Cox/Maze III Operation Versus Radiofrequency Ablation for the Surgical Treatment of Atrial Fibrillation: A Comparative Study

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Background. **The purpose of this study was to evaluate the efficacy of radiofrequency (RF) ablation in the treatment of atrial fibrillation, by comparatively analyzing the outcomes of the patients who underwent RF ablation with those of patients who underwent Cox/Maze III surgery.**

Methods. **Between April 1995 and June 2002, 70 patients underwent surgery for atrial fibrillation and open-heart surgery at the Department of Cardiovascular Surgery of the University of Bologna: 30 patients underwent the surgical Cox/Maze III procedure (group 1), and 40 patients underwent the RF ablation according to the Maze III configuration at least on the left atrium (group 2). There were 14 males and 56 females, with a mean age of 61.5 ± 12.5 years (range 22 to 80 years old).**

Results. **Groups 1 and 2 did not differ in terms of baseline characteristics. The perioperative mortality rate was not significantly different between the two groups (6.6% in group 1 vs 7.5% in group 2). The overall cumulative rates of sinus rhythm were 68.9% in group 1 and 88.5% in group 2 (not statistically significant). Biatrial contraction was assessed by transthoracic echocardiography in 70.4% of the patients in group 1 and 76.5% of the patients in group 2 ($p = 0.65$).**

Conclusions. **The RF ablation procedure offers as good results as the Cox/Maze III operation, allowing recovery of the sinus rhythm and atrial function in the great majority of patients with atrial fibrillation who underwent open heart surgery; it is a safe and effective means of curing atrial fibrillation with negligible technical and time requirements.**

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Atrial fibrillation (AF) is a common arrhythmia present in 0.4% of the general population and in more than 1% of the population more than 60 years of age. About 40% to 60% of patients undergoing mitral valve surgery have AF, thus compromising the clinical outcome. The detrimental sequelae of AF are: irregular heartbeat, compromised hemodynamics due to the absence of a synchronous atrioventricular contraction, and the risk of systemic thromboembolic events.

Restoration of the sinus rhythm (SR) with atrioventricular resynchronization may be difficult in patients with lone or chronic AF. The procedure consists of an open-heart surgical approach, as described by James Cox, namely making linear lesions in the right and left atria to prevent the occurrence of multiple reentering circuits. This surgical procedure is extensive and time consuming and requires great surgical skill. In contrast, more recently, Haissaguerre and coworkers [1] have demonstrated that radiofrequency (RF) ablation is able to confine the origin of AF to the rapidly firing foci in the pulmonary veins. The efficacy of RF ablation, in patients with chronic AF undergoing open-heart surgery, has been evaluated and the clinical outcome compared with those of patients who underwent the Cox/Maze III procedure.

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Material and Methods

Patients

Between April 1995 and June 2002, 70 patients with chronic AF underwent open-heart surgery and surgery to treat AF at the Department of Cardiovascular Surgery of the University of Bologna. The preoperative characteristics of the patients are shown in Table 1. Every patient signed an informed consent before undergoing surgery. All the operations were performed by the same surgeon. All patients underwent cardiopulmonary bypass with bicaval and aortic cannulation under moderate hypothermia (32°C); myocardial protection was assured by antegrade crystalloid cardioplegia. Between April 1995 and March 2001 we performed the Maze III operation and from April 2001 we begun to perform the RF ablation, because it is faster and safer, avoiding any additional incision apart from the conventional left atriotomy. According to the surgical technique, the patients were divided into two groups: group 1 underwent Maze III procedure, according to Cox. In group 2 patients underwent the RF ablation technique: RF energy was admin-

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Table 1. Preoperative Characteristics and Surgical Procedures

