

# Radiofrequency Ablation of Atrial Fibrillation in Patients With Mechanical Mitral Valve Prostheses

## Safety, Feasibility, Electrophysiologic Findings, and Outcomes

Ayman A. Hussein, MD,\* Oussama M. Wazni, MD,\* Serge Harb, MD,\* Lee Joseph, MD,\* Mohammed Chamsi-Pasha, MD,\* Mandeep Bhargava, MD,\* David O. Martin, MD,\* Thomas Dresing, MD,\* Thomas Callahan, MD,\* Mohamed Kanj, MD,\* Andrea Natale, MD,† Bruce D. Lindsay, MD,\* Walid I. Saliba, MD\*

*Cleveland, Ohio; and Austin, Texas*

<b>Objectives</b>	The purpose of this study was to evaluate the feasibility, safety, and outcomes of radiofrequency ablation of atrial fibrillation (AF) in patients with mechanical mitral valve replacement (MVR).
<b>Background</b>	The role of ablative therapy in patients with MVR is not yet established, with safety concerns and very few outcome data.
<b>Methods</b>	Between January 2003 and December 2008, we followed up 81 patients with MVR undergoing first-time AF ablation (compared with 162 age- and sex-matched controls). Arrhythmia recurrences were identified by symptoms with documentation, event monitoring, Holter monitoring, and electrocardiograms.
<b>Results</b>	All MVR and control patients underwent ablation under therapeutic international normalized ratio. No entrapment of catheters or stroke occurred. There were no differences in terms of procedure-related complications between the groups ( $p = \text{NS}$ ). Patients with MVR had larger atria ( $p < 0.0001$ ), lower left ventricular ejection fractions ( $p = 0.0001$ ), and more concomitant atrial flutter at baseline ( $p < 0.0001$ ). Over a 24-month follow-up, they had higher recurrence rates compared with controls (49.4% vs. 27.7% after a single ablation, $p = 0.0006$ ). The creation of flutter lines significantly reduced recurrences in patients with any history of atrial flutter (16.7% vs. 60.9%, $p = 0.009$ ). At last follow-up, 82.7% of MVR patients had their arrhythmia controlled (69.1% not receiving antiarrhythmic drugs).
<b>Conclusions</b>	Radiofrequency ablation is feasible and safe for patients with MVR. It allowed restoration of sinus rhythm in a substantial proportion of patients undergoing ablation. An abnormal atrial substrate underlies recurrences in these patients. The ablation procedure needs to be further refined with a focus on extra pulmonary vein triggers and concomitant flutters to improve outcomes. (J Am Coll Cardiol 2011;58:596–602) © 2011 by the American College of Cardiology Foundation

Atrial fibrillation (AF), the most common cardiac arrhythmia, frequently complicates the course of mitral valve disease (1,2). Among patients undergoing mitral valve replacement (MVR), many have AF, and in many others, AF and atrial flutter (AFL) develop after their surgery. It is not uncommon that AF becomes resistant to medical

management in patients with MVR, and these patients are referred for radiofrequency ablation.

Pulmonary vein isolation (PVI) and ablation of left atrial flutter are effective treatments for drug resistant atrial arrhythmias (3). The role of ablative therapy in patients with mechanical MVR is not yet established, with very few data in the literature on feasibility, safety, and outcomes (4,5). In this distinct group of patients, the procedure carries a risk of prosthetic valvular damage and entrapment of the ablation catheter within the prosthesis, necessitating open-heart surgery. Furthermore, patients with MVR have a particular atrial substrate of their arrhythmia with surgical scarring, fibrosis around the mitral annulus (MA), and probable atrial myopathy from chronic mitral valve disease. An abnormal atrial substrate may potentially contribute to arrhythmia recurrences in these patients. We aimed to evaluate the feasibility, safety, and

From the \*Center for Atrial Fibrillation, Cleveland Clinic, Cleveland, Ohio; and the †Texas Cardiac Arrhythmia Institute, St David's Medical Center, Austin, Texas. Dr. Martin is on the advisory board of Medtronic. Dr. Dresing has received speaking honoraria from Boston Scientific, Cardionet, Medtronic, and St. Jude Medical; and research support from Boston Scientific, Medtronic, St. Jude Medical, and Biotronik. Dr. Callahan receives speaking honoraria from Biotronik and Boston Scientific. Dr. Lindsay is a consultant to Biosense Webster. All other authors have reported that they have no relationships to disclose.

Manuscript received January 1, 2011; revised manuscript received March 2, 2011, accepted March 21, 2011.

outcomes of radiofrequency ablation of AF in patients with MVR.

