Original Article

Catheter Ablation of Atrial Fibrillation in Hypertrophic Cardiomyopathy

Long-Term Outcomes and Mechanisms of Arrhythmia Recurrence

Pasquale Santangeli, MD*; Luigi Di Biase, MD, PhD, FHRS*; Sakis Themistoclakis, MD; Antonio Raviele, MD; Robert A. Schweikert, MD, FACC, FHRS; Dhanunjaya Lakkireddy, MD; Prasant Mohanty, MD; Rong Bai, MD; Sanghamitra Mohanty, MD; Agnes Pump, MD; Salwa Beheiry, RN; Richard Hongo, MD, FACC, FHRS; Javier E. Sanchez, MD; G. Joseph Gallinghouse, MD; Rodney Horton, MD; Antonio Dello Russo, MD, PhD; Michela Casella, MD, PhD; Gaetano Fassini, MD; Claude S. Elayi, MD; J. David Burkhardt, MD; Claudio Tondo, MD, PhD; Andrea Natale, MD, FHRS, FACC

Background—Pulmonary vein (PV) antrum isolation in patients with hypertrophic cardiomyopathy and atrial fibrillation (AF) has been reported to have satisfactory results at the mid- and short-term follow-up. We determined the outcomes at the long-term follow-up of PV antrum isolation in these patients.

Methods and Results—We enrolled 43 patients with hypertrophic cardiomyopathy and AF (28% paroxysmal AF). PV antrum isolation (paroxysmal AF) and posterior wall isolation with complex fractionated atrial electrogram ablation (persistent and longstanding persistent AF) were the end points at the time of the index procedure and for repeat procedures during the first year of follow-up. In case of recurrent arrhythmia >1 year, high-dose isoproterenol challenge was used to disclose non-PV trigger sites. During the first year, the success rate reached 91% (mean of 1.6 procedures). After a median follow-up of 42 months (range, 38–48 months), 49% of the patients remained free from AF/atrial tachycardia. All patients underwent an additional procedure. PV antrum and posterior wall remained isolated in 82% of the cases, and extra-PV triggers were documented in all patients and targeted for ablation. After a median follow-up of 15 months (range, 8–19 months) subsequent to the last procedure, 94% of the patients remained free from AF/atrial tachycardia off antiarrhythmic drugs.

Conclusions—PV isolation in patients with hypertrophic cardiomyopathy is feasible and safe, although is not effective in preventing late (≥1 year) AF recurrences in ≈50% of patients. Non-PV triggers seem to be responsible of late recurrences, which supports the appropriateness of a more extensive ablation beyond PV isolation to improve the long-term arrhythmia-free survival. **(*Circ Arrhythm Electrophysiol*. 2013;6:1089-1094.)**

Key Words: atrial fibrillation ■ catheter ablation ■ cardiomyopathies ■ cardiomyopathy, hypertrophic

Atrial fibrillation (AF) is highly prevalent in patients with hypertrophic cardiomyopathy (HCM) and constitutes one of the most common reasons for hospitalization.[1] There is a paucity of data on the effectiveness of rhythm control with antiarrhythmic agents in this patient population. Amiodarone represents the most studied one and is considered the drug of choice by current guidelines.[2] Few data support the efficacy of sotalol or dofetilide in HCM patients with AF,[3] as well as the antiarrhythmic effectiveness of disopyramide, which has been shown to be safe when prescribed for control of left ventricular outflow tract obstruction.[2,3] Pulmonary vein antrum isolation (PVAI) has been recently reported as a feasible and safe therapeutic strategy in HCM patients with drug-refractory AF, with satisfactory short- and mid-term results.[4–6] Thus far, scant data are available on the long-term results of PVAI in patients with HCM.[4] In this

Clinical Perspective on p 1094

Received October 20, 2012; accepted September 26, 2013.

From the Texas Cardiac Arrhythmia Institute, St David's Medical Center, Austin, TX (P.S., L.D.B., P.M., R.B., S.M., A.P., J.E.S., G.J.G., R.H., J.D.B., A.N.); Albert Einstein College of Medicine at Montefiore Hospital, New York, NY (L.D.B.); University of Foggia, Foggia, Italy (P.S., L.D.B.); Cardiac Electrophysiology, Ospedale Dell'Angelo, Mestre, Italy (S.T., A.R.); Heart & Vascular Center, Akron General Medical Center, OH (R.A.S.); Division of Cardiovascular Diseases, University of Kansas, MO (D.L.); California Pacific Medical Center, San Francisco (S.B., R.H., A.N.); Cardiac Arrhythmia Research Center, Centro Cardiologico Monzino, Milan, Italy (A.D.R., M.C., G.F., C.T.); and University of Kentucky, Lexington (C.S.E.).

*Drs Santangeli and Di Biase are cofirst authors.

