



Sinus Rhythm Restoration after Radiofrequency Ablation Improves Survival in Patients Undergoing Mitral Valve Surgery : A Eight Year Single Center Study

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Abstract

Background: The usefulness of radiofrequency (RF) ablation in restoring sinus rhythm in patients with permanent atrial fibrillation (AF) undergoing surgery for mitral valve has been demonstrated. But whether sinus rhythm recovery affects long-term survival is Less Clear.

Methods: This study included 301 consecutive patients (126 men and 175 women, age 69±6 years) undergoing radiofrequency ablation of persistent atrial fibrillation along with mitral valve surgery. Radiofrequency ablation was performed using unipolar probe in 55.3%, bipolar probe in the remaining 44.7% of cases.

Results: Four patients died during hospitalization. At follow-up, sinus rhythm was present in 76% of the surviving patients. 71 patients never recovered sinus rhythm after hospital discharge. Mortality and recurrent hospitalization were significantly lower in patients with sinus rhythm at the end of follow-up in comparison to permanent AF. The incidence of stroke was also lower in patients with stable sinus rhythm. Larger atria, pulmonary hypertension and history of rheumatic disease were associated with the persistence of AF despite radiofrequency ablation. Although survival and functional capacity were significantly lower in patients with permanent AF at multivariate analysis only age and pulmonary artery pressure before surgery were independently associated with mortality.

Conclusions: Sinus rhythm restoration by RF ablation in patients undergoing mitral valve surgery is associated with an improved long-term survival. However our results suggest that a more severe hemodynamic impairment, expressed by higher pulmonary artery pressure, and increasing age are the only independent factors related to long-term survival.

Introduction

Less than 20% of patients with permanent atrial fibrillation(AF) spontaneously convert to (sr) after mitral valve surgery.^{[1],[2]} The persistence of AF after surgery is associated with a decreased exercise tolerance, an increased risk of systemic embolization^[3] and higher long-term mortality.^[4]

Original surgical treatment – (“cut and saw”) –^[5] has been progressively substituted by other tissue-ablation technologies radiofrequency -(RF)- and cryo ablation are the most common. Several different lesion sets have been proposed; including pulmonary vein isolation and other left-sided ablation lines, while the bi-atrial maze lesion set is less commonly used due to the need for right atrial atriotomy and longer times of cardiopulmonary bypass.^[6] Radiofrequency may be unipolar or bipolar.^{[7]-[9]} The main limitation of monopolar catheter is the high probability to not obtain transmural lesions in comparison to bipolar probes: moreover the latter have a reduced risk of damaging adjacent structures such as the esophagus.^{[10]-[11]}

Key Words

Mitral valve surgery, Atrial fibrillation, Monopolar and bipolar radiofrequency ablation, Survival.

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Several studies have reported a high rate of success using both monopolar and bipolar RF on rhythm recovery for short and intermediate term. Evaluation of long-term effects of these procedures has been hampered by several variables. This includes clinical characteristics of patients (age, concomitant valve surgery, etiology of valve heart disease, left ventricular function, pulmonary artery pressure), follow-up strategies and finally the type of energy used along with the set of lesions performed. Few studies however examined the effects of AF RF ablation along concurrent with mitral valve surgery regarding patients' survival, along their functional capacity, and quality of life.^[7]

The aim of the present study was to prospectively assess the effects of sinus rhythm maintenance on survival after left-sided RF ablation of AF along with mitral valve surgery.

Methods

In the study, all patients underwent unipolar or bipolar RF ablation along with mitral valve surgery between 1/1/2003 to 12/31/2011 at the Heart Surgery Department of the Azienda Ospedaliera Universitaria di Careggi Hospital in Florence.

The time of onset of AF and functional capacity expressed as NYHA(New York Heart Assoc) functional class were recorded at hospital admission. Electrocardiogram(ECG) was obtained examination was performed to confirm the presence of arrhythmia. All patients underwent transthoracic echocardiography with a 2.5 and 3.5 MHz probe (Sequoia C256 Accuson Siemens Mount View, California). Left atrium AP diameter (mm), 2D left and right

Table 1: Clinical characteristics of patients

Gender (M/F)	126/175
Age (years)	69.1 ± 9.7
Preoperative AF duration (months)	36.9 ± 49.7
LVEF (%)	51.6 ± 9.8
LA (mm)	53.7 ± 8
LA area (cm ²)	32.5 ± 10
RA area (cm ²)	22.3 ± 6.7
Systolic Pulmonary pressure (mmHg)	44.2 ± 14.9
NYHA class	2.9 ± 0.6

AF= atrial fibrillation, LVEF = left ventricular ejection fraction, LA = left atrium, RA = right atrium
 atrial area (cm²) and left ventricular ejection fraction (LVEF) were measured. End-diastolic and end-systolic images were synchronized on ECG. Since patients were in AF we considered the average value of five measurements. Pulmonary systolic pressure (PAP) was calculated adding tricuspid valve pressure gradient to estimated right atrial pressure assessed by inferior vena cava diameter and response to respiration.