## Methods

**Ablation protocol.** Our PVI and periprocedural anticoagulation protocols have been described in details (6,7). Briefly, all antiarrhythmic drugs were stopped 4 to 5 half-lives before ablation, with the exception of amiodarone, which was stopped a minimum of 4 to 5 months before the procedure. Warfarin was continued at a therapeutic international normalized ratio (INR) level at time of ablation. A transesophageal echocardiogram was obtained for patients presenting in AF if they had a subtherapeutic INR within 3 weeks before ablation to exclude a left atrium (LA) appendage thrombus. Light to moderate sedation was used during the procedure. For cardioversion, deep sedation was used briefly; otherwise, deep sedation was avoided to allow monitoring for neurologic complications.

A 10-F 64-element phased-array intravascular ultrasound catheter (Siemens AG, Malvern, Pennsylvania) was used for intracardiac echocardiography (ICE) imaging during the procedure. The ICE catheter was positioned in the right atrium (RA) and rotated clockwise to obtain the standard trans-septal view. In all patients, ICE was used to assist with trans-septal punctures, to define pulmonary vein (PV) anatomy, and most importantly in this particular group of patients, to obtain direct views of the LA and monitor for complications including pericardial effusion or damage to native or prosthetic valves. The ICE catheter remained in the RA for the entire duration of the procedure. For all mapping and ablations near the prosthetic valves, continuous real-time ICE imaging and frequent fluoroscopy checks were used to accurately localize the catheters relative to the prosthetic valves to prevent entrapment. The electrocardiographic tracing screens were also monitored for any artifacts that may result from the catheters being close to the metallic valves, but every effort is made to avoid any contact of the catheters with the valves.

After trans-septal puncture, the activated clotting time was maintained in the range of 350 to 450 s. Two catheters were advanced into the LA for mapping and ablation guided by ICE. All PVs were isolated in all patients under ICE guidance.

The cornerstone for ablation was PVI, including ablation of the antrum encompassing most of the posterior wall. Electrical isolation was confirmed with absence of PV potentials along the antrum or inside the veins by use of a circular mapping catheter. At the discretion of the operator, further ablation was performed along the septum. For patients in AF, ablation in the coronary sinus or base of the appendage was considered. When a non-PV trigger was identified during the procedure, this was also targeted. For patients in sinus rhythm (SR), the endpoint of the procedure was PVI. For patients in AF, PVI and restoration of SR was an endpoint for ablation. For patients in whom

another tachycardia developed during the procedure, the arrhythmia was mapped and ablated with SR restoration as an endpoint. For patients with a history of AFL, attempts to induce the arrhythmia were made in almost all patients, and this was mapped and ablated with SR restoration as an endpoint. For patients in whom we failed to restore SR by ablation, cardioversion was performed. For all patients, when a non-PV trigger was identified after restoring SR, this was targeted by ablation. The superior vena cava (SVC) was mapped in all patients, and potentials were ablated when there was no phrenic nerve stimulation.

In patients with typical AFL, ablation of the cavotricuspid isthmus (CTI) was performed. For atypical flutters, the critical isthmus of the arrhythmia was defined by electroanatomic activation mapping and by entrainment. Ablation was then performed to transect the identified isthmus. The endpoint of flutter ablation was its termination, demonstration of bidirectional block across the isthmus, and noninducibility of AFL by right and left atrial rapid and programmed pacing without drug use and then after isoproterenol infusion (up to 20  $\mu\text{g}/\text{min}$ ). Mitral block was determined by pacing maneuvers described by the Bordeaux group (8,9). Roof block was confirmed by pacing from the appendage and by demonstrating low to high activation in the posterior wall. Patients were monitored for complications during the procedure and their overnight hospital stay. We defined as major complication any complication that results in death, prolongation of hospital course, or requires an intervention. Otherwise, complications were considered minor.

**Study population and follow-up.** Between January 2003 and December 2008, all patients with MVR referred to our electrophysiology laboratory for first-time AF ablation were included. For each patient with MVR, we identified 2 age- and sex-matched patients from our AF ablation database who underwent PVI during the same period. When multiple matches were available, we selected as controls the ablations performed by the same operator on the case during the same period (priority given to controls closer in time to cases). All cases and controls had failed at least 2 antiarrhythmic drugs plus a negative dromotropic agent. A 24-month follow-up was considered for the study population (with additional 24 months after last ablation in patients with repeat ablation). Clinical data were collected before ablation and during subsequent follow-up visits

## Abbreviations and Acronyms

<b>AF</b>	= atrial fibrillation
<b>AFL</b>	= atrial flutter
<b>AT</b>	= atrial tachycardia
<b>CTI</b>	= cavotricuspid isthmus
<b>ICE</b>	= intracardiac echocardiography
<b>INR</b>	= international normalized ratio
<b>IQR</b>	= interquartile range
<b>LA</b>	= left atrium
<b>MA</b>	= mitral annulus
<b>MVR</b>	= mitral valve replacement
<b>PVI</b>	= pulmonary vein isolation
<b>RA</b>	= right atrium
<b>SR</b>	= sinus rhythm

scheduled at 3, 6, 12, and 24 months. More frequent follow-ups were scheduled for patients who experienced symptoms, arrhythmia recurrence, or complications from the procedure. All patients had transthoracic echocardiograms within 3 months before ablation and after PVI to assess for procedure-related mechanical valve dysfunction.