Variable	Group 1 (n = 30)	Group 2 (n = 40)	*p* Value
Age (years)	60.9 ± 13.9	62 ± 11.6	NS
Sex (male)	6	8	NS
Sex (female)	24	32	NS
LA dimension (mm)	56.4 ± 8.1	56.05 ± 7.6	NS
AF duration (months)	53.5	61.9	NS
Ejection fraction (%)	58 ± 11.4	56.8 ± 13.3	NS
NYHA	2.7 ± 0.7	2.8 ± 0.5	NS
MVR	4	13	
MVR + TVP	13	11	
MVR + AVR	4	8	
MVR + AVR + TVP	8	5	
TVP + ASD and VSD repair	1	—	
TVP + ASD repair	—	1	
AVR	—	1	
AVR + CABG	—	1	
Redo	6 (20%)	6 (15%)	NS

AF = atrial fibrillation; ASD = atrial septal defect; AVR = aortic valve replacement; CABG = coronary artery bypass graft; LA = left atrial; MVR = mitral valve replacement; NYHA = New York Heart Association; TVP = tricuspid valveplasty; VSD = ventricular septal defect.

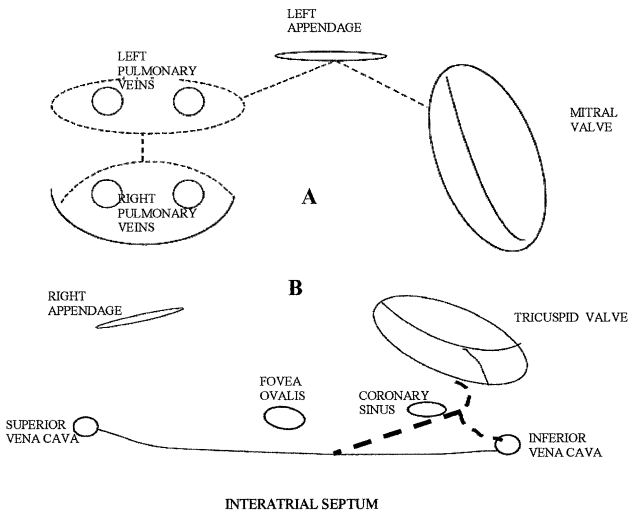

Fig 1. The surgical scheme of the radiofrequency ablation in (A) the left atrium and in (B) the right atrium. Solid lines *represent the surgical incisions (the conventional left and right atriotomies), and* dashed lines *represent the radiofrequency energy ablation lines.*

istered by using a hand-held probe (Cobra Flex; Boston Scientific, San Jose, CA). The ablation procedure was done in a bloodless operating field and temperature-guided energy applications were performed with a preselected catheter tip temperature of 70°C for 2 minutes in the left atrium and 90 seconds in the right atrium. The aorta was cross-clamped and the heart was arrested with cold cardioplegic solution. Access to the inside of the left atrium was gained through a standard atriotomy in the interatrial groove, as for a mitral valve (MV) procedure. After excision of the left atrial appendage and resuturing of the amputation site with a 4-0 Prolene (Ethicon, Somerville, NJ) the left-sided RF ablation was performed by linear ablation lines, as illustrated in Figure 1A. In addition to the incision in the interatrial groove, isolation of the right pulmonary veins was completed by an unilateral ablation line. The left pulmonary veins were encircled and a connecting line was drawn between both islands of pulmonary veins. Ablation lines were also performed from the ablation line isolating the left pulmonary vein to the base of the left atrial appendage amputation site and to the posterior MV annulus. Subsequently the MV procedure was carried out. After rewarming and the cross-clamp was released, the RF ablation was completed with an ablation line drawn on the right-sided aspect of the interatrial septum starting from the middle of the posterior longitudinal right atriotomy, across the interatrial septum up to the caudal aspect of the os of the coronary sinus extended to the inferior vena cava cannulation site (Fig 1B). Antiarhythmic prophylactic treatment was carried out on a routine basis. Amiodarone was the drug of choice. Its administration was begun after induction of anesthesia: 300 mg intravenous bolus, followed by 1200 mg/24 hours intravenously until the end of the first postoperative day; beginning with the second postoperative day, oral administration of 200 mg/24 hours was begun. After discharge, a maintenance regimen of 200 mg/24 hours was continued. The pharmacologic treatment was discontinued 6 months after the operation.