Ablation technique

Medtronic Cardioablate surgical ablation systems (Medtronic, Minneapolis USA) were used for monopolar and bipolar treatment. Detailed description of left sided ablation lines has been previously reported.^[12] The extra time on cardiopulmonary by-pass for ablation was on average 15±8 min.

Post-operative management

To favor maintenance of sinus rhythm after RF ablations amiodarone bolus of 300 mg was administered i.v. followed by a continuous infusion of 1,200 mg in the first 24 hours; thereafter it was prescribed 200 mg orally every 12 hours until discharge. A maintenance regimen of 200 mg/day was prescribed for 3 months. Patients with persistent AF after RF ablation underwent at least one attempt of external cardioversion by biphasic DC-shock. Oral anticoagulation was given to maintain the International Normalized Ratio(INR) between 2.5 and 3.5 for the first 6 months in all patients, and life-long in patients who received mechanical valves or who had persistent AF or both.

Follow-up

Patients were seen at the outpatient clinic 3 months, 6 months, and 12 months after the surgical procedure and annually thereafter. Between visits, their referring physician attended patients on a regular basis and routine ECGs were obtained at each clinic visit regardless of symptoms. Event monitors were prescribed for patients who complained of palpitations or symptoms compatible with AF during follow-up. Between visits, all patients were encouraged to seek 12-lead ECG documentation for any symptom suggestive of AF/atrial flutter recurrence and a physician routinely performed trans-telephonic monitoring of any symptoms and complications.

Table 2: Etiology of mitral regurgitation

	%
Mitral valve prolapse	26.3
Rheumatic mitral valve disease	28.7
Rheumatic mitral-aortic valve disease	19
Ischemic mitral regurgitation	12.7
DCMP related mitral regurgitation	2

DCMP – dilated cardiomyopathy

The follow-up evaluation consisted of a detailed history, physical examination and 24-h Holter monitoring. Success and AF recurrence were defined as per the HRS/EHRA/ECAS expert consensus document.^[13] Informed consent was obtained by all patients and the study approved by the Ethical Committee of our Institution.

Statistical analysis

Data are presented as means ± SD for continuous variables and

Table 3: Type of intervention performed

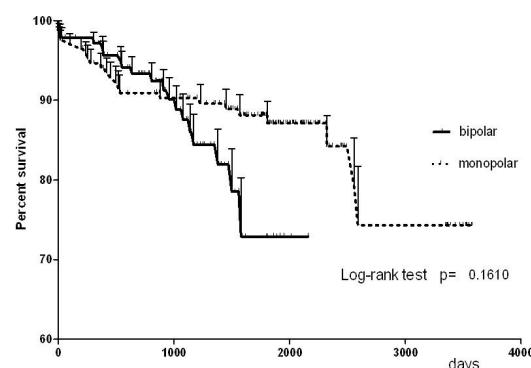
	%
Mechanical MVR	12.7
Biologic MVR	13.7
Mitral valve repair	30
MVR / mitral valve repair and AVR	18.7
Mitral valve repair and CABG	10.3
MVR and CABG	4.3
DCMP related mitral regurgitation	10.3

MVR – mitral valve replacement , AVR- aortic valve replacement CABG -coronary artery by-pass graft

as percentages for categorical variables. Continuous variables were compared through the use of Student's 2 tailed unpaired-sample test. Categorical variables were compared using the chi-square test or Fisher's exact test if appropriate. Differences among groups were evaluated using ANOVA test. Multivariate analysis was performed using stepwise Cox regression method. Kaplan-Meier curves were used for the survival analysis. Differences between groups were compared using Log-Rank test. A probability value < 0.05 was considered significant. Statistical analysis was performed using SPSS 22.0 software (SPSS, Inc., Chicago, IL, USA).

