



Original Article

Intermediate term outcome after electrogram guided segmental ostial pulmonary vein isolation using an 8 mm tip catheter for paroxysmal atrial fibrillation



Prashant Pawar, Ramalingam Vadivelu, Neeta Bachani, Kathiresan Jeyashree, Rajeev Sharma, Chetan Rath, Jaipal Jadwani, Debabrata Bera, Yash Lokhandwala*

Department of Cardiology, Holy Family Hospital and Research Institute, Bandra West, Mumbai, India

ARTICLE INFO

Article history:

Received 14 May 2019

Accepted 25 November 2019

Available online 6 December 2019

Keywords:

Atrial fibrillation

Radiofrequency ablation

Pulmonary vein isolation

ABSTRACT

Introduction: Pulmonary vein isolation (PVI) is the most widely used procedure for ablation in patients with paroxysmal atrial fibrillation (AF). Notwithstanding recent advancements in this field, including sophisticated three-dimensional (3D) based imaging and advanced ablation catheters with contact force technology, many patients and healthcare systems in developing countries will not afford such an expensive therapeutic procedure. There are no data from India analyzing the efficacy of PVI for PAF using conventional mapping and ablation. In this article, we have summarized the intermediate term outcome following PVI in patients with PAF using electrogram-based mapping and a 8 mm tip ablation catheter. **Method:** A total of 42 consecutive patients who underwent PVI for symptomatic PAF not controlled with at least one antiarrhythmic drug were studied in a tertiary care institute from March 2011 to June 2018. Patients with rheumatic AF were excluded. The pulmonary vein (PV) anatomy was assessed by pulmonary angiography during the ablation procedure. Using conventional electrophysiologic mapping, a variable curve Lasso catheter placed in the PVs was used to guide the earliest site of breakthrough. The segmental ostial PVI was performed using a 8 mm tip radiofrequency (RF) ablation catheter. Elimination of all PV ostial potentials and complete entrance block into the PV were considered indicative of complete electrical isolation. Follow-up visits were scheduled at one, three, and six months after the procedure, and every six months thereafter. History, symptom review, clinical examination, and 12-lead ECG were performed at each follow-up.

Results: At pre-discharge, 34 patients (81%) were in sinus rhythm, while eight patients (19%) continued to have atrial fibrillation. The age of the study population was 51.5 ± 11.7 yrs. The mean follow-up duration was 44 ± 21 months (range 6–84 months). The number of PVs isolated included one (five patients, 11.9%), two (20 patients, 47.6%), three (12 patients, 28.6%), and four (five patients, 11.9%). In 42 patients, a total of 101 PVs were isolated. The right superior PV (RSPV) was isolated in 37 patients, the left superior PV (LSPV) was isolated in 39 patients, the left inferior PV (LIPV) was isolated in 14 patients, and the right inferior PV (RIPV) was isolated in six patients. The procedure duration was 125 ± 29 min and the fluoroscopy time was 47 ± 13 min. The number of patients who remained in sinus rhythm at 1, 6, 12, and 24 months were 34 (81%), 32 (76%), 30 (71%), and 26 (62%), respectively. Two patients of these underwent repeat PVI, which was successful, and they had freedom from AF episodes. Complications were rare. One patient had a minor pericardial effusion, and one patient had transient sinus pauses, which were conservatively managed.

Conclusion: Conventional RF ablation using PV potential-based mapping and ablation with 8 mm tip catheters is safe for patients with PAF. The intermediate term outcome is satisfactory and cost-effective in our setting with limited resources.

© 2019 Cardiological Society of India. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

* Corresponding author. Holy Family Hospital and Research Institute, Bandra West, Mumbai, 400050, India.

E-mail address: yashlokhandwala@hotmail.com (Y. Lokhandwala).

1. Introduction

Atrial fibrillation (AF) is the most common form of sustained arrhythmia in the world, and it is a major cause of stroke, apart from being symptomatic and sometimes leading to tachycardia-induced cardiomyopathy. When compared with the western population, Indians develop AF a decade earlier,^{1,2} and hence, the impact of the disease is very significant.

Haissaguerre et al demonstrated the importance of pulmonary veins (PVs) for the initiation of paroxysmal AF, which started the era of ablation treatment for this arrhythmia.³ Catheter ablation aims to electrically isolate the foci within the PV, from the atria. It has emerged as a treatment modality for symptomatic patients who have not responded to medication.^{4,5} Reports of AF ablation demonstrated that PVI achieved short-term arrhythmic resolution in 80–85% of paroxysmal AF patients^{6,7} although some patients required repeat procedures.