Follow-Up

The primary endpoint of our study was the restoration of SR, both early and at a later date after surgery; the secondary endpoint included atrial contraction, adverse events, and survival. The mean follow-up time was 15.5 months (range: 7–74 months). Clinical history and 12-lead electrocardiogram (ECG) were taken during each follow-up visit. Sinus rhythm was defined as a supraventricular rhythm with P waves on the standard 12-lead ECG. Six-months after surgery, echocardiography was performed, including transmitral and transtricuspid Doppler echocardiography. Detection of E and A waves was used in evaluating the atrial contraction. At least one Holter monitoring of rhythm was performed in each group 6-months after hospital discharge.

Statistical Analysis

Continuous variables were expressed as the mean ± SD. The Student unpaired *t* test was used to compare the variables between the two groups. The significance of each variable as a prognostic marker was first tested univariately. Then variables identified as significantly associated with the outcome were examined multivariately. Differences of p less than 0.05 were considered to be statistically significant. The survival rates and cumulative rates of SR were calculated according to the Kaplan-Meier method and the groups were compared using the log-rank test, with a statistically significant difference assumed at p less than 0.05.

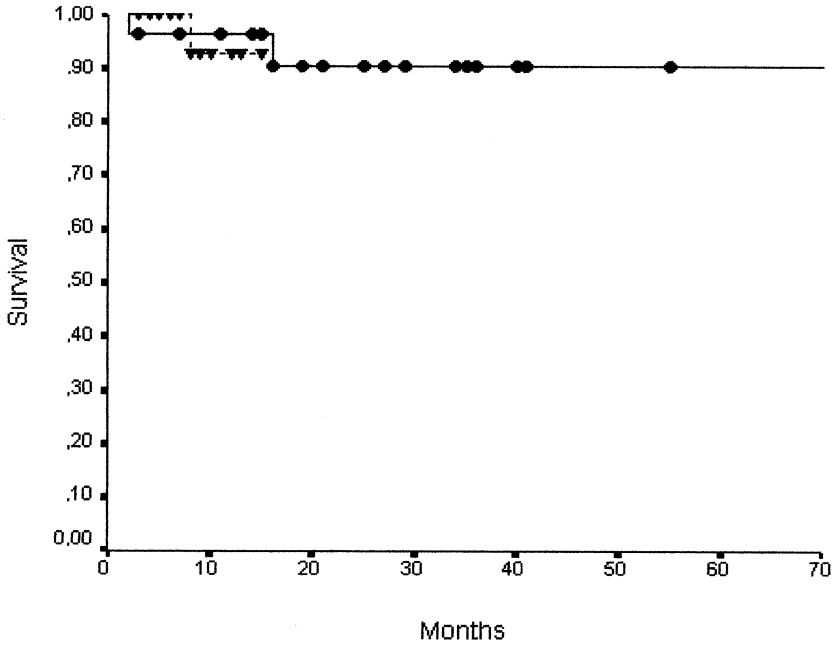

Fig 2. The overall survival at follow-up. (▼ = radiofrequency ablation; ● = Maze.)