After ablation, all patients were given an event recorder to monitor for arrhythmias during the first 3 months, and recorded on a weekly basis and whenever symptomatic. Additional event recorder monitoring was obtained beyond the 3-month period in patients with arrhythmia or symptoms consistent with arrhythmia within the first 3 months. Patients had 24-h Holter recordings at 3, 6, 12, and 24 months after ablation. Arrhythmia recurrence was identified if an atrial tachyarrhythmia, lasting 30 s or more, was captured on a 12-lead electrocardiogram, event recording, or Holter monitor. Atrial arrhythmias occurring during the first 2 months after PVI (blanking period) were not counted as recurrences. Antiarrhythmics were used in the first 2 months after ablation then stopped, unless continued arrhythmia mandated their use. Amiodarone was never used after ablation. All success rates were determined off antiarrhythmic drugs.

**Statistical analysis.** Results are presented as percentages for categorical variables and mean ± SD for continuous variables. Nonnormally distributed variables are presented as median (interquartile range [IQR]). The matching process for age and sex aimed to minimize the impact of noncardiovascular confounders. For subsequent analyses, the cases and controls were compared as independent samples to highlight the anatomical differences between the groups and their clinical implications. Clinical characteristics were compared by the Student *t* test or Wilcoxon rank-sum test for continuous variables as appropriate. For categorical variables, the chi-square test or Fisher exact test was used as appropriate. Kaplan-Meier survival curves were used to present arrhythmia-free survival after ablation (differences between the groups tested by using the log-rank test). Cox proportional hazards analyses were employed to assess for factors associated with arrhythmia recurrence in patients with MVR. A 2-sided *p* value <0.05 was considered statistically significant. All statistical analyses were performed with SPSS software (version 15.0, SPSS, Chicago, Illinois).

## Results

**Population characteristics.** The study included 81 patients with MVR and 162 age- and sex-matched controls. Their baseline characteristics are summarized in Table 1. The indications for MVR were mitral regurgitation (MR) in 52.5% of patients, mitral stenosis (MS) in 5%, both MR/MS in 11.3%, rheumatic valvular disease in 25%, congenital mitral disease in 2.5%, and unknown in 3.8%. They had their valve prostheses for a median of 6 years (IQR: 2 to 10 years; minimum and maximum: 1 and 36

**Table 1** Baseline Clinical Characteristics

Parameter	No MVR (n = 162)	MVR (n = 81)	<i>p</i> Value
Age, yrs	56.9 ± 11.5	56.2 ± 11.2	
Female	55.9	55.6	
Hypertension	29.7	41.9	0.01
Diabetes mellitus	7.9	7.4	0.88
Coronary disease	14.9	14.7	0.91
Nonparoxysmal AF	32.7	29.6	0.62
Concomitant AFL	14.8	43.2	<0.0001
Concomitant AT	3.1	4.9	0.12
AF duration, yrs	6 (3–8)	5 (3–7)	0.61
LVEF, %	54.5 ± 8.5	49.2 ± 10.6	0.0001
LAS, cm <sup>2</sup>	23.1 ± 5.4	30.3 ± 8.0	<0.0001

AF = atrial fibrillation; AFL = atrial flutter; AT = atrial tachycardia; LAS = left atrial size; LVEF = left ventricular ejection fraction; MVR = mitral valve replacement.

years) before ablation, and 28 of them (34.6%) had a maze procedure (10 radiofrequency, 8 cryothermal, 4 “cut and sew,” 6 unknown) at time of their initial surgery.

Compared to controls, Patients with MVR were more likely to have hypertension (*p* = 0.01) but as likely to have diabetes mellitus or coronary disease (*p* = NS). In the MVR group, 29.6% of patients underwent ablation for nonparoxysmal AF compared with 32.7% of patients in the control group (*p* = 0.62). The arrhythmia duration before ablation was also similar in the groups (6 [IQR: 3 to 8] years vs. 5 [IQR: 3 to 7] years, *p* = 0.61). Importantly, concomitant AFLs were more frequent in patients with MVR (43.2% vs. 14.8%, *p* < 0.0001). Patients with MVR had lower left ventricular ejection fractions (*p* = 0.0001) and larger atria (*p* < 0.0001) compared with controls. The INRs on day of the procedure were similar in both groups (2.47 ± 0.6 vs. 2.62 ± 0.8, *p* = 0.82).

**Radiofrequency ablation data.** All MVR patients and controls underwent isolation of all 4 PVs. The SVC potentials were found and ablated more frequently in patients without MVR (84.7% vs. 64.2%, *p* = 0.002). More patients in the MVR group required ablation in the coronary sinus (24.7% vs. 14.2%, *p* = 0.04). The ablation procedures were longer (154 ± 23 min vs. 123 ± 19 min, *p* = 0.03) and required more fluoroscopy (37 ± 12 min vs. 17 ± 8 min, *p* < 0.01) in patients with MVR.