Correspondence to Andrea Natale, MD, Texas Cardiac Arrhythmia Institute, St David's Medical Center, 1015 E 32nd St, Suite 516, Austin, TX 78705. E-mail dr.natale@gmail.com

Circ Arrhythm Electrophysiol is available at http://circep.ahajournals.org

DOI: 10.1161/CIRCEP.113.000339

study, we aimed to evaluate the long-term outcomes and the mechanisms of arrhythmia recurrence after radiofrequency catheter ablation of AF in patients with HCM to assess the optimal ablation strategy.

Methods

We included 43 consecutive patients (age, 59±8 years) with HCM and drug-refractory symptomatic AF. The diagnosis of HCM followed the American College of Cardiology/European Society of Cardiology guidelines.[7] Definitions of paroxysmal, persistent, and longstanding persistent AF followed the American Heart Association/American College of Cardiology/European Society of Cardiology guidelines.[8] Patients were in long-term treatment with therapeutic warfarin, which was not discontinued during the periprocedural period.[9] Antiarrhythmic drugs were discontinued ≥5 half-lives before the procedure. Patients receiving amiodarone therapy discontinued the drug 4 to 6 months before the ablation procedure. Informed consent was obtained from all patients, and all the data were entered in a central hub database approved by the Institutional Ethical Committee.

Instrumentation for Electrophysiological Study

Procedures were performed under either general anesthesia or conscious sedation. An esophageal probe was inserted in all patients to monitor esophageal temperature during ablation. Four venous accesses were obtained: 2 in the right femoral vein, 1 in the left femoral vein, and 1 in the right internal jugular vein. Right internal jugular vein access was used to place a 20-pole catheter in the coronary sinus, with the proximal 10 poles positioned along the crista terminalis. The left femoral venous access was catheterized with an 11F venous sheath to insert a 10F 64-element phased-array ultrasound imaging catheter (intracardiac echocardiography [ICE]; AcuNav, Acuson, Mountain View, CA) in the right atrium under fluoroscopic guidance. A bolus of unfractionated heparin (10 000 U in men and 8000 U in women) was administered before the transseptal access, and intermittent infusion was adopted to maintain an activated clotting time >300 s. Left atrial access was obtained with a double transseptal puncture.

Catheter Ablation

Index Procedure and Repeat Procedures During the First Year of Follow-Up

Patients with paroxysmal AF underwent PVAI and isolation of the superior vena cava. The technique of PVAI has been described extensively elsewhere.[10] Briefly, a 3.5-mm irrigated-tip catheter (NaviStar ThermoCool; Biosense Webster, Diamond Bar, CA) and a circular mapping catheter (Lasso; Biosense Webster) were used. ICE was used to identify the PV antra to guide the positioning of the circular catheter and radiofrequency delivery and to look for all potential complications. Electroanatomic mapping was performed using the CARTO system (Biosense Webster, Diamond Bar, CA) or the EnSite NavX Navigation system (St Jude Medical, St Paul, MN). Radiofrequency energy was set at a power of 40 W (≤45 W) and at a catheter tip temperature of no more than 41°C. On the posterior wall, power was reduced to 35 W; energy delivery was further reduced when the baseline esophageal temperature increased and was discontinued when the temperature reached 39°C. The end point of the procedures was elimination of all PV potentials along the antra with entry block. After isolation of all the PV antra and the posterior wall contained between the PVs, the circular mapping catheter was placed above the junction between the right atrium and superior vena cava at the level of the lower border of the pulmonary artery as imaged by ICE. Before radiofrequency delivery, maximum output pacing (≤20 mA) was performed at any site of the posterolateral side of the superior vena cava. If diaphragmatic stimulation was present, ablation in this site was not performed to avoid injury to the phrenic nerve. The end point of ablation was to eliminate any potential along the mapping catheter (entry block).

In patients with persistent and longstanding persistent AF, the electric isolation of the PVs was extended to the entire posterior wall down to the coronary sinus and the left side of the septum.[11] Ablation of complex fractionated atrial electrograms in the left atrium and the coronary sinus was also performed.

If the AF organized into an atrial tachycardia, activation and entrainment mapping were performed to attempt termination. Otherwise, patients were cardioverted after elimination of all complex fractionated atrial electrogram sites. For recurrences occurring during the first year of follow-up, repeat procedures targeted only sites of reconnection around the PV antrum, posterior wall, interatrial septum, and coronary sinus. If patients presented with organized atrial arrhythmia (ie, atrial flutter/tachycardia), activation and entrainment mapping were performed to terminate the arrhythmia.

Repeat Procedures for Recurrences Beyond 1 Year (Late Recurrences)

For repeat procedures ≥1 year after the index procedure, in addition to the ablation strategy mentioned above (ie, ablation of sites of reconnection, mapping and ablation of organized atrial tachyarrhythmias), high doses of isoproterenol (20–30 μg/min) for 15 to 20 minutes were administrated to check for extra-PV firings (Figure 1), which were mapped as previously reported.[12] No specific hemodynamic compromise beyond that expected during isoproterenol test was encountered in this series of patients. The anesthesiologist participating in the procedure used phenylephrine to manage blood pressure decrease and allow the completion of the isoproterenol test. Non-PV triggers were defined either as consistent (≥10 in 1 minute) atrial premature depolarizations or as firing inducing AF/atrial tachyarrhythmia.