Results

The patients did not differ in terms of their baseline characteristics (age, duration of AF before surgery, left atrial dimensions, and preoperative ejection fraction). Concomitant surgical procedures were: mitral valve replacement (4 in group 1 vs 13 in group 2), mitral valve replacement plus tricuspid valveplasty (13 vs 11), combined mitral and aortic valve replacement (4 vs 8), and combined mitral and aortic valve replacement plus tricuspid valveplasty (8 vs 5). Moreover, in group 1, 1 patient underwent tricuspid valveplasty plus atrial and ventricular septal defect repair; whereas, in group 2, 1 patient underwent tricuspid valveplasty plus atrial septal defect repair and 2 patients required aortic valve replacement (one of whom also required coronary artery bypass graft). The mean cardiopulmonary bypass time was 155.5 $\pm$ 40.4 minutes in group 1 and 126.3 $\pm$ 33.4 minutes in group 2 ($p = 0.002$), while the cross-clamp time was 113.3 $\pm$ 26.1 minutes in group 1 and 104.8 $\pm$ 31.5 minutes in group 2, without statistically significant difference between the two groups ($p = 0.23$). The mean intensive care unit stay was 4.8 days in group 1 and 2.4 days in group 2 (p = NS). The cumulative in-hospital mortality was not statistically significantly different between the two groups (6.6% in group 1 vs 7.5% in group 2). One patient in group 1 died of multiorgan failure and 1 patient died of a left ventricular disruption after a mitral valve replacement. One patient in group 2 died of sepsis, 1 patient died of severe hepatic cirrhosis (from 20 years), and 1 patient died of left ventricular disruption. The 2 patients with ventricular disruption were not related to the arrhythmia surgery itself, but we believe they occurred because of the severe and very deep calcifications of the annulus of the mitral valve and the subvalve apparatus.

Two patients in group 1 (6%) and 3 patients in group 2 (7%) had permanent pacemakers implanted because of postoperative bradycardia. No patient in either groups had transitory neurologic symptoms after the surgical procedure. The cumulative rates of SR at discharge were 73.3% in group 1 and 85% in group 2 ($p = 0.2$).

Follow-Up

Every discharged patient completed at least 7 months of follow-up. The duration of the follow-up ranged from 20 to 91 months (mean 73.2 $\pm$ 4.2) in group 1 and from 7 to 22 months (mean 16.5 $\pm$ 2.5) in group 2, with a statistically significant longer follow-up in group 1 ($p < 0.05$). The cumulative rates of survival for complete follow-up were 90.4% for group 1 and 92.8% for group 2 ($p = 0.91$) (Fig 2). At the 12-lead ECG, the cumulative rates of SR were 68.9% for group 1 and 88.5% for group 2 ($p = 0.53$) as illustrated in Figure 3. Biatrial contraction was assessed by transthoracic doppler echocardiography in 70.4% of the patients in group 1 and in 76.5% of the patients in group 2 ($p = 0.65$) (Table 2). We observed that 12 patients (40%) in group 1 and 29 patients (72.5%) in group 2 were under treatment with warfarin sodium; on the other hand 10 patients (33.3%) in group 1 and 9 patients (22.5%) in group 2 were undergoing antiarrhythmic therapy (sotalol or amiodarone). We noted a significant improvement of the New York Heart Association (NYHA) functional class.

Without any differences between the two groups: in group 1, 3 patients (10%) were in NYHA I, 23 patients (76.6%) were in NYHA II and 4 patients (13.3%) in NYHA III; in group 2, 20 patients (50%) were in NYHA I and 20 (50%) in NYHA II.

