

# Pulmonary vein antrum isolation for treatment of atrial fibrillation in patients with valvular heart disease or prior open heart surgery

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## KEYWORDS

Atrial fibrillation;  
Pulmonary vein  
isolation;  
Valvular heart disease;  
Open-heart surgery

**OBJECTIVES** The goal of this study was to assess the safety and efficacy of pulmonary vein antrum isolation in patients with moderate valvular heart disease or open-heart surgery and atrial fibrillation (AF).

**BACKGROUND** Valvular heart disease and open-heart surgery are commonly associated with AF and increase the risk of adverse events in AF patients.

**METHODS** A total of 391 consecutive patients who had pulmonary vein antrum isolation performed between December 2000 and December 2002 were screened. A total of 142 of these patients had clinically significant valvular disease or prior cardiac surgery. End points included AF recurrence and pulmonary vein antrum isolation complication rates.

**RESULTS** Patients with valvular heart disease or prior open-heart surgery were older, had larger left atria and a more advanced New York Heart Association class. They did not differ significantly with respect to gender, but had a longer history of AF. Procedure times were similar between patients with and without valvular heart disease or prior open-heart surgery. After  $18 \pm 7$  months in the lone AF patients,  $11 \pm 5$  months in patients with valvular heart disease, and  $10 \pm 5$  months in patients with prior open heart surgery, there was a trend toward lower recurrence of AF in patients with lone AF who enjoyed a 98% overall cure rate after up to 2 pulmonary vein antrum isolations versus 93% among patients with valvular heart disease ( $P = .04$ ) and prior open heart surgery ( $P = .07$ ). Complication rates were comparable between groups.

**CONCLUSIONS** Pulmonary vein antrum isolation is safe and effective in patients with moderate valvular heart disease and the patients who developed AF after open-heart surgery. These results have implications for our understanding of the pathophysiology of AF in patients with moderate valvular heart disease or past cardiac surgery and should be considered when discussing treatment options in these patients.

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Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia.<sup>1</sup> It causes considerable disability, im-

pairs quality of life, and is difficult to treat.<sup>2–4</sup> The discovery that atrial ectopics originating in the pulmonary veins (PV) and other atrial sites could initiate AF has led to the era of catheter-based therapy for AF with sequential advent of linear ablation, focal PV ablation and, more recently, isolation at the level of the PV antrum.<sup>5–19</sup> This therapy has shown 6-month cure rates up to 90% in selected cases. However, patients undergoing PV antrum isolation may

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(Received December 10, 2003; accepted February 4, 2004.)

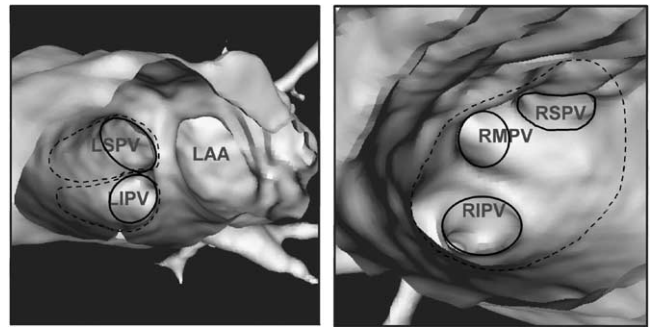
suffer from cardiac perforation and tamponade or have a cerebrovascular event (CVA) during the procedure. In addition, despite ablation at the antrum of the PVs, patients are still exposed to the potential risk of developing significant PV stenosis. To date, most patients undergoing radiofrequency ablation for AF have been younger with few comorbidities, whose quality of life has been drastically diminished secondary to symptomatic arrhythmia refractory to medical therapy. Paradoxically, the so-called "lone" AF accounts for only 3% of patients with AF.<sup>20</sup> While AF is far more common in patients with valvular heart disease, left ventricular (LV) dysfunction, history of cardiac surgery, and in the elderly,<sup>2</sup> these conditions have been considered a relative contraindication for PV antrum isolation at many centers. The combination of AF and structural heart disease is thought to be associated with a different substrate and possibly with a higher risk of procedural complications. Outcomes of PV antrum isolation in patients with low LV ejection fraction and the elderly have been found to match those in younger patients and those with normal LV ejection fraction. Results of AF ablation in patients with valvular heart disease and prior open heart surgery have not been well described. This study was performed to assess safety and efficacy of AF ablation procedures in these patients compared to those with lone AF.

