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Cardiac Autotransplantation for the Treatment of Permanent Atrial Fibrillation Combined with Mitral Valve Disease

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ABSTRACT

Objective: The results of current surgical options for the treatment of permanent atrial fibrillation associated with mitral valve surgery are widely different, particularly for extremely dilated left atria. The aim of this study is to assess the efficacy of cardiac autotransplantation in restoring a normal sinus rhythm via a consistent reduction in the left atrium volume associated with a complete isolation of the pulmonary veins.

Methods: From April 2000 to April 2002, 28 patients (men/women, 5/23) underwent cardiac autotransplantation for the treatment of mitral disease and concomitant permanent atrial fibrillation (>1 year). A modified surgical technique derived from bicaval heart transplantation procedures maintained the connection of the right atrium with the inferior vena cava in all but 3 cases. In 2 patients, the mitral valve was repaired, and it was replaced in 26 patients. Associated procedures were 6 aortic valve replacements, 2 tricuspid valve annuloplasties, and 2 coronary revascularizations.

Results: No hospital deaths were recorded, but 1 patient died of pneumonia 3 months postoperatively. At a mean follow-up period of 17.2 ± 6.7 months (range, 6-30 months), 24 patients (88.9%) were in sinus rhythm, and 3 (11.1%) were in atrial fibrillation. The Santa Cruz Score was 0 for 3 patients, 2 for 1 patient, and 4 for the remaining 23 patients (85.2%). The mean left atrial diameter decreased from 65.4 ± 17.1 mm (range, 50-130 mm) before the operation to 48.4 ± 5.6 mm (range, 37-78 mm) postoperatively ($P < .001$), and the mean left atrial volume decreased from 119 ± 70.5 mL (range, 60-426 mL) to 69.1 ± 35.1 mL (range, 31-226 mL) ($P < .0001$).

Conclusion: Cardiac autotransplantation is a safe and effective surgical option for the treatment of permanent atrial fibrillation in patients with long-lasting mitral valve disease and severe enlargement of the left atrium.

INTRODUCTION

Atrial fibrillation (AF) is present in 0.15% to 1.0% of the general population [Onundarson 1987] and in 10% of the population aged more than 70 years [Kannel 1982]. Although up to 11% of affected patients have no aberrant cardiac morphology [Kopecky 1987], the arrhythmia is present in approximately 79% of patients with mitral valve disease [Hirosawa 1987], and most patients remain in AF following mitral valve surgery with no combined AF ablation surgery [Chua 1994]. AF may cause palpitations, hemodynamic compromise, and systemic embolism, and the Cox maze procedure, designed to prevent chronic and paroxysmal AF and flutter, has been demonstrated to be effective by several studies. Moreover, other alternative approaches, including cryosurgery, radiofrequency energy ablation, laser surgery, and ultrasound, have been introduced in clinical practice with the goal of treating AF and respecting the same anatomical and physiological principles of the Cox procedure.

Nevertheless, most cases of AF with mitral valve disease are due to atrial enlargement [Keren 1987, Sanfilippo 1990], and the low rate of efficacy of linear ablation procedures in patients with severe left atrium (LA) dilation has been demonstrated [Kobayashi 1998, Kosakai 2000].

Furthermore, thromboembolism is a risk for patients with a giant LA, even if the patient presents with sinus rhythm (SR), and is treated with anticoagulation drugs.

This study shows our initial experience with cardiac autotransplantation as a method to treat AF during mitral surgery, which is designed for patients with a very enlarged left atrial cavity and allows a complete isolation of the pulmonary veins and a real surgical reduction in LA volume.

MATERIALS AND METHODS

All patients included in the study had an indication for cardiac surgery, as determined by the presence of structural mitral valve disease irrespective of AF. Inclusion criteria for the treatment of AF with the autotransplantation technique were (a) the presence of "permanent" AF, (b) AF lasting for more than 1 year, and (c) a left atrial diameter ≥50 mm.

Rhythm characteristics (presence and duration of AF) were assessed by using the patient's history and previous electrocardiograms.

Echocardiogram examinations were performed for sizing atrial dimensions and assessing atrial contractility (Sequoia 512; Acuson, Mountain View, CA, USA).