At time of ablation, 27 of 81 (33.3%) patients with MVR presented in AF, 16 (19.8%) presented in AFL, 1 (1.2%) in atrial tachycardia (AT), and 37 (45.7%) in SR. Of 37 patients presenting in SR, 11 patients (29.7%) had AF during the procedure (terminated by ablation in 8, by cardioversion in 3). For those who presented with atrial tachyarrhythmia, ablation was performed in the presenting rhythm in 37 patients (AF terminated by ablation in 30 and by cardioversion in 7) and after cardioversion in 7 patients (SR maintained for the total duration of the procedure).

In addition to PVI and SVC ablation in patients with MVR, LA triggers were found and ablated in 36 patients (44.4%). Additional targeted areas included the septum in

**Table 2** Electrophysiologic Findings on 22 Patients With Mitral Valve Prostheses and Concomitant AFL

	Mode of AFL Termination
6 patients with right AFLs	
3 CTI flutters	All 3 with CTI ablation
3 RA incisional flutters	Line connecting surgical scar to the SVC Line connecting surgical scar to the SVC to TCL prolongation to spontaneous conversion to AT; terminated with focal ablation to high crista terminalis Line connecting surgical scar to tricuspid annulus
5 patients with left AFLs	
2 MA flutters	Ablation at LA lateral wall close to MA Multiple lines in LA to TCL prolongation but not termination; cardioverted to sinus rhythm
3 macro-re-entry around PVs	PVI in 1 patient, and LA roof ablation line in 2 patients
11 patients with both RA and LA flutters	
8 CTI flutters	
2 CTI + LA roof flutter	CTI ablation + left AFL terminated with LA roof line
1 CTI + MA flutter	CTI ablation + left AFL terminated with line from MA to RIPV
1 CTI + LA anterior septum AFL	CTI ablation + left AFL terminated with anterior septal line
1 CTI + RA incisional flutter and left-side flutter	CTI ablation + line from RA scar to SVC to PVI to AFL spontaneously converted to a slow AT; terminated during ablation of the carina region
3 CTI + multiple re-entrant circuits in both RA and LA	CTI ablation plus multiple empiric flutter lines did not terminate; cardioverted to sinus rhythm
3 without CTI flutter had multiple re-entrant circuits	Multiple flutter lines did not terminate; cardioverted to sinus rhythm

CTI = cavotricuspid isthmus; LA = left atrium; MA = mitral annulus; PV = pulmonary vein; PVI = pulmonary vein isolation; RA = right atrium; SVC = superior vena cava; TCL = tachycardia cycle length; other abbreviations as in Table 1.

29 patients (35.8%), coronary sinus in 20 patients (24.7%), MA in 13 patients (16.0%), and RA/crista in 26 patients (32.1%), in addition to flutter ablation lines in patients with concomitant AFLs (Table 2).

To note that AFL were more commonly encountered in patients with prior maze (67.9%, vs. 30.8% in patients without maze,  $p = 0.0013$ ). Moreover, 27 of 28 patients with prior maze (96.4%) were found to have conduction recovery around the lines encircling the PVs.

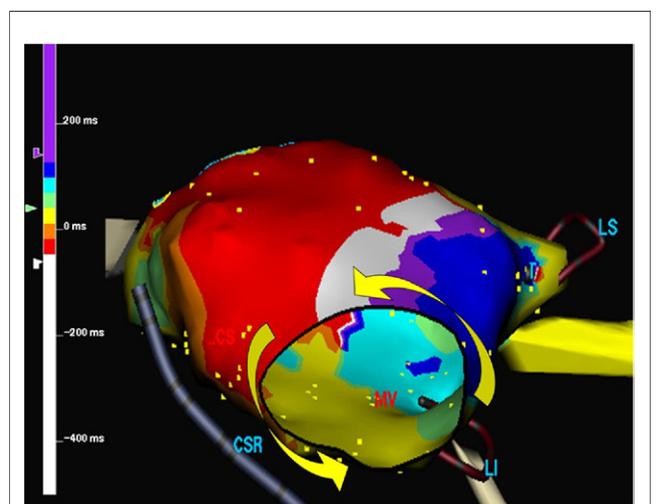
Among patients with MVR and history of concomitant flutters (35 patients, 43.2%), 16 (45.7%) presented in SR, 2 (5.7%) in AF, 1 (2.9%) in AT, and 16 (45.7%) in AFL. During catheter manipulation in the atria and by isoproterenol induction (in 2 patients), 9 more patients (25.7%) had AFL. Overall, 25 patients (71.4%) either presented in AFL or had AFL during the procedure, but electroanatomic mapping of AFLs was performed in 22 of them. In the remaining 3, flutters occurred during ablation but self-terminated in 2 and during PVI in 1 of them. No further mapping of the flutters was performed, and all 3 had empiric CTI ablation.