Follow-Up

The follow-up was performed at 3, 6, 9, 12, and then every 6 months after the procedure, with physical examination, 12-lead ECG, and 7-day Holter monitoring. All patients received an event recorder for the first 5 months to record any symptomatic events. In addition, random recordings were performed 2× to 3× per week to monitor for any asymptomatic episodes of AF. Recurrence was considered to be any episode of AF/atrial tachycardia lasting for ≥30 seconds after a blanking period of 3 months from the procedure. Repeat ablation was not allowed during the blanking period.

Late recurrence was defined as AF/atrial tachycardia recurrence occurring beyond 1 year after the index procedure. Antiarrhythmic drugs (class III agents—sotalol or dofetilide in 41 cases, amiodarone in 2 cases) were systematically used for the blanking period and discontinued after the end of the blanking period if patients were in sinus rhythm.

Statistical Analysis

Descriptive statistics are reported as mean±SD (or median and interquartile range for skewed distributions) for continuous variables

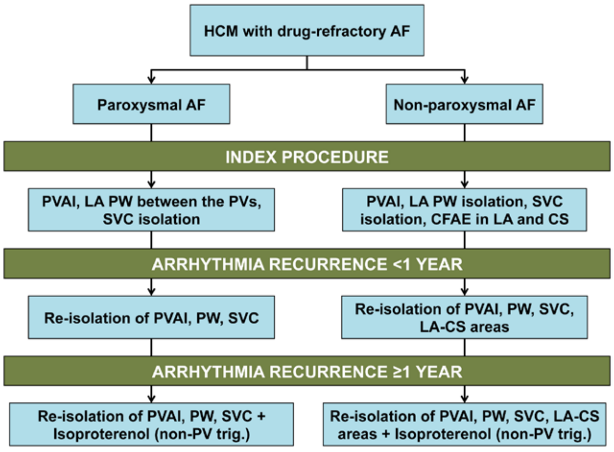

Figure 1. Study design and ablation strategy adopted in the study. AF indicates atrial fibrillation; CFAE, complex fractionated atrial electrograms; CS, coronary sinus; HCM, hypertrophic cardiomyopathy; LA, left atrial; PV, pulmonary vein; PVAI, PV isolation; PW, posterior wall; and SVC, superior vena cava.

and as absolute frequencies and percentages for categorical variables. Between-group comparisons were performed with the unpaired Student *t* test for continuous data (Mann–Whitney *U* test when normality assumption was not possible) and with the Fisher exact for categorical variables. Long-term arrhythmia-free survival was reported as crude event rates and assessed through a time-to-event analysis by the Kaplan–Meier method. All tests were 2-sided, and a $P<0.05$ was considered statistically significant. To adjust for type I error while making multiple pairwise comparisons for the type of recurrent arrhythmia in paroxysmal versus persistent and longstanding persistent AF populations, the *P* value for rejecting null hypothesis was set at a conservative level ($P=0.01$). Statistical analyses were performed by STATA version 11.1 (StataCorp, College Station, TX) software.

Results

The majority of patients had persistent (18 [41%]) and longstanding persistent (13 [31%]) AF (Table). The mean left atrial diameter was 50.8±6.8 mm, and the left ventricular ejection fraction was 59±6%. Maximum left ventricular wall thickness was 19.8±3.9 mm. All patients had failed treatment with ≥1 antiarrhythmic drug.

Index Procedure and First Year of Follow-Up

PVAI and isolation of the posterior wall between the PVs and of the superior vena cava were achieved in all patients with paroxysmal AF. In those with persistent and longstanding persistent AF, ablation was extended to the entire posterior left atrial wall and to areas with complex fractionated atrial electrograms in the left atrium and coronary sinus.[13] The average radiofrequency time in patients with paroxysmal AF was 34±6 minutes and was significantly longer in patients with persistent and longstanding persistent AF (71±9 minutes; $P<0.001$

Table. Clinical Characteristics of the Patients Included in the Study

Variable	N=43
Age, y	59±8
Sex, males	29 (67)
AF type	
Paroxysmal	12 (28)
Persistent	18 (42)
Longstanding persistent	13 (30)
NYHA functional class I	9 (21)
NYHA functional class II	31 (72)
NYHA functional class III	3 (7)
AF duration, mo (median, IQR)	36 (51)
LA diameter, mm	50.8±6.8
Maximum LV thickness, mm	19.8±3.9
LV ejection fraction, %	59±6
Implantable cardioverter-defibrillator	27 (63)
Failed antiarrhythmic drugs	
Amiodarone	36 (84)
Sotalol	31 (72)
Dofetilide	8 (19)
Class IC agents	4 (9)

Values are expressed as mean±SD or n (%). AF indicates atrial fibrillation; IQR, interquartile range; LA, left atrial; LV, left ventricle; and NYHA, New York Heart Association.

for comparison with paroxysmal AF). The median fluoroscopy time was 49 minutes (range, 29–53 minutes), with a median procedural time of 176 minutes (range, 161–189 minutes).