## Methods

Baseline clinical and demographic variables as well as procedural details and outcomes of follow-up have been prospectively collected for 391 consecutive patients undergoing PV antrum isolation for AF at the Cleveland Clinic Foundation Center for Atrial Fibrillation between August 2000 and December 2002.

### PV antrum isolation approach

Circular mapping in combination with PV angiography was used in the first 56 patients as previously described.<sup>18</sup> In the remaining 335 patients, PV antrum isolation was performed with the assistance of intracardiac echocardiography using a 10Fr 64-element phased array ultrasound imaging catheter (AcuNav, Accuson, Mountain View, California).<sup>1</sup> Intravenous heparin bolus and infusion adjusted to achieve activated clotting time of 350 to 400 seconds (F. Hoffman-LaRoche Ltd., Basel, Switzerland) was administered while the catheters were in the left atrium. Ablation lesions were created in the PV antrum proximal to the tube-like portion of the PV (Figure 1). In the first 160 patients, a 35°C target temperature was chosen for radiofrequency energy delivery through the cooled-tip catheter (EP Technologies, Sunnyvale, California). At each site, energy was delivered for 45 seconds. Monitoring for microbubble formation with intracardiac echocardiogram and lowering delivered energy appropriately to avoid the microbubble generation was prac-



**Figure 1** Three-dimensional computed tomography reconstruction of the pulmonary vein ostia. **Solid lines** represent ostial ablation guided by fluoroscopy and angiography. **Dashed lines** represent more proximal ablation lesions delivered at the antrum of the pulmonary veins using intracardiac-echocardiogram-guided circular mapping. LAA = left atrial appendage; LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary vein; RIPV = right inferior pulmonary vein; RMPV = right middle pulmonary vein; RSPV = right superior pulmonary vein.

ticed in the remaining 231 patients.<sup>21–23</sup> The goal of PV antrum isolation was abolition of all PV potentials as measured by the circular mapping catheter. No linear lines from the PV to the mitral annulus were performed in any of our patients. Isolation of the superior vena cava (SVC) was performed in all the patients included in this series.<sup>13,24–26</sup> Pacing from the tip of the ablation catheter before radiofrequency delivery to detect phrenic nerve stimulation and avoid right diaphragmatic palsy was used during isolation of the SVC. Each patient received 325 mg of aspirin immediately after the procedure and resumed warfarin the night of the ablation and continued for at least 3 months if there were no AF recurrences. Patients with permanent or persistent AF were treated with half dose of subcutaneous enoxaparin (0.5 mg/kg twice daily) for 3 days after ablation.

### Follow-up and end points

After the procedure, recurrence of AF was assessed by an external transtelephonic loop recorder 1 and 3 months after ablation. Monthly telephone interviews, 24-hour Holter monitor at 3, 6, and 12 months, and 12-lead electrocardiogram (ECG) at 2, 3, 6, and 12 months were obtained in all patients. Additional monitoring with a loop recorder or a Holter monitor was considered in symptomatic patients. Interrogation of implanted devices is also used to confirm recurrence of arrhythmias. Any episode of AF, including asymptomatic AF, lasting more than 10 seconds, identified on a Holter monitor, loop recorder, or ECG was considered a recurrence. Left ventricular systolic function (ejection fraction) was obtained using transthoracic echocardiography in all patients pre-PV antrum isolation and reassessed 3 months after PV antrum isolation. Spiral computed tomography was performed 10 to 12 weeks after ablation in all patients to assess for PV stenosis. Severe PV stenosis was defined as any vein narrowing greater or equal to 70%. Use

**Table 1** Patient demographics

	Lone AF	Valve disease	CVSx
Patients, n (%)	194	102	40
Women	40 (21)	22 (22)	8 (20)
Age (y)	54 ± 12	58 ± 10*	59 ± 10 <sup>‡</sup>
LA size (cm)	4.4 ± 2.4	4.7 ± 2.0	4.8 ± 0.4 <sup>‡</sup>
Mean EF (%)	55 ± 4	52 ± 10	51 ± 11
NYHA, n (%)			
I	187 (96)	82 (80) <sup>§</sup>	28 (70) <sup>§</sup>
II	6 (3)	4 (4)	2 (5)
III	1 (0.5)	15 (15)	8 (20)
IV	0	1 (1)	2 (5)
Duration of AF (years)	6 ± 4	8 ± 8 <sup>†</sup>	6 ± 4
Type of AF, n (%)			
Paroxysmal	111 (58)	37 (37) <sup>  </sup>	12 (30) <sup>¶</sup>
Persistent	18 (9)	12 (12)	7 (18)
Permanent	64 (33)	52 (51)	22 (55)
Number of anti-arrhythmic drugs tried before PVI	3.2 ± 1.1	3.0 ± 1.1	3.0 ± 1.4