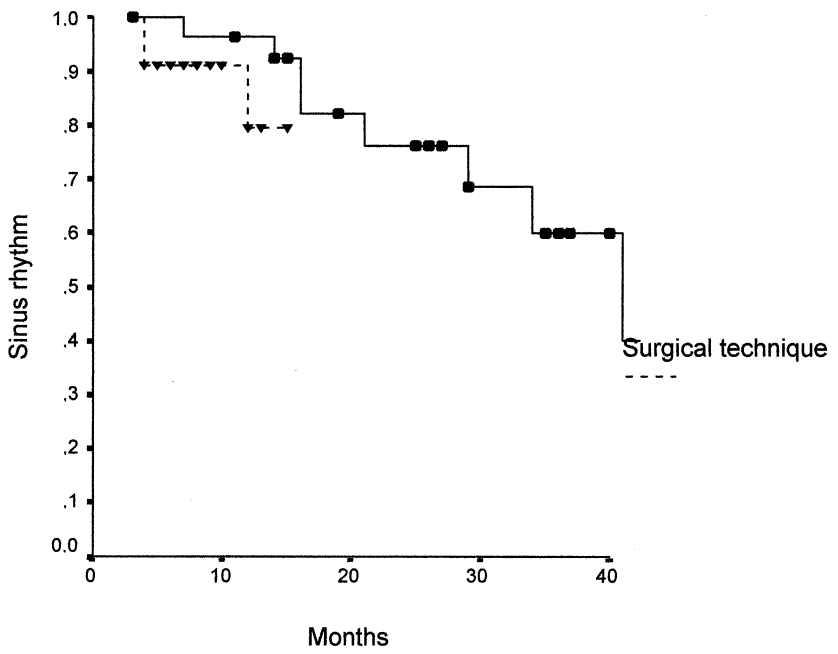

Fig 3. Trend of the sinus rhythm during the follow-up in the two groups. (▼ = radiofrequency ablation; ■ = Maze.)

Comment

This study analyzes data obtained in patients undergoing surgery for AF, in addition to other open-heart surgical procedures, comparing the Cox/Maze III procedure with that of RF ablation. In 1991, Cox and associates [2–6] described a new procedure for the radical surgical treatment of atrial fibrillation: the Maze procedure. Initially it was performed as an isolated cardiac procedure. However, as experience with this technique has grown, it has been performed concomitantly with other cardiac procedures [7, 8]. It has been noted that the correction of the underlying cardiac pathology alone usually fails to abolish AF [9]. Kosakai and coworkers [10] have reported the advantage of the Maze procedure for atrial fibrillation in patients undergoing simultaneus open-heart surgery. The negative effects of AF are widely known, particularly in combination with valve diseases. Therefore, a specific surgical intervention is needed to eliminate AF. Excellent results have been described for the surgical treatment of chronic AF associated with organic heart disease at the expense, however, of extensive atrial incisions, suturing, and greater blood loss as well as longer cardiac arrest [11, 12]. In an attempt to reduce the procedure time and to simplify the surgical technique, modifications of the original Maze procedure have been developed [13], including the application of RF energy [14]. In this case all the lesions are made in the endocardium and replace most of the surgical incisions of the previous techniques. The RF ablation procedure requires 15 to 20 minutes of elective cardiac arrest time in contrast to at least 50 to 60 minutes of the Cox/Maze III procedure [15, 16]. The treatment of AF by the application of RF in the atria is based on the concept of preventing functional macroreentrant circuits [14, 15]. Haissaguerre and colleagues [1] demonstrated that the vast majority of atrial premature beats that initiate frequently atrial fibrillation originate in the pulmonary veins. These foci trigger atrial fibrillation with a burst of rapid discharges and respond to local radiofrequency ablation with a catheter [1]. We also performed a RF ablation in the isthmus, between the tricuspid valve annulus and the inferior vena cava to interrupt the conduction along the coronary sinus to avoid the development of postsurgical atrial flutter. In our experience with 70 patients, we retrospectively compared the outcome of patients undergoing the Cox/Maze III procedure with that of patients undergoing the RF ablation procedure. In our study, patients had a long duration of AF (53.5 months in group 1 and 61.9 months in group 2, p = NS) and large left atrial dimensions (56.4 $\pm$ 8.1 mm in the group 1 and 56.05 $\pm$ 6 mm in the group 2, p = NS). The cumulative rates of SR at discharge were 73.3% in group 1 and 85% in group 2 (p = 0.2). At follow-up restoration of SR was demonstrated in 68.9% of patients in group 1 and 88.5% in group 2. These data are comparable to the results documented by different groups [17–22], who found restoration of SR between 70% and 98%, depending on patient preoperative characteristics (lone AF, concomitant heart diseases) and the surgical techniques. All our patients had chronic AF. In