All patients completed the follow-up monitoring, with all being compliant to the 7-day Holter monitoring. The compliance to all the required transtelephonic transmission during the initial 5 months was ≈88%. At 1 year, the overall freedom from recurrent AF/atrial tachycardia after a single procedure was 53% (75% in patients with paroxysmal AF versus 45% in those with persistent and longstanding persistent AF; $P=0.08$ for comparison), with most of the recurrences occurring between 3 and 9 months after the index procedure. Specifically, the recurrent arrhythmia was atypical atrial flutter in 65% of cases (69% in paroxysmal AF versus 71% in persistent and longstanding persistent AF; $P>0.99$) and AF in the remaining 35% (33% in paroxysmal AF versus 29% in persistent and longstanding persistent AF; $P>0.99$). All patients with recurrence underwent repeat ablation (average 1.6±0.7 procedures [1–3]). Recovery of conduction across the previously targeted areas (most frequently in the PV antrum) was noted in all patients undergoing a repeat ablation; all areas demonstrating reconnection were reisolated during the repeat procedure (Figure 1). In patients presenting with atypical atrial flutter, repeat isolation of areas with reconnection always resulted in acute termination of the flutter. The overall secondary success rate at 1 year was 76% off antiarrhythmic drugs and reached 91% including patients who were successfully treated with previously ineffective antiarrhythmic drugs. No major complications occurred. Minor complications (minor hematoma at the femoral vein access sites) occurred in 2 (4.6%) patients.

Long-Term Follow-Up

After the first year of follow-up, an additional 18 patients experienced recurrent arrhythmia, with a cumulative success rate of 49% at a median follow-up of 42 months (range, 38–48 months; Figure 2A). In particular, long-term arrhythmia-free survival was achieved in 67% of patients with paroxysmal AF, 56% with persistent AF, and 23% with longstanding persistent AF (Figure 2B).

Most of the late recurrences occurred between 16 and 23 months (Figure 2A and 2B), and all patients underwent an additional procedure (Figure 1). Atypical atrial flutter was the dominant mode of recurrence in these patients, occurring in 89% of cases, whereas the remaining 11% presented with recurrent AF. Among the clinical variables, only type of AF was found to predict long-term success, with the highest risk of recurrence among patients with longstanding persistent AF (odds ratio, 2.58; 95% confidence interval, 1.11–6.05; $P=0.028$).

Mechanism of Long-Term Recurrence, Ablation Strategy, and Outcomes

Persistent isolation of the previously targeted areas (ie, PV antra and posterior wall) was confirmed in 82% of patients. In the 16 patients presenting with atypical atrial flutter, activation and entrainment mapping were performed, and the arrhythmia was successfully terminated with ablation in 69% of cases. In the 2 patients presenting with recurrent AF, persistent isolation of the previously targeted areas was confirmed at repeat ablation, and the patients were converted to sinus rhythm with

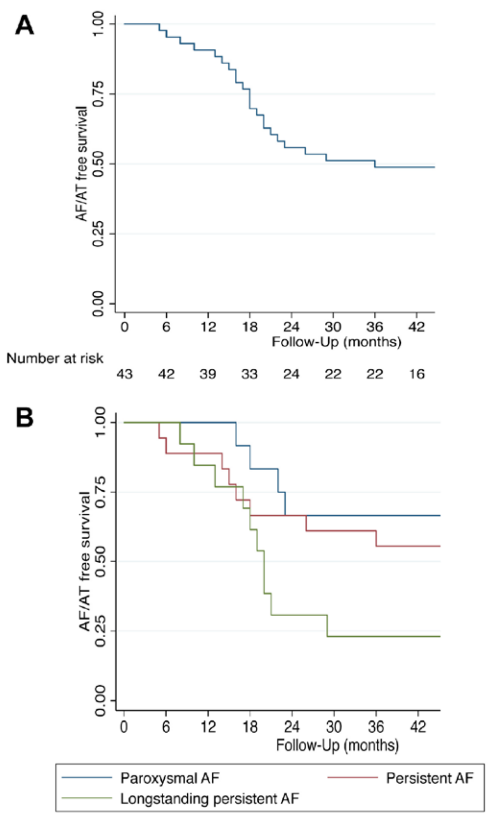

Figure 2. A, Kaplan–Meier survival curve showing multiple-procedure freedom from any atrial arrhythmia recurrence after pulmonary vein (PV) and posterior wall isolation (without ablation of non-PV triggers). **B**, Kaplan–Meier survival curve showing multiple-procedure freedom from any atrial arrhythmia recurrence after PV and posterior wall isolation (without ablation of non-PV triggers) according to the type of presenting atrial fibrillation (AF). Time zero is the last ablation targeting the PV and posterior wall without non-PV trigger ablation. AT indicates atrial tachycardia.