Other strategies for PAF include PV antrum isolation, balloon-based radiofrequency (RF)/cryoablation and wide circumferential ablation (WACA) around the PVs. Many of these techniques involve expensive equipment and three-dimensional mapping. The resultant cost is not affordable for most patients in India. Hence, we analyzed our experience using conventional electrophysiology method based on PV mapping using a Lasso catheter. An 8 mm tip catheter was used to ensure better contact, minimize the number of energies necessary, and shorten the procedure time.

2. Method

2.1. Patient selection

A total of 42 consecutive patients admitted with symptomatic PAF for catheter ablation in a tertiary care teaching hospital from March 2011 till June 2018 were prospectively enrolled for this study. All patients gave written and informed consent. All procedures were performed by a single operator.

Inclusion criteria: All patients 18 years or older who had symptomatic non-rheumatic PAF not controlled with at least one antiarrhythmic drug were included for the study.

Exclusion criteria: Patients with rheumatic AF were excluded. Other exclusion criteria were persistent AF (symptoms lasting for more than seven days but less than a year), long-standing persistent AF (symptoms lasting for more than a year), left atrial (LA) thrombus, LA anteroposterior diameter exceeding 50 mm, unstable angina in the previous three months, bleeding disorders, pregnancy, patients with contraindications for anticoagulation, decompensated heart failure, and unwillingness to give informed consent.

2.2. Mapping and ablation technique

PV isolation (PVI) was performed solely by conventional Electrophysiology equipment (EP Tracer, Model V074 version), without using 3D mapping. Before the procedure, PV anatomy was assessed by trans-esophageal echocardiogram (TEE) in all patients: the PVs were visualized and their diameters assessed (mid-esophageal 0° view for right PVs and mid-esophageal 50° view for left PV); the LA was visualized for thrombus, and the LA appendage velocity was assessed (mid-esophageal 90° left and right and 45° views). Cardiac CT was used to assess the PV anatomy in selected patients (Fig. 1A and B).

Before the procedure, 25 patients were on oral anticoagulation with vitamin K antagonists or NOAC, while the remaining 17 were taking aspirin. A day prior to the procedure, an oral anticoagulation dose was omitted. All patients underwent TEE prior to the

procedure, after confirming that the international normalized ratio (INR) was less than 2. The procedure was performed under local anesthesia. Vascular access was through the femoral veins; two in the right femoral vein (one for ablation catheter and other for SRO sheath/Lasso catheter) and one access from the left femoral vein was used for placing the decapolar catheter in the coronary sinus. Totally, five patients developed AF during the procedure; two reverted with ibutilide, two with DC version, and one needed both modalities. A left femoral artery sheath was used to monitor blood pressure and for guiding trans-septal puncture. Trans-septal catheterization was performed using RAO 30° and LAO 50° fluoroscopic views, and systemic anticoagulation was achieved with intravenous heparin to maintain an activated clotting time of 250–350 s. Pre-ablation selective angiography of individual PVs was performed in the AP and LAO 40° views (Fig. 2A). The ostia of the PVs were marked.

In addition, the mapping catheter was used to determine the ostium of the vein as the site immediately before the catheter fell off the venous ridge into the LA during a slow pullback along the trunk of the vein. Through the SRO sheath, a Lasso catheter was placed in the PV and gradually withdrawn to within 5 mm of the ostium. A Webster 7F thermocouple 8 mm tip catheter was inserted into the LA either through the same trans-septal puncture site or through a second trans-septal puncture and used for ablation (Fig. 2B). Ablation of some of the PVs (especially the right inferior) was not performed in the following situations:

- i) The vein was electrically silent
- ii) The vein could not be cannulated
- iii) The vein was too small in caliber to accommodate the Lasso catheter
- iv) There was frequent triggering ectopy that was clearly originating from other (usually superior) PVs.

Focal/segmental PVI was performed during sinus rhythm (right-sided veins) or during distal coronary sinus pacing (left-sided veins) by delivering RF energy at ostial sites that had the earliest breakthrough bipolar potentials (Fig. 2C). RF energy was delivered at the PV ostium with a target temperature of 50–60 °C and a maximum power output of 30–50 W for 20–30 s. Ablation was stopped if the patient had severe pain during ablation.