\* p < 0.0001 compared with others; †p = 0.04 compared with others; ‡p = 0.006 compared with others; §p < 0.006 for the difference in NYHA functional class distribution compared with others; ||p = 0.0002 for the difference in AF type distribution compared with others; ¶p = 0.001 for the difference in AF type distribution compared with others.  
 AF = atrial fibrillation; EF = ejection fraction; LA = left atrium; NYHA = New York Heart Association.

**Table 3** Complications and recurrences, n (%)

	Lone AF n = 194	Valve disease n = 102	CVSx n = 40
CVA	0	1 (1)	0
TIA	1 (0.5)	0	0
Tamponade	4 (2)	0	0
Access site			
hematoma	1 (0.5)	1 (1)	0
Severe PV stenosis	2 (1)	1 (1)	0
Combined adverse outcomes	8 (4)	3 (3)	0
Recurrence	31 (16)	17 (17)	6 (15)
Controlled on antiarrhythmic drug	4 (2)	5 (5)	3 (8)
2nd PVI	27 (14)	12 (12)	3 (8)
On antiarrhythmic drug post 2nd PVI	0	2 (2)	0
Follow-up, mo	18 ± 7	11 ± 5	10 ± 5

AF = atrial fibrillation; CVA = cerebrovascular accident; PV = pulmonary vein; TIA = transient ischemic attack.

of these data for research purposes was approved by the institutional ethics review board.

## Results

### Baseline patient characteristics

Patient demographics and clinical characteristics are shown in Table 1. Of 391 patients, 197 (50%) patients had structural heart disease, including 94 (24%) patients with LV dysfunction, defined as ejection fraction below 40%, 102 (26%) with known clinically significant valvular dis-

ease defined as moderate stenosis or insufficiency of the mitral or aortic valve, and 40 (10%) patients with history of prior cardiac surgery, including 22 patients with history of aortocoronary bypass grafting, 4 patients with aortic valve replacement, 7 patients with mitral valve replacement, and 5 patients with history of other open-heart surgery. A total of 55 patients with LV dysfunction alone were excluded from this analysis. The remainder of LV dysfunction patients had either concomitant moderate valve disease or history of prior cardiac surgery and were analyzed in those groups.

### PV antrum isolation in patients with valvular heart disease

Significant valvular dysfunction was present in approximately half of the structural heart disease patients. Patients with valve disease were older at the time of PV antrum isolation than those with lone AF and had a higher New York Heart Association functional class. They did not differ significantly with respect to gender. These patients had AF for a longer period of time with half of the patients in permanent AF before ablation. Nevertheless, the number of antiarrhythmic drugs attempted before PV antrum isolation was similar between groups.

Total procedure and fluoroscopy times were similar between patients with lone AF and those with significant valvular heart disease as shown in Table 2.

After a mean follow-up of 11 ± 5 months, patients with significant valvular dysfunction had a higher rate of AF recurrence. However, after a second procedure in this group, there was a 93% overall cure rate compared with 98% after a mean follow-up of 18 ± 7 months in patients with lone AF (P = .04) (Table 3).

**Table 2** Pulmonary vein isolation and follow-up results

	Lone AF	Valve disease	CVSx
Fluoroscopy time (min)	83 ± 26	85 ± 20	84 ± 26
Procedure time (h)	4 ± 1	4 ± 1	4 ± 1
Mean number of RF lesions/PV (min)	9.4 ± 3.4	9.7 ± 2.6	9.5 ± 2.0

p = not significant.  
 AF = atrial fibrillation; PV = pulmonary vein; RF = radiofrequency.