electric cardioversion. At high-dose isoproterenol challenge, non-PV sites of firing were detected in all patients. Non-PV triggers were most commonly mapped in the coronary sinus, left atrial appendage, interatrial septum, and right atrium/crista terminalis (Figure 3). Trigger ablation was performed with the aim of achieving electric isolation when triggers arose from the coronary sinus or left atrial appendage (LAA) or with focal ablation in other areas, such as the interatrial septum and the crista terminalis. In these cases, the amount of ablation increased by an average of 14±3 minutes for the coronary sinus (with the end point of complete isolation) or by an average of 31±4 minutes for achieving LAA isolation. No patient experienced any major complication, whereas 2 patients had a minor complication not requiring intervention (ie, 1 femoral pseudoaneurysm, 1 groin hematoma). No clinical variable was found to significantly predict non-PV triggers, although patients with non-PV triggers were older (62±9 versus 57±7 years; P=0.07), had larger left atrial diameters (52±7 mm versus 49±6 mm; P=0.29), and had lower left ventricular ejection fraction (58±5% versus 61±6%; P=0.08). At a median follow-up of 15 months (range, 8–19 months) after the last procedure, 94% of the patients remained free from AF/atrial tachycardia off antiarrhythmic drugs.

Discussion

The present study reports the results of catheter ablation of AF in a large series of patients with HCM, with the longest follow-up to date. The major findings are as follows: (1) catheter ablation of AF in patients with HCM is a safe and effective approach to achieve long-term freedom from recurrent arrhythmia; (2) PV and posterior wall isolation alone are insufficient to obtain satisfactory long-term results even when permanent isolation is achieved; (3) non-PV triggers can be demonstrated in the majority of HCM patients with late arrhythmia recurrence; and (4) ablation of non-PV triggers is associated with a significant improvement in the long-term arrhythmia-free survival.

AF has a major effect on morbidity and mortality in patients with HCM.[14] Radiofrequency catheter ablation has been proposed as an effective rhythm-control treatment for HCM patients with AF.[4,6,15] Specifically, PV antrum isolation (with or without additional left atrial linear ablation)[4–6,15] has shown satisfactory results at mid-term follow-up. The present study shows that the benefit of PV antrum and posterior wall isolation is limited at the long-term follow-up, even when persistent isolation is achieved. Rather, non-PV triggers seem highly prevalent in these patients. These results support the concept

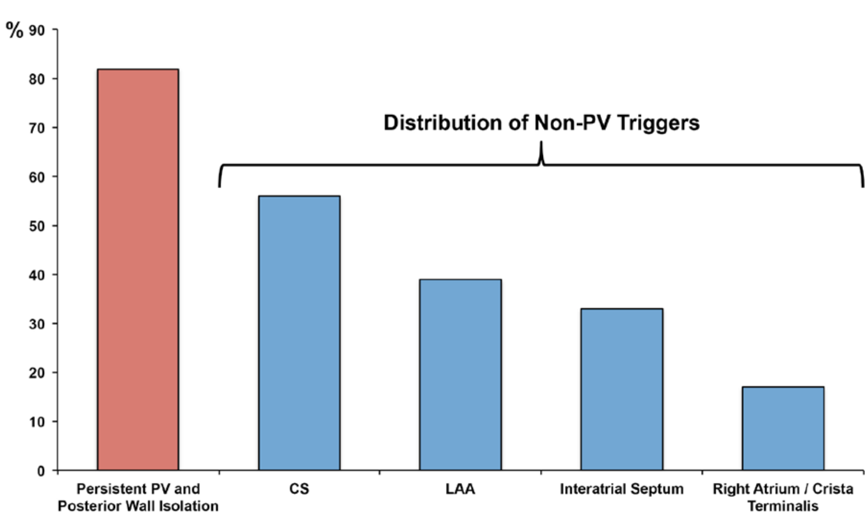

Figure 3. Electrophysiological findings at repeat procedures in patients presenting with late (≥1 year) atrial arrhythmia recurrence. PV indicates pulmonary vein.

that HCM patients with AF represent a specific population in whom PV isolation alone should not be considered sufficient as a stand-alone approach, and a more extensive ablation beyond the PV antrum and posterior wall is necessary to increase the long-term arrhythmia-free survival.

From a pathophysiological perspective, the effect of chronic atrial stretch because of diastolic dysfunction leading to diffuse atrial fibrosis,[16] the presence of mitral regurgitation caused by systolic anterior motion of the mitral valve, and the underlying atrial myopathy caused by the sarcomere protein gene mutations[14] might provide the substrate for multiple arrhythmogenic areas beyond the PVs in such patients. Previous studies evaluating the role of PV isolation in patients with HCM have shown that enlarged left atria, increasing age, and more advanced heart failure symptoms are predictors of arrhythmia recurrence after PV isolation[4]; the presence and role of non-PV triggers were not investigated in such studies, and the electrophysiological mechanisms underlying the lack of clinical response to PV isolation during follow-up remained undefined. Non-PV triggers could provide an explanation for the lack of sustained response to PV isolation shown in previous studies[4] because older age,[17] enlarged left atria,[18] and more advanced heart failure[19] have all been linked to a higher prevalence of non-PV triggers.