Of 22 patients who underwent flutter mapping, 6 had RA flutters (3 CTI flutters terminated with CTI ablation, 3 incisional flutters), 5 had LA flutters (all with prior maze), and 11 had both RA and LA flutters (7 with prior maze).

Of 5 patients with LA flutters, 2 had MA flutters (terminated with ablation in the left lateral atrial wall close to the MA in 1 of them, by cardioversion after failure of multiple flutter lines “MA to left inferior and right superior PVs, lines in roof, septum and posterior wall” to terminate). The remaining 3 patients with LA flutters had macro re-entry around the PVs (terminated with PVI in 1, roof

line in 1, and cardioversion after failure of multiple lines to terminate the flutter in 1).

Of 11 patients with both RA and LA flutters, 8 had a CTI dependent flutter successfully ablated in all of them. Two of them had a LA roof flutter (terminated with LA roof line), 1 had a MA flutter (Fig. 1) terminated with a line from MA to right inferior PV, 1 had an anterior septum flutter (terminated with anterior septal line), 1 had an RA incisional flutter and a LA flutter (after CTI ablation, an RA incisional flutter was



**Figure 1** Map of Counter-Clockwise Perimitral Flutter

Inferior anterior view of NAVX (St. Jude Medical, Minneapolis, Minnesota) map of a counter-clockwise perimitral flutter. CSR = catheter in coronary sinus; LI = left inferior pulmonary vein; LS = left superior pulmonary vein; MV = mitral valve.

identified but did not terminate with a line from the SVC to the scar; during PVI, the flutter spontaneously converted to a slow AT that terminated during ablation of the carina region of the left PVs). The remaining 3 patients had multiple re-entrant circuits in both RA and LA (multiple empiric lines failed to terminate, and both patients had PVI and then cardioverted to SR). Of 11 patients with both RA and LA flutters, 3 did not have CTI flutters. All had multiple re-entrant circuits with failure of flutter lines to restore SR. All were cardioverted after successful PVI.

Overall, AFLs were terminated by ablation in 15 of 22 patients in whom electroanatomic mapping was performed (68.2%).

**Clinical outcomes.** All but 3 patients with MVR (3.7%) and 7 patients without MVR (4.3%) completed the study follow-up. All 10 patients with incomplete follow-up had recurrence requiring repeat ablations in 2008 and 2009. All had at least 12 months of follow-ups after their last ablation, with recurrence of AF in 1 patient with MVR and 2 patients without MVR. These patients were accounted for in the overall analysis of recurrence and success rates.

Patients with MVR had more recurrences than controls (49.4% vs. 27.8%,  $p = 0.0006$ ). The recurrent arrhythmia was more likely to be AFL (54.8% vs. 40%) or AT (2.4% vs. 0%) and less likely to be AF (59.6% vs. 93.3%) in patients with MVR ( $p = 0.04$ ). The clinical characteristics and echocardiographic and ablation data according to arrhythmia recurrence in patients with MVR are summarized in Table 3. Patients with arrhythmia recurrence had older prostheses in place (time since MVR 7 [3 to 12] years vs. 4 [2 to 8] years,  $p = 0.03$ ) and were more likely to have had AF for longer duration (7 [4 to 10] years vs. 5 [2 to 8] years,  $p = 0.04$ ). In univariate Cox proportional hazards analyses, factors found to have a significant association with arrhythmia recurrences were time since MVR (hazard ratio for +1 year change: 1.04, 95% confidence interval: 1.01 to 1.12,  $p = 0.04$ ) and longer duration of AF before ablation (hazard ratio for +1 year change: 1.03, 95% confidence interval: 1.01 to 1.09,  $p = 0.05$ ). There was a significant decrease in LA size in patients with MVR at 3 months after ablation (mean difference  $-3.6 \text{ cm}^2$ , standard error 0.7,  $p < 0.0001$ ), but this change in atrial size did not predict ablation outcomes (hazard ratio for  $-1 \text{ cm}^2$  change: 0.58, 95% confidence interval: 0.12 to 2.71,  $p = 0.49$ ).

Among patients with a history of AFL, those who underwent mapping of their flutters with subsequent ablation had lower recurrence rates compared with patients who did not have flutter mapping and ablation (16.7% vs. 60.9%,  $p = 0.009$ ). Of 7 patients with failure of ablation to terminate the flutters and subsequent cardioversion to SR, all 3 patients in whom ablation resulted in prolongation of the tachycardia cycle length remained arrhythmia free whereas the remaining 4 patients had recurrence.

