persistent	68	49	ASD direct closure, MVP, MAP, TAP	yes			
6	F	72	ASD, MR, TR	no	Persistent	4	53	ASD patch closure, MAP, TAP	yes	Cardiac tamponade, AF		
7	М	67	Residual shunt of ASD	yes	Paroxysmal	90	30	ASD patch closure	yes			

8	М	58	ASD, TR	no	Persistent	4	50	ASD patch closure, TAP	yes			
9	F	16	Congenital MR	no	Paroxysmal	2	46	MVP, MAP	no	Cerebral infarction		
10	F	42	partial AVSD, MR	yes	Persistent	13	40	MVP, MAP	no			
11	М	55	partial AVSD, MR	yes	Persistent	2	59	MVP, MAP	no			
12	М	71	partial AVSD, MR	yes	Persistent	10	57	MVP, MAP	yes	Atrial flutter	Sick sinus syndrome	Pacemaker implantation
13	F	33	PA with IVS, PR	yes	Paroxysmal	56	N/A	PVR	yes			
14	F	37	TOF, PR	yes	Paroxysmal	11	N/A	PVR	yes		Atrial fibrillation	
15	F	33	TOF, PR, TR	yes	Paroxysmal	12	23	PVR, TAP	yes	Atrial tachycardia	Atrial tachycardia	Catheter ablation
16	F	61	VSD	no	Persistent	28	54	VSD Patch Closure	yes			
17	F	53	VSD, TR	yes	Persistent	10	46	TAP	no			

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ASD. AVSD. atrial septal defect: atrioventricular septal defect; IVS, intact ventricular septum; MAP, mitral annuloplasty; regurgitation; MVP. MR. mitral mitral valvuloplasty; MVR, mitral valve replacement; pulmonary atresia; PR. pulmonary PA. regurgitation; PVR, pulmonary valve replacement; TOF, tetralogy of Fallot; TAP, tricuspid annuloplasty; TR, tricuspid regurgitation; TVP, tricuspid valvuloplasty; VSD, ventricular septal defect; RF, radiofrequency

# DISCUSSION

The results of the Cox-maze procedure IV for AF in ACHD were shown in the present study. There was no early and late death. There were 2 operative complications except for arrhythmia. The free rate of arrhythmia recurrence and secondary intervention for arrhythmia was  $81.6\pm18.4\%$ .

In terms of early mortality, this result is similar to the other reports about the Cox-maze procedure for patients with CHD reported a lower early mortality rate of 0-4% [8-10]. However, in the present study there were 2 operative complications except for arrhythmia. Cardiac tamponade was occurred in a patient on the 14th POD because of excessive administration of warfarin, this was, however, not strongly related with the procedure. Cerebral infarction was occurred in a patient on the 7th POD even though the patient kept normal sinus rhythm. This patient was discharged without any neurological dysfunction. These results showed that the Cox-maze procedure concomitantly with primary repair for patients with congenital heart disease is a relatively safe procedure.

In the present study, freedom from arrhythmia recurrence and secondary intervention for arrhythmia at 5 years was 81.6±18.4%. Two patients underwent additional surgery or catheter intervention for arrhythmia. This result was comparable to other reports of the Coxmaze procedure for patients with CHD. Im et al. performed a biatrial Cox-maze procedure in 33 patients with an atrial septal defect and reported that normal sinus rhythm was maintained without any episode of atrial fibrillation recurrence at 2 and 5 years in 82% and 69% of patients, respectively [8]. Gutierrez et al. performed the Cox-maze procedure III in 24 patients with congenital heart disease and reported that 74% of survivors remained arrhythmia-free for a mean follow-up of 2.8 years after the procedure [11].

The retrospective study design and the small sample size of patients are notable limitations of our study. Besides, radiofrequency ablation was not used in all patients, and a 24-hour recording from a Holter monitor was not undertaken routinely at the time of regular follow-up. In the future, the accumulation of cases, a unified procedure, and the accurate evaluation of arrhythmia using a routine 24-hour Holter monitor are necessary for further evaluation of this method.

# **CONCLUSION**

The Cox-maze procedure III for AF concomitantly with primary repair in ACHD was relatively safe and valid method. This method should be considered as a treatment for AF in ACHD.

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# **AUTHOR'S BIOGRAPHY**

#### **Corresponding Author**



Akihisa Furuta, MD, Seirei Hamamatsu General Hospital, Department of Cardiovascular Surgery

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