**Table 4** Complications and recurrences in PVI, "no-bubbles", n (%)

	Lone AF n = 127	Valve disease n = 11	CVSx n = 6
CVA	0	1 (9)	0
TIA	1 (1)	0	0
Tamponade	2 (2)	0	0
Access site hematoma	0	0	0
Severe PV stenosis	2 (2)	1 (9)	0
Combined adverse outcomes	3 (2)	2 (18)	0
Recurrence	24 (19)	2 (18)	0
Controlled on antiarrhythmic drug	3 (2)	0	0
2nd PVI	21 (17)	2 (18)	0
On antiarrhythmic drug post 2nd PVI	0	2 (18)	0
Follow-up, mo	22 ± 3	21 ± 3	21 ± 2

CVA = cardiovascular accident; PV = pulmonary vein; TIA = transient ischemic attack.

Of 10 patients with valvular dysfunction who had PV antrum isolation before using microbubbles to titrate energy delivery (Table 4), 1 had a stroke, and 1 developed severe PV stenosis. Among the 91 patients treated using microbubbles to titrate energy delivery (Table 5), 1 developed a clinically significant access site hematoma, but no other complications were seen.

### PV antrum isolation in patients with previous cardiac surgery

A total of 40 patients in our cohort had prior cardiac surgery. These were the oldest among the structural heart disease patients, with the average age of  $59 \pm 10$  years. Even though AF duration in this subgroup was similar to the lone AF patients, most of them had permanent AF. As a group, these patients had the worst New York Heart Association functional class distribution. Left atria were consistently larger among these patients.

Patients with history of previous cardiac surgery had similar procedural and fluoroscopy times as the others (Table 2). Six of the cardiac surgical patients recurred after PV antrum isolation (Table 5). The overall cure rate in patients with history of prior cardiac surgery after a mean follow-up of  $10 \pm 5$  months was 93% compared with 98% after a mean follow-up of  $18 \pm 7$  months in patients with lone AF ( $P = .07$ ). No complications were recorded in the subgroup of patients with history of prior cardiac surgery.

Complication rates in patients with valvular heart disease and prior open heart surgery compared favorably with those in patients with lone AF. One patient with lone AF had a transient ischemic attack, which took place before microbubble pattern was used to titrate energy delivery during ablation. Four patients in the lone AF group had a cardiac

perforation with tamponade during the procedure. One patient had a clinically significant access site hematoma, and 2 patients had severe PV stenoses. None of these took place after the microbubble pattern was used to titrate energy delivery during ablation.

### Discussion

Patients with structural heart disease in our series were older, had AF for a longer period of time with greater prevalence of chronic AF. There was a trend for larger left atria among these patients. This reached statistical significance for those with prior open-heart surgery. Patients with structural heart disease had worse New York Heart Association functional class and, likely, higher LV filling pressures. This may have led to hypertrophy of the atrial myocardium and enlargement of PV ostia making ablation more challenging.

Despite these challenges, PV antrum isolation appeared effective in patients with structural heart disease. Procedure and fluoroscopy times were similar between lone AF patients and those with valvular heart disease or history of prior open-heart surgery. Cure rates after 2 procedures were 98% in patients with lone AF and 93% in patients with structural heart disease. This difference did reach statistical significance for patients with history of valvular heart disease. In addition, many of the patients who were previously refractory to multiple antiarrhythmics and experienced recurrence after the first procedure were subsequently controlled on medication.

**Table 5** Complications and recurrences in PVI, bubbles, n (%)

	Lone AF n = 67	Valve disease n = 91	CVSx n = 34
CVA	0	0	0
TIA	0	0	0
Tamponade	2 (3)	0	0
Access site hematoma	1 (1.5)	1 (1)	0
Severe PV stenosis	0	0	0
Combined adverse outcomes	5 (7)	1 (1)	0
Recurrence	7 (10)	15 (16)	6 (18)
Controlled on antiarrhythmic drug	1 (1)	5 (5)	3 (9)
2nd PVI	6 (9)	10 (11)	3 (9)
On antiarrhythmic drug post 2nd PVI	0	0	0
Follow-up, months	10 ± 5	10 ± 4	8 ± 4

AF = atrial fibrillation; CVA = cerebrovascular accident; PV = pulmonary vein; PVI = pulmonary vein isolation; TIA = transient ischemic attack.

The success of PV antrum isolation was not without cost. One (1%) of the patients with valvular heart disease had a neurologic event, 1 (1%) developed an access site hematoma, and 1 (1%) had severe PV stenosis. The complication rates, however, were similar to those in patients with lone AF.