There was a trend toward better outcomes in patients having prior maze compared with patients not having prior maze (recurrence rate 39.3% vs. 55.8%,  $p = 0.16$ ). The

**Table 3** Clinical Characteristics, Echocardiographic Data, and Ablation Data According to Arrhythmia Recurrence in Patients With MVR

Parameter	No Recurrence	Recurrence	p Value
n (%)	41 (50.6)	40 (49.4)	
Age, yrs	55.8 ± 10.6	56.5 ± 11.8	0.78
Female	46.3	65	0.09
Hypertension	56.1	47.5	0.44
Diabetes mellitus	9.8	5	0.41
Coronary disease	12.2	17.5	0.11
Time since MVR, yrs	4 (2–8)	7 (3–12)	0.03
Prior maze	42.5	25	0.14
Indication for MVR			0.5
MR	55	50	
MS	2.5	7.5	
MR/MS	12.5	10	
Rheumatic MS	25	25	
Congenital	0	5	
Unknown	5	2.5	
Nonparoxysmal AF	26.8	32.5	0.58
Concomitant AFL	46.3	40	0.56
Concomitant AT	4.9	5	0.98
AF duration, yrs	5 (2–8)	7 (4–10)	0.04
AF before MVR	53.7	47.5	0.58
4 PVs isolated	100	100	1.0
Left atrial triggers	48.8	40	0.43
Right atrial triggers	26.8	37.5	0.3
SVC ablation	58.5	70	0.28
LVEF, %	49.3 ± 11.3	49.2 ± 10.1	0.96
LAS, cm <sup>2</sup>	29.8 ± 8.4	30.7 ± 7.7	0.64

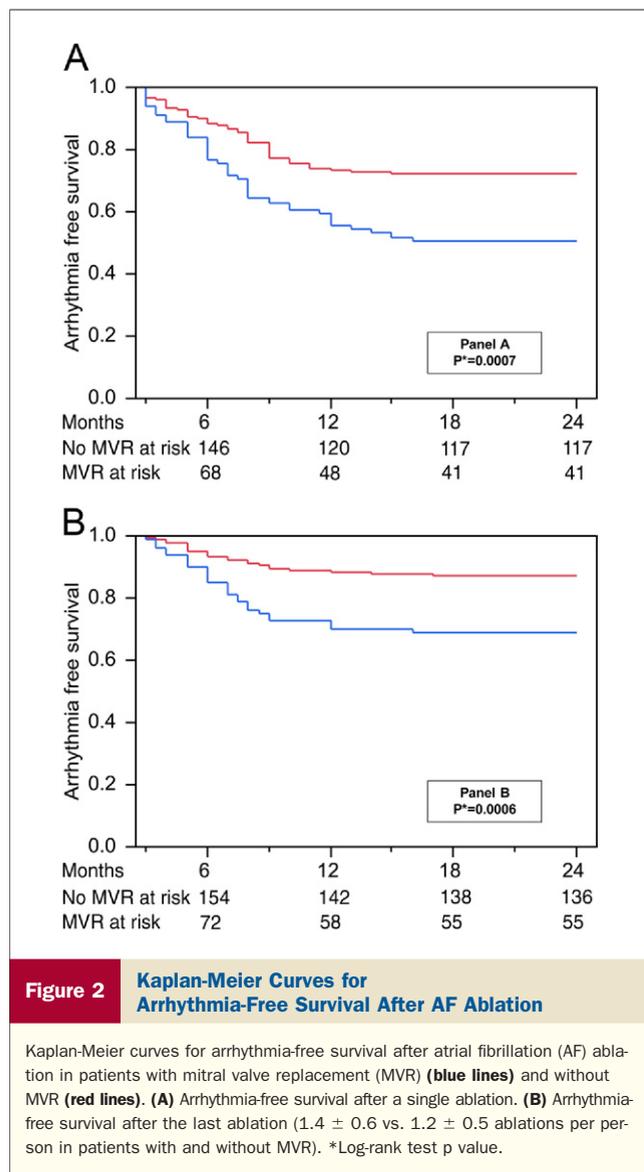
Values are n (%), mean ± SD, %, or median (range).

MR = mitral regurgitation; MS = mitral stenosis; MVR = mitral valve regurgitation; other abbreviations as in Tables 1 and 2.

recurrent arrhythmia were more likely to be AFL or AT in patients with prior maze (AFL 63.7% vs. 51.6%; AT 9.1% vs. 0%;  $p = 0.04$ ).

**Repeat ablations and outcomes at last follow-up.** Of patients with arrhythmia recurrence, 29 patients with MVR (72.5%, 24 with 2 ablations, 5 with 3 ablations) and 33 patients without MVR (73.3%, 26 with 2 ablations, 7 with 3 ablations) had repeat ablations. All repeat ablations were performed in the presenting rhythm. Overall, more ablations per person were required in MVR patients ( $1.4 \pm 0.6$  vs.  $1.2 \pm 0.5$ ,  $p = 0.003$ ) but failed to achieve similar success rates at last follow-up (69.1% vs. 87.0%,  $p = 0.0006$ ). The arrhythmia-free survival in patients with and without MVR after single or repeat ablations is outlined in Figure 2. At last follow-up, of 81 patients with MVR, 56 (69.1%) were arrhythmia free while not taking antiarrhythmic drugs, 11 (13.6%) had their arrhythmia controlled with antiarrhythmic drugs that had previously failed, and 14 (17.3%) had drug-resistant AF and were managed with rate control.