The present study also allows to draw clinically relevant conclusions on the optimal ablation strategy in these patients by showing that non-PV trigger ablation is associated with a significant arrhythmia-free survival benefit. More than 90% of patients were free from any recurrent arrhythmia without antiarrhythmic medications at an average of 14 months after the last procedure. The majority of patients with late arrhythmia recurrence presented with atypical atrial flutter, which was successfully mapped and ablated in approximately two thirds of cases. Flutter termination was not found to predict the long-term outcome in our patient cohort (P=0.49); again, trigger ablation seemed to be the only reliable predictor of success. These findings are in line with the concept that postablation-organized reentrant arrhythmias are the consequence of spontaneous triggering from specific structures, such as the PV, the coronary sinus, the LAA or the interatrial septum/right atrium.[20]

Study Limitations

This study had a prospective nonrandomized design and included a relatively small sample of patients. The presence of non-PV triggers was not assessed at the time of the index procedure and for repeat procedures during the first year of follow-up because of concerns of inducing or worsening intraventricular obstruction during isoproterenol test. However, no complications were observed during high-dose isoproterenol test at repeat procedures beyond 1 year, thus suggesting that isoproterenol challenge is safe in these patients, albeit we did not actively assess the presence of a dynamic gradient during the isoproterenol challenge. In addition, we could not evaluate whether non-PV triggers were already present at the time of the first ablation or only represented a late phenomenon responsible for arrhythmia recurrence at long-term follow-up. The lack of assessment for PV exit block might represent another limitation. Most of the late recurrences were observed between 16 and 23 months after the index procedure, which might be explained by the fact that most of the follow-up beyond 1 year occurred within that time frame. It is possible that, if the follow-up was longer, more late recurrences might be seen. Finally, assessment of the left atrial function after ablation was not an end point of the study and was performed only in patients undergoing extensive anterior ablation, including isolation of the LAA.

Conclusions

PV isolation in patients with HCM is feasible and safe, although is not effective in preventing late (≥1 year) AF recurrences in ≈50% of patients. Non-PV triggers seem to be responsible for late recurrences in the majority of these patients. This supports the appropriateness of a more extensive ablation strategy targeting multiple structures other than the PV antra to improve long-term success.

Disclosures

Dr Natale has received consultant fees or honoraria from Biosense Webster, Boston Scientific, Medtronic, Biotronik, and LifeWatch. Dr Biase is a consultant for Biosense Webster and Hansen Medical. The other authors report no conflicts.

References

1. Spirito P, Seidman CE, McKenna WJ, Maron BJ. The management of hypertrophic cardiomyopathy. *N Engl J Med*. 1997;336:775–785.
2. Gersh BJ, Maron BJ, Bonow RO, Dearani JA, Fifer MA, Link MS, Naidu SS, Nishimura RA, Ommen SR, Rakowski H, Seidman CE, Towbin JA, Udelson JE, Yancy CW; American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines; American Association for Thoracic Surgery; American Society of Echocardiography; American Society of Nuclear Cardiology; Heart Failure Society of America; Heart Rhythm Society; Society for Cardiovascular Angiography and Interventions; Society of Thoracic Surgeons. 2011 ACCF/AHA guideline for the diagnosis and treatment of hypertrophic cardiomyopathy: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2011;124:2761–2796.
3. Wann LS, Curtis AB, January CT, Ellenbogen KA, Lowe JE, Estes NA 3rd, Page RL, Ezekowitz MD, Slotwiner DJ, Jackman WM, Stevenson WG, Tracy CM, Fuster V, Rydén LE, Cannom DS, Le Heuzey JY, Crijns HJ, Lowe JE, Curtis AB, Olsson S, Ellenbogen KA, Prystowsky EN, Halperin JL, Tamargo JL, Kay GN, Wann LS, Jacobs AK, Anderson JL, Albert N, Hochman JS, Buller CE, Kushner FG, Creager MA, Ohman EM, Ettinger SM, Stevenson WG, Guyton RA, Tarkington LG, Halperin JL, Yancy CW; 2006 Writing Committee Members; ACCF/AHA Task Force Members. 2011 ACCF/AHA/HRS focused update on the management of patients with atrial fibrillation (Updating the 2006 Guideline): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Heart Rhythm*. 2011;8:157–176.
4. Di Donna P, Olivotto I, Delcrè SD, Caponi D, Scaglione M, Nault I, Montefusco A, Girolami F, Cecchi F, Haissaguerre M, Gaita F. Efficacy of catheter ablation for atrial fibrillation in hypertrophic cardiomyopathy: impact of age, atrial remodelling, and disease progression. *Europace*. 2010;12:347–355.
5. Bunch TJ, Munger TM, Friedman PA, Asirvatham SJ, Brady PA, Cha YM, Rea RF, Shen WK, Powell BD, Ommen SR, Monahan KH, Haroldson JM, Packer DL. Substrate and procedural predictors of outcomes after catheter ablation for atrial fibrillation in patients with hypertrophic cardiomyopathy. *J Cardiovasc Electrophysiol*. 2008;19:1009–1014.
6. Kilicaslan F, Verma A, Saad E, Themistoclakis S, Bonso A, Raviele A, Bozbas H, Andrews MW, Beheiry S, Hao S, Cummings JE, Marrouche NF, Lakkireddy D, Wazni O, Yamaji H, Saenz LC, Saliba W, Schweikert RA, Natale A. Efficacy of catheter ablation of atrial fibrillation in patients with hypertrophic obstructive cardiomyopathy. *Heart Rhythm*. 2006;3:275–280.