The superoinferior diameter (D1), measured from the mitral valve plane toward the pulmonary veins and measured on B-mode in the 4-chamber apical view, was considered as

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Table 1. Clinical and Echocardiographic Data*

Age (range), y	62 ± 9.1 (45-78)
Sex M/F, n	5/23
NYHA class (range), n	3.2 ± 0.6 (2-4)
Embolic antecedent, n	4 (14.3%)
Previous operations, n	6 (21.4%)
Etiology	
Rheumatic, n	26 (92.9%)
Degenerative, n	2 (7.1%)
AF duration (range), y	6.6 ± 6.5 (1-25)
AF duration >10 y, n	12 (42.8%)
EF (range), %	58.6 ± 6.3 (41-70)
LVEDD (range), mm	54.1 ± 8.1 (42-72)
LA superoinferior diameter (range), mm	65.4 ± 17.1 (50-130)
LA volume, mL	119.3 ± 70.5 (60-426)
Mitral valve lesions	
Stenosis, n	9 (32.1%)
Incompetence, n	6 (21.4%)
Mixed lesion, n	12 (42.9%)
Mitralic prosthesis dysfunction, n	1 (3.6%)
Associated valve lesions	
Aortic disease, n	6
Tricuspid disease, n	4

*M indicates male; F, female; NYHA, New York Heart Association; AF, atrial fibrillation; EF, ejection fraction; LVEDD, left ventricle end diastolic diameter; LA, left atrium.

the left atrial diameter. The lateromedial (D2) and anteroposterior (D3) left atrial diameters also were measured to enable calculation of the left atrial volume by the formula: (D1 × D2 × D3 × 0.53)/1000.

Postoperative atrial contractility was assessed with pulse Doppler in the 4-chamber apical view, with the sample volume immediately under the mitral valve plane and with color flow Doppler used to find the best alignment. The atrial transport function was considered effectively restored when the transvalvular peak A wave was ≥20 cm/s.

Results of atrial contraction function were expressed in terms of the Santa Cruz Score (SCS) [Melo 1997].

From April 2000 to April 2002, 28 patients (5 men, 23 women) with mitral valve disease and associated permanent AF were operated on in our unit with the autotransplantation technique. The clinical and echocardiographic characteristics are listed in Table 1. In particular, the mean time of AF duration was 6.6 ± 6.5 years (range, 1-25 years), and in 12 patients (42.9%) the AF duration was more than 10 years. The preoperative mean left atrial diameter and volume were 65.4 ± 17.1 mm (range, 50-130 mm) and 119.3 ± 70.5 mL (range, 60-426 mL).

Surgical Technique

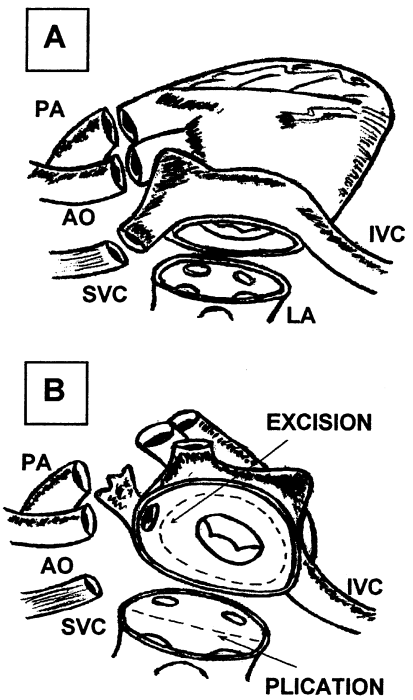
Through a median sternotomy, normothermic cardiopulmonary bypass was instituted via the use of standard aortic and bicaval cannulation. After aortic cross-clamping, myocardial protection was obtained through retrograde cold blood cardioplegia with warm reperfusion (24 cases) or by continuous normothermic retrograde blood perfusion and a beating heart (4 cases).

In 3 patients, the heart was removed from the chest according to the bicaval heart transplantation technique, and in 25 patients the connection of the inferior vena cava was maintained (Figure, A). The valvular surgery time was accomplished with the heart on the bench or rotated into the pericardial cavity. Before the heart was reimplanted, the left atrial volume was reduced by (a) excising the left atrial appendage and redundant atrial wall from the heart and (b) longitudinally plicating the posterior left atrial wall between the orifices of right and left pulmonary veins with a double running suture (Figure, B). In 4 patients with severe dilation of the right atrium, a reduction of this cavity was obtained by excising the right appendage and a large part of the right atrium's free wall.

Protocol of Postoperative Treatment

Amiodarone administration (5 mg/kg by slow administration of an intravenous bolus and an infusion of 10 mg/kg per 24 hours) was started intraoperatively only in cases of unstable SR with AF episodes and a need of internal cardioversion. Postoperative atrial arrhythmias were treated with amiodarone (5 mg/kg by slow administration of an intravenous bolus and an infusion of 10 mg/kg per 24 hours), which was combined with external cardioversion if necessary. In these patients, amiodarone oral therapy (200 mg/day) was continued after discharge of the patient and was withdrawn after 3 months.