Patients who had recurrent documented AF paroxysms and consistent PAC morphologies suggestive of a particular vein (usually the upper PVs) underwent isolation of these veins initially. After this, if no further arrhythmias were seen despite isoprenaline, the other veins (usually lower) were left alone. Additionally, 10 PVs showed no electrical activity. Elimination of all PV potentials and complete entrance block into the PV were considered indicative of complete electrical isolation. After ablation, selective angiography of the PVs was performed to look for stenosis. None of the patients had PV stenosis, which usually starts off immediately after ablation. Follow-up cardiac CT scan was not done to assess PV stenosis.

Immediately after PVI, oral anticoagulation was started with warfarin, dabigatran, or apixaban. If warfarin was used, there was a 48 h overlap with enoxaparin or fondaparinux. The anticoagulation was continued for at least three months.

2.3. Follow-up after ablation

Patients were discharged usually within two days after the ablation. Following the procedure, a vitamin K antagonist or direct oral anticoagulant was continued for at least three months. Patients taking an antiarrhythmic drug before the procedure were advised to continue the medication for three months after ablation; this was discontinued thereafter if the patient was free of an AF relapse.

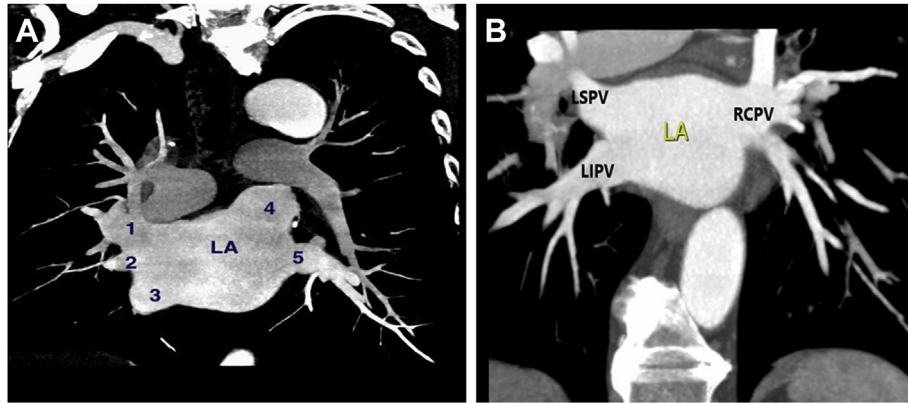


Fig. 1. (A): Posteroanterior projection of cardiac CT showing three left PVs and two right PVs. Labels: LA: Left atrium. 1: Left superior PV. 2: Left middle PV. 3: Left inferior PV. 4: Right superior PV. 5: Right inferior PV. (B): Posteroanterior projection of cardiac CT showing two left PVs and a single right common PV. Labels: LA: Left atrium. LSPV: Left superior pulmonary vein. LIPV: Left inferior pulmonary vein. RCPV: Right common pulmonary vein.

Follow-up visits were scheduled at one, three, and six months, and every six months thereafter. An ECG, symptom review, and clinical examination were performed at each follow-up. AF episodes less than 30 min duration are not a significant risk factor for stroke. So, while we may have missed silent AF recurrences in sleep, it is improbable that any significant episodes during the waking hours were missed.

2.4. Freedom from AF

Freedom from AF was defined as no occurrence of even a single episode of documented atrial arrhythmia lasting more than 30 s at any time within the study period after the procedure. No blanking period was used in this study, as there has been conflicting evidence of its validity. Therefore, arrhythmias were classified as recurrent even within the first few weeks of the procedure.

2.5. Statistical analysis

Clinical and laboratory parameters (age, gender, duration of AF, diabetes mellitus, hypertension, hyperthyroidism, coronary artery disease, structural heart disease, (alcoholism, BMI) were assessed for their impact on the outcome of PVI. Discrete variables are described in terms of the frequency and proportion and compared using the χ^2 or Fisher's exact test. Continuous variables are described as the mean $\pm$ SD and compared using unpaired *t*-tests for normally distributed data; the median (IQR) was compared using the Mann–Whitney *U* test. Univariable and multivariable predictors of freedom from AF were examined using logistic regression using forward conditional modeling. Kaplan–Meier analysis was used to analyze AF-free survival. Where applicable, two-tailed tests were used in all analyses. A *p* value ≤ 0.05 was considered significant for all tests. Analyses were performed using IBM SPSS Statistics software V.21.