7. Maron BJ, McKenna WJ, Danielson GK, Kappenberger LJ, Kuhn HJ, Seidman CE, Shah PM, Spencer WH III, Spirito P, Ten Cate FJ, Wigle ED; Task Force on Clinical Expert Consensus Documents. American College of Cardiology; Committee for Practice Guidelines. European Society of Cardiology. American College of Cardiology/European Society of Cardiology clinical expert consensus document on hypertrophic cardiomyopathy. A report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents and the European Society of Cardiology Committee for Practice Guidelines. *J Am Coll Cardiol*. 2003;42:1687–1713.
8. Fuster V, Ryden LE, Cannom DS, Crijns HJ, Curtis AB, Ellenbogen KA, Halperin JL, Le Heuzey JY, Kay GN, Lowe JE, Olsson SB, Prystowsky EN, Tamargo JL, Wann S, Smith SC Jr, Jacobs AK, Adams CD, Anderson JL, Antman EM, Hunt SA, Nishimura R, Ornato JP, Page RL, Riegel B, Priori SG, Blanc JJ, Budaj A, Camm AJ, Dean V, Deckers JW, Despres C, Dickstein K, Lekakis J, McGregor K, Metra M, Morais J, Osterspey A, Zamorano JL, American College of Cardiology/American Heart Association Task Force on Practice G, European Society of Cardiology Committee for Practice G, European Heart Rhythm A, Heart Rhythm S. ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation. A report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation): developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. *Circulation*. 2006;114:e257–e354.
9. Di Biase L, Burkhardt JD, Mohanty P, Sanchez J, Horton R, Gallinghouse GJ, Lakkireddy D, Verma A, Khaykin Y, Hongo R, Hao S, Beheiry S, Pelargonio G, Dello Russo A, Casella M, Santarelli P, Santangeli P, Wang P, Al-Ahmad A, Patel D, Themistoclakis S, Bonso A, Rossillo A, Corrado A, Raviele A, Cummings JE, Schweikert RA, Lewis WR, Natale A. Periprocedural stroke and management of major bleeding complications in patients undergoing catheter ablation of atrial fibrillation: the impact of periprocedural therapeutic international normalized ratio. *Circulation*. 2010;121:2550–2556.
10. Kanj M, Wazni O, Natale A. Pulmonary vein antrum isolation. *Heart Rhythm*. 2007;4(3 Suppl):S73–S79.
11. Elayi CS, Verma A, Di Biase L, Ching CK, Patel D, Barrett C, Martin D, Rong B, Fahmy TS, Khaykin Y, Hongo R, Hao S, Pelargonio G, Dello Russo A, Casella M, Santarelli P, Potenza D, Fanelli R, Massaro R, Arruda M, Schweikert RA, Natale A. Ablation for longstanding permanent atrial fibrillation: results from a randomized study comparing three different strategies. *Heart Rhythm*. 2008;5:1658–1664.
12. Bhargava M, Di Biase L, Mohanty P, Prasad S, Martin DO, Williams-Andrews M, Wazni OM, Burkhardt JD, Cummings JE, Khaykin Y, Verma A, Hao S, Beheiry S, Hongo R, Rossillo A, Raviele A, Bonso A, Themistoclakis S, Stewart K, Saliba WI, Schweikert RA, Natale A. Impact of type of atrial fibrillation and repeat catheter ablation on long-term freedom from atrial fibrillation: results from a multicenter study. *Heart Rhythm*. 2009;6:1403–1412.
13. Di Biase L, Santangeli P, Natale A. How to ablate long-standing persistent atrial fibrillation? *Curr Opin Cardiol*. 2013;28:26–35.
14. Olivotto I, Cecchi F, Casey SA, Dolara A, Traverse JH, Maron BJ. Impact of atrial fibrillation on the clinical course of hypertrophic cardiomyopathy. *Circulation*. 2001;104:2517–2524.
15. Gaita F, Di Donna P, Olivotto I, Scaglione M, Ferrero I, Montefusco A, Caponi D, Conte MR, Nistri S, Cecchi F. Usefulness and safety of transcatheter ablation of atrial fibrillation in patients with hypertrophic cardiomyopathy. *Am J Cardiol*. 2007;99:1575–1581.
16. Sciagrà R, Sotgia B, Olivotto I, Cecchi F, Nistri S, Camici PG, Pupi A. Relationship between atrial fibrillation and blunted hyperemic myocardial blood flow in patients with hypertrophic cardiomyopathy. *J Nucl Cardiol*. 2009;16:92–96.
17. Santangeli P, Di Biase L, Mohanty P, Burkhardt JD, Horton R, Bai R, Mohanty S, Pump A, Gibson D, Couts L, Hongo R, Beheiry S, Natale A. Catheter ablation of atrial fibrillation in octogenarians: safety and outcomes. *J Cardiovasc Electrophysiol*. 2012;23:687–693.
18. Mohanty S, Mohanty P, Di Biase L, Bai R, Pump A, Santangeli P, Burkhardt D, Gallinghouse JG, Horton R, Sanchez JE, Bailey S, Zagrodzky J, Natale A. Impact of metabolic syndrome on procedural outcomes in patients with atrial fibrillation undergoing catheter ablation. *J Am Coll Cardiol*. 2012;59:1295–1301.
19. Lin D, Frankel DS, Zado ES, Gerstenfeld E, Dixit S, Callans DJ, Riley M, Hutchinson M, Garcia F, Bala R, Verdino R, Cooper J, Marchlinski FE. Pulmonary vein antral isolation and nonpulmonary vein trigger ablation without additional substrate modification for treating longstanding persistent atrial fibrillation. *J Cardiovasc Electrophysiol*. 2012;23:806–813.
20. Bai R, Di Biase L, Mohanty P, Dello Russo A, Casella M, Pelargonio G, Themistoclakis S, Mohanty S, Elayi CS, Sanchez J, Burkhardt JD, Horton R, Gallinghouse GJ, Bailey SM, Bonso A, Beheiry S, Hongo RH, Raviele A, Tondo C, Natale A. Ablation of perimitral flutter following catheter ablation of atrial fibrillation: impact on outcomes from a randomized study (PROPOSE). *J Cardiovasc Electrophysiol*. 2012;23:137–144.