All patients were treated with spirolactone 100 mg daily during their hospital stay.



Modified autotransplantation. A, Disconnection of the heart maintaining the inferior vena cava (IVC) connection. B, Rotation of the heart and left atrial size reduction. PA indicates pulmonary artery; AO, aorta; SVC, superior vena cava; LA, left atrium.

Table 2. Operative Data*

Primary cardiac procedures, n	
MVR	20 (71.4%)
MVP	2 (7.1%)
MVR + AVR	6 (21.5%)
Associated cardiac procedures, n	
CABG	2 (7.1%)
TVP	2 (7.1%)
RAVR	4 (14.3%)
Myocardial protection, n	
RCBC + blood reperfusion	24 (85.7%)
Totally beating heart	4 (14.3%)

*MVR indicates mitral valve replacement; MVP, mitral valvuloplasty; AVR, aortic valve replacement; CABG, coronary artery bypass grafting; TVP, tricuspid valvuloplasty; RAVR, right atrium volume reduction; RCBC, retrograde cold blood cardioplegia.

Oral anticoagulation treatment was suspended after the third month in patients without a mechanical prosthesis and with echocardiographic evidence of effective biatrial contraction.

All patients were assessed for rhythm and atrial contractility at hospital discharge, the third month, and every 6 months thereafter by means of electrocardiography and echocardiography.

After patient discharge, new AF or atrial flutter episodes were treated with external cardioversion. The surgical treatment was considered ineffective when the patient needed more than 2 cardioversions during the first 3 months following surgery. After this time, the recurrence of AF or flutter was defined as permanent AF, and no more external cardioversion treatment was used.

RESULTS

Operative Findings and Clinical Follow-up

All patients underwent mitral valve surgery alone or in association with other procedures (Table 2). Two patients underwent mitral valve repair consisting of a posterior leaflet quadrangular resection and a posterior annular ring implantation. Twenty patients underwent isolated mitral valve replacement with biological (7 cases) or mechanical (13 cases) prostheses, and 6 patients had a double mitro-aortic valve replacement with mechanical prostheses. Associated procedures were coronary artery bypass grafting (2 cases), De Vega tricuspidal annuloplasty (2 cases), and right atrial volume reduction (4 cases).

Mean cardiopulmonary bypass and aortic cross-clamp times were 164 ± 31 minutes and 108 ± 22 minutes, respectively; with continuous blood perfusion, the mean total myocardial anoxic ischemic time was 72 ± 33 minutes (Table 2).

Postoperative complications were 1 case of reoperation for bleeding, 1 case of acute renal insufficiency successfully treated with continuous venovenous hemofiltration, and 1 case of prolonged mechanical ventilation (72 hours) for acute respiratory failure. The mean length of hospital stay was 9.4 ± 4.4 days (range, 5-23 days). No hospital deaths occurred in this series.

The mean follow-up interval was 17.2 ± 6.7 months (range, 6-30 months), and during this time 1 patient (3.6%) died from bilateral pneumonia occurring 3 months after hospital discharge. The mean New York Heart Association functional class for the 27 survivors was 1.4 ± 0.6, and no embolic accident has been recorded as of this writing.

Cardiac Rhythm and Atrial Function

Table 3 shows the rhythm and atrial contractility at hospital discharge and at different intervals of follow-up.

At the end of the operation, 21 patients (75%) recovered SR, 6 patients (21.4%) presented junctional rhythm, and 1 patient (3.6%) remained with AF. Three patients (10.7%) presented with intraoperative AF recurrence that required treatment with internal cardioversion and amiodarone infusion.

During the rest of the hospital stay, 11 patients (39.2%) presenting with AF recurrence (9 patients) or atrial flutter (2 patients) were successfully treated with amiodarone infusion alone in 2 cases or combined with external cardioversion in 7 cases. In 2 patients the treatment was ineffective.

At hospital discharge, 23 patients (82.2%) recovered SR, 2 patients had a junctional rhythm, and 3 patients (10.7%) maintained AF. The SCS was 0 for 3 patients, 2 for 4 patients, 3 for 1 patient, and 4 for 20 patients (71.4%).

At mean follow-up durations of 11.9 ± 5.3 months and 17.2 ± 6.7 months, 24 patients (88.9%) presented stable SR, and 3 patients (11.1%) maintained AF.