3. Results

3.1. Baseline characteristics

A total of 42 patients were studied (Table 1). The study population had 30 (71.4%) males and 12 (28.6%) females, aged 51.5 ± 11.7 years (range 24–75 years). The BMI was 22.5 ± 2.55 ; a BMI > 25 was present in 10 (23.8%) patients. Diabetes was present in 11 (26%) patients, hypertension in 13 (31%), and structural heart disease in

two (4.8%) patients. One anti-arrhythmic drug (AAD) had been tried in two (4.8%) of the patients, two AADs in 25 (59.5%) and three AADs in 15 (35.7%) patients. Hence, a mean of 2.31 ± 0.0 AADs had been ineffective in preventing recurrence before the ablation procedure. The commonly used AADs include amiodarone, beta blockers, and flecainide.

3.2. Echocardiographic parameters

The anteroposterior LA diameter was 40.5 ± 4.1 mm and the LVEF was 0.58 ± 0.21 . The LA diameter > 46 mm was present in six (14.3%) patients, and among them, the failure rate was high: 5/6 (83.3%).

3.3. Procedural details (Table 2)

The procedure duration was 125 ± 29 min, while the fluoroscopy time was 47 ± 13 min. After the procedure, 34 patients were arrhythmia-free, while eight patients continued to have AF episodes. The mean number of PVs isolated was 2.4 ± 0.8 . The number of PVs isolated were one (five patients, 11.9%), two (20 patients, 47.6%), three (12 patients, 28.6%), and four (5 patients, 11.9%). The RSPV was isolated in 40, the LSPV in 39, the LIPV in 17, and the RIPV in five patients. The number of RF energy applications was 18 ± 7 .

3.4. Complications

Complication occurred in two patients; one patient developed a moderate pericardial effusion and one patient had short-lived sinus pauses, which were conservatively managed.

3.5. Follow-up

The mean follow-up duration was 44 ± 21 months (range 6–84 months). The number of patients who had freedom from AF at 1, 6, 12, and 24 months were 34 (81%), 32 (76%), 30 (71%), and 26 (62%), respectively. The only parameter that showed significant difference between patients who remained in sinus rhythm and AF recurrence was a LA size of ≥ 45 mm (Table 3). The mean LA size was larger in patients with failed ablation as compared to the success group, 47.8 ± 2.4 mm vs 39.8 ± 2.3 mm ($p < 0.001$).