Results

In the period under investigation 301 patients, 126 men and 175 women, mean age of 69.1 ± 9.7 years underwent RF

**Figure 1:** Kaplan Meyer survival curves of patients treated with monopolar and bipolar RF ablation

ablation in conjunction with mitral valve surgery. The clinical and echocardiographic characteristics are reported in [Table 1]. Four patients died in the immediate postoperative period (1.2%). One patient died of a cerebral hemorrhage, one of myocardial infarction, the remaining 2 of septic shock. 297 patients were included in the study. At the time of surgery 80% patients had severe functional impairment (III-IV NYHA class). Rheumatic mitral valve disease, lone or combined with aortic valve disease, (47.7%), and mitral valve prolapse were the more frequent indication to surgery [Table 2].

Table 4: Clinical characteristics of patients treated with monopolar or bipolar RF ablation			
	Monopolar	Bipolar	p
Age (years)	169	132	
Sex M/F	67.8±9	70.7±9.0	0.019
Duration AF	99/70	76/56	0.9
SR at follow-up %	38±43	35±56	0.55
LVEF (%)	100/69	74/58	0.63
LA (mm)	52±10	51±9	0.63
LA area (cm ²)	49±6	53±8	0.001
RA area (cm ²)	32±10	32±9	0.8
Syst Pulmonary pressure (mmHg)	22±6	22±6	0.8
Etiology	44±15	42±14	0.5
Mitral valve prolapse	48	31	0.06
Rheum MVD	57	29	
Rheum MAVD	25	32	
Ischemic MR	20	18	
Dilated Cardiomiopathy	19	22	
NYHA class			
I	0	1	0.05
II	28	40	
III	117	78	
IV	24	13	

SR= sinus rhythm , LVEF = left ventricular ejection fraction, LA = left atrium, RA = right atrium , MVD= mitral valve disease, MAVD= mitro-aortic valve disease, MR= mitral regurgitation

Details on surgical interventions performed are reported in [Table 3]. Radiofrequency ablation was performed using catheter unipolar probe in 55.3%, and bipolar in the remaining 44.7% of cases. There were no significant differences between clinical characteristics of the two groups except for age and left atrial LA diameter [Table 4].

Rhythm analysis

At the end of follow-up 69.4% patients were alive. Among them 76% were in sinus rhythm at the last follow-up visit. During follow up (mean duration about 8 years) 40.9% of patients remained in sinus rhythm at periodic clinical examinations and never experienced clinically demonstrated recurrent AF. 9 patients discharged in AF were in sinus rhythm at the end of follow up. One hundred and three patients (35.2%) had at least one symptomatic AF episode during follow-up. Finally 24% had permanent AF despite radiofrequency treatment and electrical CV attempts. Atrial tachycardia, was recorded in 6.9%. twenty-seven patients underwent definitive pacing, 8 during hospitalization, 19 during the follow-up period. The clinical and echocardiographic characteristics before surgery of the three groups of patients (stable sinus rhythm, recurrent AF, persistent AF) are shown in [Table 5]. Patients with persistent AF despite treatment were on average older, by up to 3 years, compared to those than those with recurrent AF or who remained in stable sinus rhythm ($p=0.03$).

We did not find any relationship between rhythm at follow-up regarding gender, surgical procedure performed, permanent pacing, left ventricular ejection fraction(LVEF) and finally NYHA class before surgery. Left atrium diameter, left and right atrial area were significantly lower in patients with stable sinus rhythm in comparison with the other two groups. Systolic pulmonary artery pressure was higher in those with persistent AF than in those with stable sinus

rhythm. Logistic multivariate analysis showed that the duration of the arrhythmia (OR 1.005 95%CI 1.00019 -1.01074 $p= 0.04$), preoperative left atrial area size(OR 1.03874 95%CI 1.00537-1.07321 $p= 0.02$), tricuspid valve repair (OR 2.07273 95%CI 1.07453-3.99821 $p=0.03$) and attempts to DC cardiovert(OR 1.9163 95%CI 1.00933 -3.63854 $p= 0.04$) were associated with permanent atrial fibrillation.

Other outcome

Ischemic stroke occurred in 8 of patients (3%) during follow-up. Among the 6 who were in permanent AF, 5 had INR values at stroke occurrence below the therapeutic range. Significant carotid stenosis was found in 1 of the 2 patients in SR.