At 11.9 ± 5.3 months, the SCS was 0 for 3 patients, 2 for 3 patients, and 4 in 20 patients. At the last follow-up time of 17.2 ± 6.7 months (range, 6-30 months), only 1 patient scored 2, 3 patients scored 0, and 23 patients (85.2%) scored 4.

No prosthesis dysfunction or mitral valvuloplasty failure was found at the last echocardiography evaluation.

The mean left atrial diameter and volume at 17.2 ± 6.7 months following the operation were 48.4 ± 5.6 mm (range, 37-78 mm) and 69.1 ± 35.1 mL (range, 31-226 mL). The reduction in the mean left atrial diameter was statistically significant when it was compared with the mean preoperative value of 65.4 ± 17.1 mm ($P < .001$). Similarly, the reduction in mean left atrial volume was statistically significant, compared with the preoperative value of 119.3 ± 70.5 mL ($P < .0001$).

Table 3. Cardiac Rhythm and Atrial Contractility

		Follow-up	
	At Discharge (n = 28)	11.9 ± 5.3 mo (n = 27)	17.2 ± 6.7 mo (n = 27)
Rhythm, n			
Atrial Fibrillation	3 (10.7%)	3 (11.1%)	3 (11.1%)
Junctional Rhythm	2 (7.1%)	0	0
Sinus Rhythm	23 (82.2%)	24 (88.9%)	24 (88.9%)
Santa Cruz Score, n			
Score 0	3 (10.7%)	3 (11.1%)	3 (11.1%)
Score 1	—	—	—
Score 2	4 (14.3%)	3 (11.1%)	1 (3.7%)
Score 3	1 (3.6%)	—	—
Score 4	20 (71.4%)	21 (77.8%)	23 (85.2%)

DISCUSSION

Permanent AF is frequently present in patients with long-lasting mitral valve disease, and the negative sequelae of this combination are widely known [Kannel 1982]. Furthermore, the presence of AF after mitral valve replacement is associated with a worse New York Heart Association functional class, increased transmitral gradients, and larger areas of both atria, compared with SR [Vaturi 2001]. Therefore, it is of unquestionable importance to make every effort to correct the arrhythmia during mitral valve surgery.

As Haines has stated [Haines 2000], the understanding of the pathophysiology of AF and the best treatment for this arrhythmia is evolving rapidly, but the treatment's development is still in its infancy.

The most accepted treatment strategy worldwide is Cox's maze procedure [Cox 1991], which is based on the compartmentalization of the atria by linear lesions to prevent the propagation of multiple reentrant wavelets.

Haissaguerre and associates [Haissaguerre 1998] have demonstrated that most AF is initiated by premature atrial beats caused by microreentrant circuits within the pulmonary veins at the level of the transition zone between the endothelium of the pulmonary veins and the endocardium of the LA and that AF is sustained by macroreentrant circuits in the atrial myocardium itself.

When the atrium starts to fibrillate, it undergoes a process described by Allessie as "atrial remodeling" [Allessie 1998]. He defines the result of this electrophysiological (and perhaps anatomical) remodeling as "atrial fibrillation begets atrial fibrillation." In other words, the more the atrium fibrillates, the more it is inclined to fibrillate.

From the treatment standpoint, the complete isolation of all 4 pulmonary veins per se would not be effective, and it is necessary to make the atria incapable of harboring the macroreentrant circuits that are the basis of AF once it is established. This is the basic concept of the maze procedure, which is actually performed with linear cryoprobes rather than with the cut-and-sew technique [Cox 2001]. Similarly, other techniques such as radiofrequency ablation [Sie 2001] have been applied to the same purpose.

Other investigators report simpler AF treatment methods during mitral valve surgery, such as the selective isolation of pulmonary veins [Sueda 2001] and epicardial and/or endocardial LA radiofrequency maze [Melo 2000, Benussi 2000], with different results. It is well known that atrial mass and size reduction may also be important components of the success of linear atrial ablation procedures [Haines 2000]. The reduction in atrial mass is essential for the recovery of SR, because the less tissue that is present where the reentrant circuit originates, the shorter will be the wavelength that allows the maintenance of the arrhythmia. For this reason, not only are linear lesions performed with the maze procedure but also both atrial appendages are amputated, and, in some cases, the atrial size is further reduced [Cox 1991, McCarthy 2000].

The theoretical assumption in the use of autotransplantation for treating AF in mitral valve surgery has been proposed (R.J. Batista, oral communication, IX Scientific Forum, Belo Horizonte, December 1999) and emphasizes the importance of wall stress in the maintenance of AF. Indeed, according to the Laplace law, it is possible to reduce wall stress in the LA in 2 ways: reducing the atrial pressure with mitral valve repair or replacement and reducing the left atrial size.