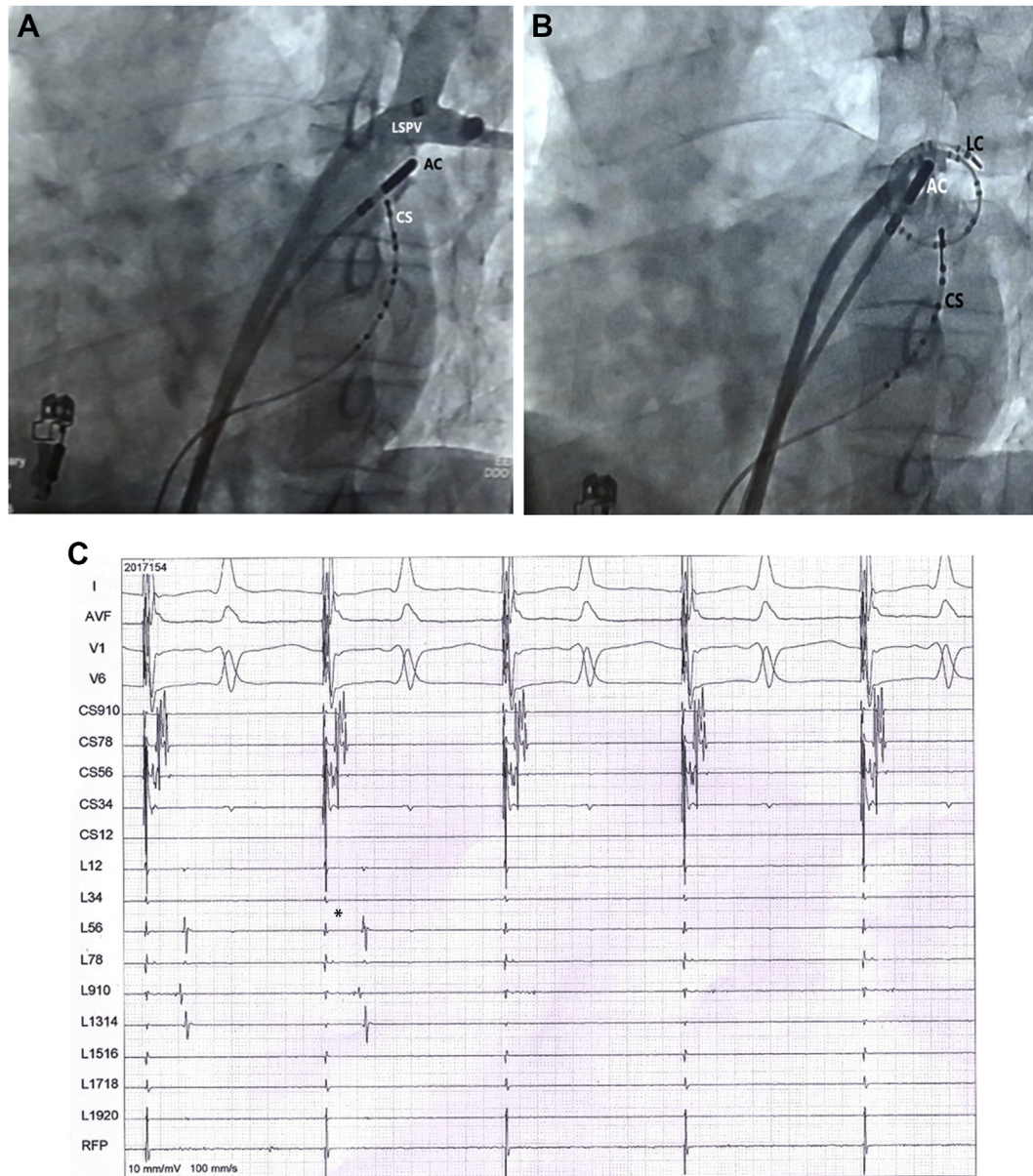


Fig. 2. (A): Preablation selective angiography of the LSPV performed in fluoroscopic LAO view. Labels: LSPV: Left superior pulmonary vein. AC: Ablation catheter. CS: Coronary sinus catheter. (B): Left anterior oblique cine-angiographic view demonstrating a Lasso mapping catheter (LC) and 8 mm tip ablation catheter (AC) at the LSPV ostium. CS: Coronary sinus catheter. (C): PVI for AF. Note how the PV potential disappears during RF ablation. CS: Coronary sinus. L: Lasso catheter.

3.6. Recurrence of AF and redo PVI

AF recurrence in the first year after initial successful PVI was seen in two patients. In the first patient during the first PVI, the RSPV was electrically silent and other three PVs were isolated, but recurrence was seen after three months. In the redo PVI, he was found to have widespread arrhythmogenic foci in RSPV, and the LIPV showed partial reconnection with good PV potentials. After a successful redo PVI, freedom from AF was noted during two years of follow-up.

In the second patient, the first time she was presented as 'focal' AF arising from the LIPV, which was successfully ablated. After six months, she had multiple hospitalizations for symptomatic PAF episodes. She was taken up for the repeat procedure, which showed good PV potentials in the RSPV, RIPV, and LSPV, which were successfully isolated. During a two-year follow-up period after this, she had freedom from AF episodes.

4. Discussion

The data on epidemiological trends of AF from India are limited.^{1,2,8,9} Though non-valvular AF is the commonest cause in the western population, in Indian settings, rheumatic heart disease still contributes to at least for half of the AF cases. In the western population, its prevalence is around 1–2% of the general population, occurring in up to 5% of people aged 75 or more.¹⁰

Although the aged population is more at risk for developing AF, the mean age of Indian patients with AF is nearly a decade younger than the western cohort.^{1,2} In our study, the age was 51.5 ± 11.6 years (range 24–75 years). Hospital data records of patients with chronic AF from Andhra Pradesh revealed a mean age of 45.4 years, with many (51%) aged < 50 years and only 16.3% older than 60 years.¹¹ In an observational hospital-based study carried among indoor patients of AF in Bihar, Vidya et al reported that the mean age of the patients was 47 years, with 48% of patients aged

Table 1
Baseline characteristics of the study population (*n* = 42).

Parameter		
Age		51.5 ± 11.7 years
Gender		
Male		30 (71%)
Female		12 (29%)
BMI		22.5 ± 2.6
Diabetes mellitus		11 (26%)
Hypertension		13 (31%)
Coronary artery disease		2 (5%)
Structural heart disease		2 (5%)
Duration of symptoms		32 ± 40 months
		1.82
Antiarrhythmics before procedure	1	2 (5%)
	2	25 (59%)
	3	15 (36%)
Antiarrhythmics after procedure	0	7 (17%)
	1	31 (74%)
	2	4 (9%)
LA diameter (AP)		40.5 ± 4.1 mm
LVEF		0.58 ± 0.21
	1	

Table 2
Procedure-related variables (*n* = 42).