It is possible that the use of intracardiac echocardiogram to titrate energy delivery and monitor catheter placement at the PV ostia has helped to increase the success rate and to reduce the risk of complications. This may have been incrementally more important in patients with structural heart disease who may have a higher baseline risk of neurologic events and other periprocedural complications. There is emerging evidence from other centers that PV antrum isolation can achieve cure of AF in 62% to 86% of the patients.<sup>7,9,12,15</sup> Most of the patients in these studies did not have structural heart disease. In 2 series, however, structural heart disease did not appear to predict recurrence of AF after PV antrum isolation.<sup>27,28</sup> On the other hand, both studies were either underpowered or did not specify the type of structural heart disease.

All patients included in this study had ablation using a cooled-tip ablation catheter. Use of different catheter design may result in varied success rates of isolation procedures.<sup>18</sup> This could be even more relevant when isolation is performed at the “antrum” of the PVs. Further prospective studies could help determine the optimal catheter type for PV antrum isolation in patients with structural heart disease.

Atrial fibrillation affects 10% to 45% of patients undergoing open-heart surgery, depending on patient profile, type of surgery, and method of arrhythmia surveillance.<sup>29–31</sup> It is possible that patients with history of valve disease, heart surgery, and other structural heart disease have a different milieu for maintaining AF compared with patients with lone AF. Involvement of the PVs in postoperative AF has not been consistently shown. Multiple hypotheses have been suggested to explain occurrence of AF in the postoperative period, including increased adrenergic tone, inflammatory pericarditis, atrial incisions, atrial ischemia, increased frequency of premature atrial beats, alterations in atrial refractory periods, and increased dispersion of refractoriness.<sup>32–34</sup> Although they may play a role, it remains unknown whether these factors are causally related or merely associated with the development of AF. All of these factors could cause increased irritability and firing from the PVs, thus explaining their link to AF. Recently, bursts of atrial tachycardia degenerating into AF and originating from the PV in a patient with AF after myectomy for hypertrophic obstructive cardiomyopathy have been reported with successful abolition of AF after PV antrum isolation.<sup>35</sup> The data presented here seem to suggest that PV antrum isolation could be a viable therapeutic option for most patients with AF occurring after cardiac surgery.

Valvular heart diseases are also associated with a higher risk of AF.<sup>2,36–40</sup> It is possible that patients with valvular heart disease may have a higher degree of atrial disarray, irreversible fibrosis, with PV ectopics playing a lesser role

in the initiation and maintenance of this arrhythmia.<sup>39,40</sup> However, the high success rate seen in our series after PV “antrum” isolation speaks to the fact that etiology of AF is similar in most patients. In our experience, the majority of patients returning for a repeat procedure showed recovery of conduction in 1 or more of the ablated PVs. Considering the incremental benefit of the second PV antrum isolation in these patients, it appears that the inability to obtain a permanent effect at the sites targeted with ablation is the most important reason for recurrences.

## Limitations

This study was a retrospective case series of patients who underwent PV antrum isolation. A double blinded, randomized placebo-controlled trial would strengthen the validity of the findings. Follow-up among patients with lone AF was significantly longer than among patients with structural heart disease because fewer of these patients were treated with PV antrum isolation early in the experience with this procedure. It is possible that, at a similar follow-up, they would accrue a higher rate of AF recurrence; however, 93% cure among patients, half of whom had chronic AF despite multiple trials of antiarrhythmic medications, warrants offering PV antrum isolation to patients with AF regardless of the presence of valvular heart disease or previous heart surgery. It is important to recognize that none of our patients had severe valvular regurgitation or stenosis at the time of the ablation. It is conceivable that patients with more advanced valvular disease could develop irreversible atrial myopathy with a lesser response to PV “antrum” isolation. However, in patients with mechanical valves undergoing our procedure, cure rates paralleled those in the overall population of patients with valve disease.

## Conclusions

Most centers still consider valvular heart disease and history of prior cardiac surgery to be a relative contraindication for this procedure. With accumulating experience, our center has become less stringent in denying PV antrum isolation to these patients. This change in attitude toward PV antrum isolation stems from the observation of similar success and complication rates in patients with and without structural heart disease. These findings should be taken into consideration when selecting patients for this procedure. [Table 3.](#)

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