Autotransplantation allows the recovery of SR while at the same time realizing 3 of the above-mentioned goals: (a) complete isolation of the 4 pulmonary veins, (b) reduction of the left atrial mass, and (c) reduction of the left atrial wall stress.

Various modifications have been proposed to simplify the technique while aiming at the same target, including the isolation of pulmonary veins and reducing the size of the left atrial cavity. Nevertheless, the autotransplantation technique, despite its apparent complexity, has the advantage of allowing comfortable access to the LA. In the first 3 cases of our series, we removed the heart from the chest as Batista has described and realized that a major concern was the reimplantation of the heart after LA reduction because of the increased distance between the caval stumps. The problem was overcome by leaving the inferior vena cava connected (Figure), dissecting free the whole length of the superior vena cava, and marking the left atrial cuff behind the superior vena cava with hemoclips to avoid excessive displacement of the vena cava during the reconnection.

Particular attention has been addressed to myocardial protection. In 24 cases, intermittent retrograde cold blood cardioplegia was employed during the disconnection of the heart and the mitral surgery. Continuous retrograde blood reperfusion was instituted at the beginning of reimplantation, thereby reducing the period of ischemic cardiac arrest. In the last 4 cases, the entire procedure was accomplished on the beating heart with continuous retrograde warm blood perfusion according to the technique described by Gersak and Sutlic [Gersak 2002]. This approach appears to be the ideal myocardial protection strategy for this kind of operation, because the optimal exposure of the mitral valve and the LA makes irrelevant, in terms of surgical comfort, the motion of the heart and the blood flow through the coronary ostia.

The results of our series in terms of stable AF conversion (88.9%) and reestablishment of normal atrial function (SCS 4, 85.2%) at 17.2 ± 6.7 months of follow-up are comparable with results reported with the maze procedure [Kosakai 2000, McCarthy 2000] and superior to those of other surgical ablation techniques [Melo 2000, Sie 2001]. Moreover, with maze-type procedures, the rate of the SR falls below 60% when the preoperative LA diameter exceeds 70 mm, and when it exceeds 87 mm, the rate of the SR can fall to 0% [Kosakai 2000]. The mean preoperative values of LA diameter and volume in our experience are considerably higher than those reported in other series of the more recent literature [Benussi 2000, Sie 2001]. The relevant and statistically significant postoperative reductions in LA diameter and volume are principally due to the autotransplantation technique.

Particular attention was directed to the demonstration of normal atrial contractility at different follow-up intervals. Some articles in the literature report a considerable gap between the percentage of SR recovery and the detection of normal atrial function with the Cox maze or maze-type

procedures [Sie 2001, Yuda 2001]. Moreover, some investigators [Albirini 1997, Kawaguchi 1996] have stated that atrial systolic function is lost with the maze operation. As shown in Table 3, an SCS of 4 was recorded postoperatively in 21 of 24 patients in SR at 11.9 ± 5.3 months and in 23 of 24 patients at 17.2 ± 6.7 months in our series, suggesting the possibility of a further late recovery of LA function, not only when a stable SR is maintained but also when a surgically effective LA volume reduction is performed. At the same time, discordant results have been published about the effectiveness of the Cox maze on the prevention of late thromboembolic events [Bando 2002, Haines 2000]. The absence of thromboembolisms at the intermediate-term follow-up in our series is encouraging and may be explained by the higher percentage of patients with SR who recovered normal atrial contractility.

Recently, some investigators [Harada 2000, Sueda 2001] have reported the results of isolated left atrial procedures to eliminate chronic AF during mitral valve operations, with a SR recovery rate ranging from 83% to 91%. These results suggest that in more than 80% of AF cases combined with mitral valve disease the LA plays an important role in maintaining the AF and the right atrium does not. The autotransplantation technique can be considered an isolated left atrial procedure as well. It allows good results, as indicated by the high AF conversion rate and by the low incidence (2 cases) of postoperative atrial flutter. In our series, only in 4 cases of a very large right atrium was a surgical reduction of the right atrial cavity combined with an excision of the right appendage, our aim being to reduce the incidence of supraventricular tachyarrhythmias in the postoperative course.

In conclusion, the autotransplantation procedure is effective in obtaining a stable SR and normal atrial function recovery in the mid term, particularly in patients with a very large LA. A longer follow-up is necessary to confirm the stability of these results.

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