Variable		
Number of veins isolated	1	5 (11.9%)
	2	20 (47.6%)
	3	12 (28.6%)
	4	5 (11.9%)
Procedure time (minutes)		125 ± 29
Fluoroscopy time (minutes)		47 ± 13

Table 3
Factors associated with successful outcome at one year after PVI (*n* = 42).

Variable	Sinus rhythm		AF	P
	Mean ± SD		Mean ± SD	
Age (years)	52.3 ± 12.7		49.8 ± 7	0.655
BMI	22.3 ± 2.6		21.2 ± 1.6	0.307
LA size (mm)	39.8 ± 2.3		47.8 ± 2.4	<0.001
	Sinus rhythm		AF	p
	N	%	N	%
Gender				
Male	20	80.0%	5	20.0%
Female	10	90.9%	1	9.1%
Diabetes mellitus				
No	22	81.5%	5	18.5%
Yes	8	88.9%	1	11.1%
HTN				
No	18	78.3%	5	21.7%
Yes	12	92.3%	1	7.7%

between 51 and 60 years.¹² Data from the IHRS-AF registry¹ and the Indian subset of REALISE AF¹³ and RELY-AF¹⁴ study also reaffirmed these findings. The mean age of Indian patients with AF in the REALISE-AF study¹³ was 60 years, while that in the IHRS-AF registry¹ was 54.2 years (range 15–96 years).

Tedrow and colleagues observed a large cohort of women and found that the risk of incident AF was linearly associated with increasing BMI.¹⁵ In our study, out of 42 patients, only eight patients had a BMI ≥25, and the mean BMI of patients in this study was 22.5 ± 2.6.

Atrial enlargement and fibrosis trigger and lead to persistence of AF through changes in the substrate of LA and subsequent electrical remodeling.¹⁶ Moreover, patients with larger LA require more energy and longer lesions to complete the ablation.

Some studies demonstrate that severe LA scarring after ablation predisposes patients to AF recurrences, which seems to result from re-connection between LA and PVs.¹⁷ Zhuang et al showed patients with recurrences had a larger LA size than those without recurrences after a single PVI (95% CI 1.26–2.48, *p* < 0.001).¹⁸ In our study also, the mean LA size was larger in patients with failed ablation than the success group, 47.8 ± 2.4 mm vs 39.8 ± 2.3 mm (*p* < 0.001). The LA diameter was >46 mm in six (14.3%) patients, and among them, PVI was successful in only one patient. Thus, our study finding of larger LA diameter as a predictor of failure of PVI is in concordance with other studies.

In our study, the number of patients who remained in sinus rhythm at 1, 6, 12, and 24 months were 34 (81%), 32 (76%), 30 (71%), and 26 (62%), respectively. Initial studies describing focal ablation within the PVs showed disappointing minimal long-term benefit and a significant risk of PV stenosis.¹⁹ Despite using irrigated tip catheters with contact force technology in PAF patients with mean age of 56 years, the success rate after single PV antral isolation in a multicenter study was 48.6% and the five-year long-term freedom from AF was only 58.3%. About 53% of the PAF patients required second redo PVI, 42% required third redo procedure, and 33% required a fourth redo procedure in that study.²⁰ Hence, our study results, which used 2D mapping, non-irrigated catheter and few redo ablations, are not inferior.

Marrouche et al²¹ clearly demonstrated that distal isolation ablation (from within PVs) eliminated AF only in 29% of the patients, whereas ostial isolation eliminated AF in all. In that study, it was also shown that the AF recurrence rate was 21% with 4 mm tip ablation catheter and 15% with cooled tip catheter at a mean follow-up period of 10 ± 3 months and 4 ± 2 months, respectively, whereas no recurrence was documented with use of 8 mm tip ablation catheter at a mean follow-up period of 6 ± 4 months. Though the literature regarding the effectiveness of 4 mm vs 8 mm tip catheter is sparse in catheter ablation for AF, we used 8 mm tip catheter in view of perceived greater effectiveness, especially in cost-constraint situations.

The latest multicentric CABANA trial did not show any significant difference in primary or secondary outcomes between ablation arm and AAD therapy arm in the treatment of AF patients.²² Regarding cost effectiveness of AF ablation, it had been shown in few decision modeling studies that RF ablation of AF might be cost effective in patients with AAD-resistant AF. The average cost of AF ablation varies between 14,000 and 18,000 US \$ in the USA,²³ and such a high cost is primarily secondary to 3D mapping system and special catheters like smart touch catheters/cryoballoon and in Indian settings, such a high cost, is beyond the reach of many deserving symptomatic AF patients. Hence, 2D mapping and 8 mm tip catheter for better contact were used in our study to get better results in a resource-constraint setting.