Table 2. Restoration of Sinus Rhythm

	Group 1	Group 2	p Value
Rhythm			
Early (12-lead ECG)	73.3%	85%	0.20
Late (Holter)	68.9%	88.5%	0.53
Biatrial contraction (Echocardiography)	70.4%	76.5%	0.65

ECG = electrocardiogram.

group 1, 26.7% of the patients underwent combined mitral and aortic valve replacement plus tricuspid valveplasty and 20% (6 patients) were redos. In group 2, 12.5% of patients underwent combined mitral and aortic valve replacement plus tricuspid valveplasty and 15% (6 patients) of the previous patients were redos. An important aim of restoring SR is to produce the contraction of both atria, restoring an adequate electromechanical synchrony, and decreasing the risk of thromboembolism. In our study, biatrial contraction was restored in 70.4% of the patients in group 1 and 76.5% of the patients in group 2: our data are equivalent to the data of other groups, reporting the occurrence of biatrial contraction in 66.7% to 99% of patients depending on the baseline characteristics: the unsurpassed success of 99%, reported by Cox in 346 patients is unique. Japanese have the most extensive experience with the Maze III and modifications in patients with valvular disease and the Kosakai's analysis [23] of the results of many Maze procedures has given the new insights into the construction of AF: a questionnaire was sent to 517 Japanese hospitals that perform cardiac surgery. Answers were returned from 288 hospitals stating that 2547 treatments for AF or flutter had been performed. In his study, Kosakai divided the patients into four groups: patients with AF alone, AF associated with congenital heart disease, no cause-and-effect relationship between the basic aillment, and AF associated with mitral valve disease; in the AF associated with mitral valve disease group he found an overall SR restoring rate of 73.2%. On the other hand, some European centers developed the largest experience with the surgical RF ablation of AF: Melo and coworkers [20] reported a success rate of 50% in restoring SR and biatrial contraction assessed by echocardiography, according to the Santa Cruz score. Sie and associates [24] reported a SR restoring rate of 72% in their study population.

The cut and sew technique is very interesting for the surgeon but it requires knowledge, time, and a good ventricular function. It could be said that this operation is potentially dangerous for bleeding, but in literature this complication is extremely rare: none of our patients suffered from bleeding. With experience in using the Maze procedure, it is possible to hybridize the surgical approach, by creating some linear lesions in specific areas with RF power. Comparing the early outcome of the two groups, we found a shorter cardiopulmonary bypass time in group 2 ($p = 0.002$) and this result does not seem to be related to the underlying valve disease procedures as Table 1 demonstrates: in effect 13 patients of group 2 and only 4 patients of group 1 underwent mitral valve replacement (MVR); 13 patients of group 1 and 11 patients of group 2 underwent MVR and tricuspid valveplasty; and 8 patients of group 2 and 4 patients of group 1 underwent MVR and aortic valve replacement. From our present experience with RF ablation, it can be stated that its use is fast and safe: bleeding after surgery is the same as for conventional mitral surgery and we have seen no myocardial infarctions or high levels of myocardial enzymes resulting from coronary artery lesions. The additional length of myocardial ischemic and operative time associated to AF surgery is negligible. This is a significant advantage in older patients with poor ventricular function or multiple valve disease, making it possible to enlarge the indications to restore sinus rhythm surgically. In conclusion, we believe that the use of RF energy is safe, effective and simplifies the Cox/Maze III procedure in patients undergoing cardiac surgery, by restoring SR and atrial contraction in the majority of patients and also reducing operating time.

Study Limitations

The first limitation of this study was that it is a retrospective, nonrandomized study. The second limitation is that atrial contraction and contribution to ventricular filling was studied with transthoracic echocardiography. This approach can induce false results specifically in patients with prosthetic valves. Episodes of postoperative asymptomatic AF may have been missed because electrocardiographic measurements and Holter recordings were routinely made during visits to the outpatient clinic or when the symptoms arose.

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