**Procedure-related complications.** Three patients in the MVR group had procedure-related complications (3.7%; 1 hematoma requiring intervention, 1 groin bleeding requiring transfusion, 1 femoral pseudoaneurysm requiring surgical repair). No patients with MVR had stroke, cardiac tamponade,



prosthetic valve damage, or entrapment of the ablation catheter within the prosthesis. The incidence of procedure related complications were similar in both groups (Table 4).

## Discussion

This is the largest study to date to evaluate the feasibility, safety, and outcomes of AF ablation in patients with MVR. We have demonstrated that the procedure is feasible and is not associated with increased risk of complications, particularly no catheter entrapment occurred. An average of 1.5 ablations per patient was required to restore SR off antiarrhythmic drugs in 70% of patients with MVR referred for ablation. Also, ablative therapy allowed arrhythmia control with medications that have previously failed in an additional 13% of patients. Only 17% continued to have drug-resistant AF. In a group of patients who have failed medical management, this may still be considered a clinical success. However, the overall success rates of radiofrequency abla-

tion were lower in patients with MVR compared to controls. Recurrent arrhythmias were more likely to be AFL or AT and less likely to be AF in patients with MVR, and occurred more frequently in patients with older prostheses in place and in those with longer duration of AF. A substantial proportion of patients with MVR had concomitant AFL at baseline. Electroanatomic mapping with creation of flutter lines, in addition to CTI ablation, significantly improved the outcomes in patients with any history of AFL during their AF course. The majority of patients having prior maze procedures were found to have conduction recovery in at least 1 of the PVs and were more likely to have concomitant flutters at baseline and to have more recurrences as AFL or AT after ablation compared to patients without a prior maze procedure.

Ablative therapy is feasible in MVR patients but requires longer fluoroscopy times (5) to prevent valvular damage or entrapment of the ablation catheter by frequently checking the position of the catheter during ablation. Furthermore, longer fluoroscopy times during mapping allow detailed reconstruction of LA anatomy and help to accurately localize the MA. These measures ultimately result in reduction of complications risk, but careful manipulation of ablation catheters in the LA remains essential to prevent them.

Previously reported complications in patients with MVR undergoing ablation in the LA are prosthesis disk embolization as a result of trauma from ablation catheters (10), transient ischemic attacks (5), and catheter entrapment within the prosthetic valve (4). None of these complications occurred in our study. Interestingly, no patients had thromboembolic complications.

We believe that performing ablation with ICE guidance and under therapeutic INRs were 2 critical factors that contributed to the safety of AF ablation in our patients. Intracardiac echocardiography allowed direct visualization of catheters in the LA and determined in real-time the position of catheters relative to the prosthetic valves, which helped along with fluoroscopy to prevent entrapment or damage to MV prostheses. The thromboembolic risk is a major concern in patients with prosthetic valves and is further increased with catheter-based ablation in the LA. It

**Table 4** **Procedure-Related Complications in Patients With and Without Mechanical MVR**

Parameter	No MVR (n = 162)	MVR (n = 81)	p Value
Minor complications, %			0.20
Pericardial effusion, no intervention	1.2	0	
Major complications, %			0.52
Bleeding requiring transfusion	0.6	1.2	
Hematoma requiring intervention	1.2	1.2	
Femoral pseudoaneurysm	0	1.2	
Tamponade	0.6	0	
Stroke	0	0	
Native or prosthetic valve damage	0	0	

MVR = mitral valve replacement.

is unknown whether appropriate bridging with heparin after warfarin discontinuation at time of ablation is a safe enough strategy to prevent these complications. In our study, warfarin was continued at therapeutic levels at time of ablation and may have protected against thromboembolic complications, but it is hard to draw any conclusions regarding this issue given the sample size. Further research will be needed to address these issues.

Lang et al. (5) reported their experience with catheter ablation in patients with MVR and enlarged atria. In their study, more procedure-related complications and more frequent post-ablation AT occurred among patients with MVR. Overall, success rates were similar in patients with or without MVR in their report but lower than success rates of surgical therapy for AF at time of MVR (10–12). Many findings in our study explain the lower success rates in patients with MVR. The observations that these patients have larger atria and lower left ventricular ejection fractions at baseline suggest that a more advanced structural heart disease underlies higher recurrence rates. Furthermore, surgical scarring and fibrosis, in addition to probable atrial myopathy from long-standing valvular disease potentially contribute to arrhythmia recurrences. An arrhythmogenic substrate explains the higher recurrence rates, suggesting that the role of PV triggers in initiating and maintaining AF in these patients is less important than it is in the general population of patients referred for AF ablation. Our ability to restore and maintain SR off antiarrhythmic drugs in a substantial proportion of patients with MVR undergoing PVI suggest that the PVs may still serve as AF triggers in these patients, but the findings suggest that modification of the atrial substrate is essential to improve ablation outcomes (4). In particular, the observations of more concomitant AFL at baseline, particularly in patients having prior maze surgery, and the findings of more recurrences as AFL and AT after AF ablation in patients with MVR underscores the importance of the atrial substrate of the arrhythmia. In fact, surgical scarring, incomplete ablation lines (13), and fibrosis around the prosthetic valve facilitate macro re-entrant tachycardia.