Complications during AF ablation include vascular access complications, PV stenosis, pericardial tamponade, cerebral embolism, atriopharyngeal fistula, cardiac perforation, and death. Currently, the risk of complication during RF ablation for AF is 2–3%, with vascular access complications being the most common, while fatal complications are rare.²⁴ We had only two complications, none of which was serious.

5. Limitations of the study

In our study, 3D mapping was not used. The current recommendation in AF ablation is to perform PVI of all four PVs, while we have done PVI of only those veins that were considered arrhythmogenic. In patients who had recurrent documented AF paroxysms and consistent PAC morphologies suggestive of a particular vein (usually the upper PVs) underwent isolation of these veins initially.

After this, if no further arrhythmias were seen despite isoprenaline, the other veins (usually lower) were left alone. We did not test with adenosine after ablation. Also, we did not check for an exit block. Our study is a single-center, single experienced operator outcome study. We need to have a multicentric data on AF ablation from developing countries with reduced resources. Our results, though not as good as with current large studies with sophisticated mapping, image merging, and ablation techniques targeting all four veins, are, nonetheless, not much inferior.

We could not analyze whether recurrences correlated with the number of veins isolated. This was because of the small numbers in each subgroup.

Our patients during follow-up did not have routine Holter, external, or internal loop recorder to assess AF recurrence. We now understand that AF episodes less than 30-min duration are not a significant risk factor for stroke. So, while we may have missed silent AF recurrences in sleep, it is improbable that any significant episodes during the waking hours were missed.

Intracardiac echo was not used in our patients due to resource constraints. Intracardiac echo would have possibly helped identify clearly the PV orifice and catheter contact and unmask electrical activity in some of the 'silent' veins.

CT pulmonary venogram was not done routinely in all patients at follow-up to look for PV stenosis due to financial constraints. Immediate postprocedural pulmonary venogram by cine angiogram may not be relied upon to predict the future occurrence of PV stenosis.

6. Summary

To the best of our knowledge, this is the first study from India reporting the intermediate term outcome of PVI for patients with symptomatic PAF. AF was more common in males and in age group >50 years; hypertension was seen in only one-third of the patients. Immediately after the procedure, 34 out of 42 patients (81%) remained free of any symptomatic and/or documented AF episode.

After PVI, the number of patients who remained in sinus rhythm at intermediate term follow-up was 62%. An 8 mm tip catheter ensures adequate contact and energy delivery and was not associated with any major complication. An anteroposterior LA diameter >46 mm was the best predictor of failure of PVI. Though larger LA diameter is associated with higher AF recurrence rates, larger atria that are associated with healthier myocardium may be easier to ablate.

Hence, this study confirms that PVI using conventional mapping techniques and a 8 mm tip catheter is a safe and economically feasible treatment modality for symptomatic patients with PAF in the Indian setting with reasonable outcomes. Our results, though not as good as with current large studies with sophisticated mapping, image merging, and ablation techniques targeting all four veins, are, nonetheless, not much inferior.

Funding

None.

Declaration of competing interest

All authors have none to declare.