Hospitalization due to cardiac cause during the follow-up period was needed in 31% of patients. The hospitalization rate was almost twofold in patients who never regained sinus rhythm after ablation in comparison with patients in sinus rhythm(SR) at the end of follow-up. The high hospitalization rate in patients with recurrent AF was mainly related to attempts of SR restoration. A significant

Table 5: Clinical characteristics of different groups

	Stable SR	AF recurrence	Permanent AF	P
Age (years)	67.7 ± 9.2	67.9 ± 10	71.9 ± 8.5	0.0494
LA (mm)	50.7 ± 7.1	53.9 ± 8.7	56.1 ± 8.4	<0.0001
LA area (cm ²)	30.7 ± 7.8	32.1 ± 8.0	37 ± 11.4	<0.0001
RA area (cm ²)	20.4 ± 4.0	21.9 ± 6.0	23.9 ± 6.8	0.0159
Systolic PAP (mmHg)	41.0 ± 11.9	44.4 ± 14.1	46.1 ± 15.4	<0.0001
Electric cardioversion before discharge (%)	9.1	20.1	28.9	0.0092
Hospitalization (%)	17.5	48.8	30.0	<0.0001

AF= atrial fibrillation, LVEF = left ventricular ejection fraction, LA = left atrium, RA = right atrium improvement in functional capacity was found after surgery.

Survival analysis

At the end of follow-up period overall survival was of 85.7%. Forty-three patients died during follow-up, 67.4% due to cardiac causes. Patients who died were older than survivors (mean age 72.9 ± 6.2 vs. 68.6 ± 9.4 years, $p=0.026$). We did not find gender related differences in mortality, there was no difference in mortality between patients who underwent monopolar or bipolar radiofrequency ablation [Figure 1].

Overall mortality was significantly higher in patients with persistent AF in comparison to those in stable sinus rhythm after discharge (Log Rank test- $p=0.009$). The survival rate however was not significantly different in patients with stable sinus rhythm during follow-up in comparison to patients who had transient AF recurrences but were in sinus rhythm at the end of follow-up [Figure 2].

Long-term mortality was higher in patients with rheumatic mitral valve disease who had a lower probability of sinus rhythm recovery, than in those suffering from mitral valve prolapse. Tricuspid valve repair was associated to a worse prognosis: it was performed in 28.6% patients who died in comparison to 14.8% survived at the end of follow-up ($p=0.041$).

Preoperative functional capacity was not related to survival. The percentage of patients in advanced NYHA class (III-IV) was not significantly different in the two groups (82% of survivors vs. 91% of deceased patients). Atrial size (both right $p=0.0023$ and left atrial area $p=0.0135$) and pulmonary artery pressure (43.3 ± 14.3 vs 49.3 ± 17.2 mmHg; $p=0.022$) were significantly lower in survived patients.

Table 6: Clinical characteristics of survived and died patients

	Survived	Died	p
Preoperative AF duration (months)	36.5 + 50	39.4 + 48.3	0.72
AF recurrence free (days)	759 + 831.5	293 + 575	0.0001
LVEF (%)	59 + 9.5	49.9 + 12.1	0.22
LA (mm)	53.4 + 27	56 + 91	0.06
LA area (cm ²)	31.1 + 7.9	36.3 + 18.7	0.0135
RA area (cm ²)	21.9 + 5.7	24.5 + 10.7	0.0328
Syst Pulmonary pressure (mmHg)	43.3 + 14.3	49.3 + 17.2	0.022

AF= atrial fibrillation, LVEF = left ventricular ejection fraction, LA = left atrium, RA = right atrium

At multivariate analysis, only age (OR= 1.1; 95% CI= 1.02-1.11; p= 0.003) and pulmonary artery pressure (OR=1.03; 95% CI= 1.02-1.12; p= 0.02) were independently associated with survival [Figure 3].

Discussion

Radiofrequency ablation along with mitral valve surgery has been reported to significantly affect rate of sinus rhythm recovery however the characteristics of the population included in each study and the use of different RF catheters (unipolar or bipolar) and ablation line sets

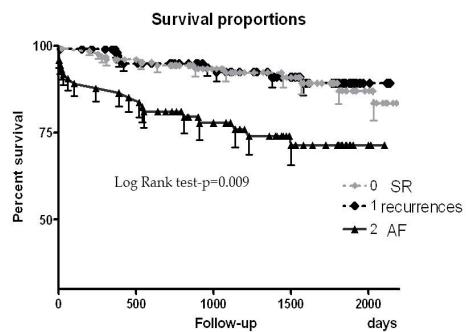


Figure 2: Kaplan Meyer survival curves : comparison among patients with stable sinus rhythm, recurrences of AF and persistent AF

may account for the large differences in success percentage observed.^{[14]-[17]} Moreover results may have been influenced by the absence of a uniform AF classification, adequate reporting of preoperative cardiac conditions or by the different methods of evaluating AF recurrences.