For patients who present in AFL or have AFL during ablation, electroanatomic mapping and ablation of these flutters is of major importance to prevent recurrences. For patients with a history of AFL but do not have the arrhythmia during ablation, induction of their flutters may be warranted to allow electroanatomic mapping and the application of flutter lines where appropriate. Furthermore, the creation of empiric flutter lines, especially in patients with obvious surgical scarring, may help to improve the ablation outcomes. It may be also reasonable to perform CTI ablation in all MVR patients with any history of AFL during their AF disease course, given the high prevalence of CTI flutters in these patients and the ease with which CTI flutters can be eliminated. All of these factors should be considered during the ablation procedure in patients with

any previously documented AFLs, given the high recurrence rates and ultimately the need for repeat ablations, but further research will be needed to address this issue.

## Conclusions

We have demonstrated that radiofrequency ablation is feasible and safe but technically challenging in patients with mitral valve prostheses. It was possible to restore SR off antiarrhythmic drugs in a substantial proportion of patients with MVR referred for AF ablation, but it seems that the ablation procedure needs to be further refined. In particular, ablation strategies with a focus on the atrial substrate, extra-PV triggers, and concomitant flutters may help to improve ablation outcomes.

**Reprint requests and correspondence:** Dr. Walid I. Saliba, Cardiac Pacing and Electrophysiology, Department of Cardiovascular Medicine/J2-2, 9500 Euclid Avenue, Cleveland, Ohio 44195. E-mail: salibaw@ccf.org.

## REFERENCES

1. Psaty BM, Manolio TA, Kuller LH, et al. Incidence of and risk factors for atrial fibrillation in older adults. *Circulation* 1997;96:2455–61.
2. Grigioni F, Avierinos JF, Ling LH, et al. Atrial fibrillation complicating the course of degenerative mitral regurgitation: determinants and long-term outcome. *J Am Coll Cardiol* 2002;40:84–92.
3. Calkins H, Brugada J, Packer DL, et al. HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for personnel, policy, procedures and follow-up. *Heart Rhythm* 2007;4:816–61.
4. Wang X, Liu X, Shi H, et al. Heart rhythm disorders and pacemakers: pulmonary vein isolation combined with substrate modification for persistent atrial fibrillation treatment in patients with valvular heart diseases. *Heart* 2009;95:1773–83.
5. Lang CC, Santinelli V, Augello G, et al. Transcatheter radiofrequency ablation of atrial fibrillation in patients with mitral valve prostheses and enlarged atria: safety, feasibility, and efficacy. *J Am Coll Cardiol* 2005;45:868–72.
6. Hussein AA, Martin DO, Saliba W, et al. Radiofrequency ablation of atrial fibrillation under therapeutic international normalized ratio: a safe and efficacious periprocedural anticoagulation strategy. *Heart Rhythm* 2009;6:1425–9.
7. Kanj MH, Wazni OM, Natale A. How to do circular mapping catheter-guided pulmonary vein antrum isolation: the Cleveland Clinic approach. *Heart Rhythm* 2006;3:866–9.
8. Jais P, Shah DC, Haissaguerre M, et al. Mapping and ablation of left atrial flutters. *Circulation* 2000;101:2928–34.
9. Matsuo S, Wright M, Knecht S, et al. Peri-mitral atrial flutter in patients with atrial fibrillation ablation. *Heart Rhythm* 2010;7:2–8.
10. Bridgewater BJ, Levy RD, Hooper TL. Mitral valve prosthesis disk embolization during transeptal atrioventricular junction ablation. *J Interv Cardiol* 1994;7:535–7.
11. Williams MR, Stewart JR, Bolling SF, et al. Surgical treatment of atrial fibrillation using radiofrequency energy. *Ann Thorac Surg* 2001;71:1939–43, discussion 1943–4.
12. Sie HT, Beukema WP, Elvan A, Ramdat Misier AR. Long-term results of irrigated radiofrequency modified maze procedure in 200 patients with concomitant cardiac surgery: six years experience. *Ann Thorac Surg* 2004;77:512–6, discussion 516–7.
13. Ernst S, Ouyang F, L ber F, Antz M, Kuck KH. Catheter-induced linear lesions in the left atrium in patients with atrial fibrillation: an electroanatomic study. *J Am Coll Cardiol* 2003;42:1271–82.

**Key Words:** atrial fibrillation ■ mitral valve prostheses ■ radiofrequency ablation.