References

- Vora A, Kapoor A, Nair M, et al. Clinical presentation, management, and outcomes in the Indian heart rhythm society-atrial fibrillation (IHRS-AF) registry. *Indian Heart J*. 2017 Jan 1;69(1):43–47.
- Bohra V, Sharma G, Juneja R. Burden of atrial fibrillation in India. *Journal of the Practice of Cardiovascular Sciences*. 2015 Sep 1;1(3):230.
- Haissaguerre M, Jais P, Shah DC, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *N Engl J Med*. 1998 Sep 3;339(10):659–666.
- Jais P, Cauchemez B, Macle L. Catheter ablation versus antiarrhythmic drugs for atrial fibrillation: the A4 study. In: Jais P, Cauchemez B, Macle L, eds. *Circulation*. vol. 118. 2008:2498.
- Wilber DJ, Pappone C, Neuzil P, et al. Comparison of antiarrhythmic drug therapy and radiofrequency catheter ablation in patients with paroxysmal atrial fibrillation: a randomized controlled trial. *Jama*. 2010 Jan 27;303(4):333–340.
- Oral H, Knight BP, Tada H, et al. Pulmonary vein isolation for paroxysmal and persistent atrial fibrillation. *Circulation*. 2002 Mar 5;105(9):1077–1081.
- Boersma LV, Wijffels MC, Oral H, Wever EF, Morady F. Pulmonary vein isolation by duty-cycled bipolar and unipolar radiofrequency energy with a multielectrode ablation catheter. *Heart Rhythm*. 2008 Dec 1;5(12):1635–1642.
- Soni A, Earon A, Handorf A, et al. High burden of unrecognized atrial fibrillation in rural India: an innovative community-based cross-sectional screening program. *JMIR public health and surveillance*. 2016 Jul;2(2).
- Saggu DK, Sundar G, Nair SG, et al. Prevalence of atrial fibrillation in an urban population in India: the Nagpur pilot study. *Heart Asia*. 2016 Apr 1;8(1):56–59.
- Kannel WB, Abbott RD, Savage DD, McNamara PM. Epidemiologic features of chronic atrial fibrillation: the Framingham study. *N Engl J Med*. 1982 Apr 29;306(17):1018–1022.
- Rao DV, Reddy RM, Srikanth K, Prakash RK, Prasad SA, Prasad GS. To study the prevalence and clinical profile of chronic atrial fibrillation in hospitalized patients. *Nitte Univ J Health Sci*. 2014 Jun 1;4(2):17.
- Vidya N, Gupta AK, Syed Mahmood, Malini Kulshrestha, Patiyal RK. Etiological profile and clinical presentation of patients with atrial fibrillation from a rural area of Bihar. *Nat J Clin Med Res*. 2012;2:124–127.
- Chiang CE, Naditch-Brulé L, Murin J, et al. Distribution and risk profile of paroxysmal, persistent, and permanent atrial fibrillation in routine clinical practice: insight from the real-life global survey evaluating patients with atrial fibrillation international registry. *Circulation: Arrhythmia and Electrophysiology*. 2012;5(4):632–639.
- Oldgren J, Healey JS, Ezekowitz M, et al. Variations in cause and management of atrial fibrillation in a prospective registry of 15 400 emergency department patients in 46 countries: the RE-LY Atrial Fibrillation Registry. *Circulation*. 2014 Apr 15;129(15):1568–1576.
- Overvad TF, Rasmussen LH, Skjøth F, Overvad K, Lip GY, Larsen TB. Body mass index and adverse events in patients with incident atrial fibrillation. *Am J Med*. 2013 Jul 1;126(7):640–e9.
- Yue L, Xie J, Nattel S. Molecular determinants of cardiac fibroblast electrical function and therapeutic implications for atrial fibrillation. *Cardiovasc Res*. 2010 Oct 20;89(4):744–753.
- Oakes RS, Badger TJ, Kholmovski EG, et al. Detection and quantification of left atrial structural remodeling with delayed-enhancement magnetic resonance imaging in patients with atrial fibrillation. *Circulation*. 2009 Apr 7;119(13):1758–1767.
- Zhuang J, Wang Y, Tang K, et al. Association between left atrial size and atrial fibrillation recurrence after single circumferential pulmonary vein isolation: a systematic review and meta-analysis of observational studies. *Europace*. 2011;14(5):638–645.
- Chen SA, Hsieh MH, Tai CT, et al. Initiation of atrial fibrillation by ectopic beats originating from the pulmonary veins: electrophysiological characteristics, pharmacological responses, and effects of radiofrequency ablation. *Circulation*. 1999 Nov 2;100(18):1879–1886.
- Teunissen C, Kassenberg W, van der Heijden JF, et al. Five-year efficacy of pulmonary vein antrum isolation as a primary ablation strategy for atrial fibrillation: a single-centre cohort study. *Europace*. 2016 Feb 2;18(9):1335–1342.
- Marrouche NF, Dresing T, Cole C, et al. Circular mapping and ablation of the pulmonary vein for treatment of atrial fibrillation: impact of different catheter technologies. *J Am Coll Cardiol*. 2002 Aug 7;40(3):464–474.
- Packer DL, Mark DB, Robb RA, et al. Effect of catheter ablation vs antiarrhythmic drug therapy on mortality, stroke, bleeding, and cardiac arrest among patients with atrial fibrillation: the CABANA randomized clinical trial. *Jama*. 2019 Apr 2;321(13):1261–1274.
- Khaykin Y, Shamiss Y. Cost of AF ablation: where do we stand? *Cardiol Res Pract*. 2011;1–6. Jan 2011.
- Bertaglia E, Zoppo F, Tondo C, Colella A, et al. Early complications of pulmonary vein catheter ablation for atrial fibrillation: a multicenter prospective registry on procedural safety. *Heart Rhythm*. 2007 Oct 1;4(10):1265–1271.