CLINICAL PERSPECTIVE

Pulmonary vein antrum (PVA) isolation has been reported as a feasible and safe treatment for patients with hypertrophic cardiomyopathy and atrial fibrillation (AF), with satisfactory short- and mid-term results. The long-term outcomes of PVA isolation in this subset of patients are still poorly defined. The present study evaluated the long-term outcomes and mechanisms of arrhythmia recurrence in a consecutive series of 43 patients with hypertrophic cardiomyopathy and AF. PVA isolation (paroxysmal AF) and posterior wall isolation with complex fractionated atrial electrogram ablation (non–paroxysmal AF) were the end points at the time of the index procedure and for repeat procedures during the first year of follow-up. With such an ablation strategy, freedom from recurrent AF/atrial tachycardia was achieved in 49% of the cases after a median follow-up of 42 months. High-dose isoproterenol challenge was used to disclose non-PV trigger sites for patients presenting with recurrent arrhythmia beyond 1 year from the index procedure. Persistent isolation of the PVA and posterior wall was documented in 82% of patients, and extra-PV triggers were found in all cases and targeted for ablation. After a median follow-up of 15 months after the last procedure, 94% of the patients remained free from AF/atrial tachycardia off antiarrhythmic drugs. The results of this study highlight that PVA isolation has suboptimal long-term results in patients with hypertrophic cardiomyopathy, possibly because of a high incidence of non-PV triggers that are responsible for late arrhythmia recurrence.

Circulation
Arrhythmia and Electrophysiology

Catheter Ablation of Atrial Fibrillation in Hypertrophic Cardiomyopathy: Long-Term Outcomes and Mechanisms of Arrhythmia Recurrence

Pasquale Santangeli, Luigi Di Biase, Sakis Themistoclakis, Antonio Raviele, Robert A. Schweikert, Dhanunjaya Lakkireddy, Prasant Mohanty, Rong Bai, Sanghamitra Mohanty, Agnes Pump, Salwa Beheiry, Richard Hongo, Javier E. Sanchez, G. Joseph Gallinghouse, Rodney Horton, Antonio Dello Russo, Michela Casella, Gaetano Fassini, Claude S. Elayi, J. David Burkhardt, Claudio Tondo and Andrea Natale

Circ Arrhythm Electrophysiol. 2013;6:1089-1094; originally published online October 10, 2013;
doi: 10.1161/CIRCEP.113.000339
Circulation: Arrhythmia and Electrophysiology is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 1941-3149. Online ISSN: 1941-3084