In our study we followed the HRS/ EHRA/ECAS expert consensus document to evaluate the success of the procedure.^[13]

In previous studies preoperative LA size, cardiothoracic ratio over 60%, fine AF wave at preoperative ECG, and no early sinus rhythm restoration, an increasing number of concomitant surgeries were reported as independent predictors of ablation failure in the intermediate follow-up period at multivariate analysis.^{[14]-[16],[18]}

An elevated mean-age of patients, the absence of paroxysmal AF and a high percentage of rheumatic valve disease may explain the relative high rate (26%) of persistence of AF at hospital discharge observed in present investigation. Atrial fibrosis^[19] may be responsible for the poor results of RF ablation in rheumatic heart disease. Duration of the arrhythmia, preoperative left atrial area, tricuspid valve repair and finally in hospital attempt of DC cardioversion were independently associated with persistence of AF.

Few studies evaluated the effects on long term survival of sinus rhythm maintenance after radiofrequency (RF) ablation in patients

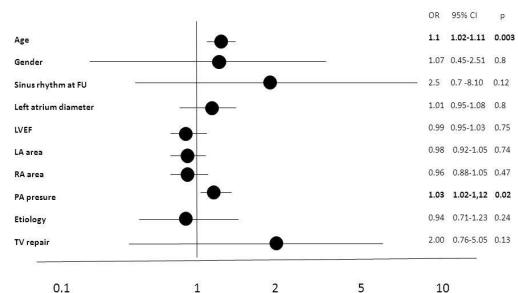


Figure 3: Results of multivariate logistic analysis on survival

with permanent atrial fibrillation (AF) undergoing surgery for mitral valve disease.

In a retrospective study an improved survival rate was reported in the subgroup of 65 patients treated with the maze procedure (SR at 81% at 5 years) in comparison with patients who underwent isolated mitral valve repair.^[20] Ad et al^[21] reported a higher four-year survival in patients who underwent Cox-maze procedure versus patients with untreated AF (OR= 2.47; P = 0.048).

At present this study is the largest with a long follow-up evaluating the relationship between RF ablation with mitral valve surgery and mortality. Survival rate is significantly lower in patients with permanent AF after surgery, in comparison with patients with stable sinus rhythm and in whom at least 1 recurrence of AF was documented during follow-up (70% vs respectively 90 and 91%). Factors associated with mortality were also related to an increased rate of persistent AF at follow-up. Only age and pulmonary artery pressure before surgery were independently associated with survival.

Limitation of the study

The absence of a control group is a limitation of the study. Few clinical studies in literature compared the results of concomitant AF ablation in open heart surgery with those of a concurrent control arm (that is leaving the AF untreated). The absence of a control arm does not allow to assess the absolute effect of the ablative procedure either because it is impossible to know how many of the patients would convert to sinus rhythm spontaneously and more relevant; the effects of confounding variables (e.g. the different degree of hemodynamic impairment).

The results of 7 matched-controlled and 4 randomized trials of the maze procedure associated with concomitant mitral valve surgery showed that freedom from AF was 77% to 95% in the maze group versus 4% to 53% in the control group at 2 and 8 year follow-up.^[22] The study by Gillinov et al^[23] randomized to surgical ablation or no ablation 260 patients with persistent or long standing persistent AF undergoing mitral valve surgery. Sinus rhythm was present in 63.2 % in the ablation group in comparison to 29.4 % (p<0.0001) in the non-ablation group. Ablation was associated with a higher risk of pacemaker implantation and no significant differences were reported in major cardiovascular or cerebrovascular adverse effects. The effects on survival are not valuable due to brief duration of follow-up (1 year). Another possible limitation related to the lesion set as this study involved only the left atrium. No randomized studies, however, have compared different RF lesion sets. In their study Gillinov et al^[23] reported no significant difference after surgical pulmonary vein

isolation alone or bi-atrial maze procedure in sinus rhythm rate at 1 year (61 vs 66%).

Patients included had long lasting AF before surgery and in patients discharged in AF late recovery of sinus rhythm occurred only in 9. Moreover on average AF recurrence occurred 750 days after surgery, a time significantly longer than standard “blanking period”.

Conclusions

The present study supports the efficacy of RF ablation (unipolar and bipolar) in restoring SR in patients with AF undergoing mitral valve surgery and demonstrates that, in patients in whom sinus rhythm is maintained after RF ablation, not only the quality of life is improved but mortality is also significantly decreased. However our results suggest that a more severe hemodynamic impairment, expressed by higher pulmonary artery pressure, and increasing age are the only independent factors related to long-term survival.

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Conflict Of Interests

None.

Disclosures

None.

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