Catheter ablation for the treatment of persistent atrial fibrillation: Maintenance of sinus rhythm with left atrial appendage and coronary sinus isolation after multiple ablation procedures

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Introduction

After seminal research demonstrated the pulmonary veins (PVs) and PV antrum contained substrates that can initiate and perpetuate paroxysmal atrial fibrillation (AF) in the majority of patients,1–3 catheter ablation with circumferential pulmonary vein isolation (PVI) has become the cornerstone treatment for the management of paroxysmal AF.4 However, in patients with persistent and long-standing persistent AF, single- and multiple-procedure recurrence rates remain high.5 Therefore, further ablation of left atrial and right atrial lines, ablation of complex fractionated atrial electrograms (CFAE), and, recently, the targeting of focal sources have been performed, with mixed results.6–8

We report on the results of multiple catheter ablation procedures in a patient with persistent AF, eventually targeting 2 specific AF substrates within the left atrial appendage (LAA) and coronary sinus (CS) after extensive ablation, including circumferential isolation of the ipsilateral PVs and superior vena cava (SVC), extensive CFAE ablation within the left atrium (LA) and right atrium (RA), and multiple linear lesions in both atria.

Case report

We present a case of a 37-year-old Syrian pilot, initially referred to our institution for the management of symptomatic, drug-resistant, long-standing persistent AF of 5 years' duration. He had failed medical therapy with flecainide, propafenone, sotalol, and amiodarone. In addition, he had undergone several attempts at electrical cardioversion; however, AF recurred after only a short period of sinus rhythm (SR). He had no other significant medical history and he was not obese. Blood pathology was essentially unremarkable, with a normal thyroid function test. Transthoracic echocardiography revealed no evidence of left ventricular systolic or diastolic dysfunction, no valvular dysfunction, and no pulmonary hypertension. The LA size was 50 mm.

The initial electrophysiology study (EPS) was performed under sedation with midazolam, sufentanil, and a continuous infusion of propofol on October 18, 2010. Via femoral venous access, an octapolar catheter was placed in the CS and double transseptal punctures were performed using 8.5 French SL1 long sheaths (St Jude Medical, St Paul, MN) and a transseptal needle. After both long sheaths were advanced into the LA, a 3.5 mm irrigated-tip ablation catheter was used in conjunction with a 3-dimensional electroanatomic mapping system (CARTO; Biosense Webster, Diamond Bar, CA) to reconstruct the LA. PV angiography was performed to identify the PV ostia, which were then marked on the LA map using tags. A 20 mm spiral catheter was used to identify the PV potentials within the PVs and ipsilateral wide circumferential lines were ablated around the septal and lateral PVs. After all PVs were isolated, the patient remained in AF and electrical cardioversion (DCR) was attempted 3 times with re-induction of AF following a few beats of SR. Through use of the spiral catheter, the earliest activation during re-induction was identified in the SVC; therefore isolation of the SVC was performed. After SVC isolation, re-attempts at DCR again resulted in re-initiation of AF, this time with the earliest activation in the CS. Ablation was then
KEY TEACHING POINTS

- Catheter ablation for atrial fibrillation (AF) is a step-wise approach.
- Iatrogenic atrial arrhythmias can occur after AF ablation.
- AF can be initiated from several different focal sources, which may be unmasked only after elimination of other sources.
- Elimination of sources that initiate AF can render patients arrhythmia-free and improve quality of life.

performed targeting fractionated signals in the posterior LA as well as the CS until no further CFAEs were seen in these areas. DCR was then repeated with conversion to and maintenance of SR.

In-hospital Holter monitoring postprocedure showed recurrent atrial tachyarrhythmias. A second EPS was therefore performed 2 days after the initial procedure. Access to the LA was obtained as described above. During the second procedure, no recovered PV conduction was seen, and an atrial tachyarrhythmia was documented with a relatively stable cycle length (CL) of 210–230 ms within the LAA during AF. CFAE ablation was therefore performed at the anterior wall of the LA near the LAA, at the area close to the posterior and lateral mitral annulus, and finally within the posterior CS, which led to conversion of AF to typical right atrial flutter with a CL of 240 ms. Therefore, ablation of a cavotricuspid isthmus (CTI) line restored stable SR. During SR, the PVs were confirmed isolated. Further ablation at the CTI and the mitral isthmus resulted in bidirectional conduction block over both atrial isthm.

Further monitoring showed recurrent atrial tachyarrhythmias with predominantly AF and occasional AT 4 days after the second procedure. Therefore, a third EPS was performed 6 days later. Three-dimensional mapping demonstrated no areas with CFAE in the LA, RA, and CS except at the LA anterior wall. Ablation at the LA anterior wall converted AF to an AT with a stable CL of 270 ms and earliest activation at the ridge and base of the LAA. Ablation at this region resulted in stable SR. PACing maneuvers were then performed to demonstrate bidirectional block of the CTI and mitral isthmus and no recovered PV conduction. LAA isolation was not performed, as no further AFs/ATs were inducible with burst pacing (shortest pacing CL = 240 ms) with and without isoproterenol at the end of the ablation procedure.

Postprocedural Holter monitoring showed only short episodes of paroxysmal AF, which was effectively suppressed with sotalol. Therefore, the patient was medically treated with sotalol 80 mg 3 times a day and flecainide 100 mg twice a day, and was anticoagulated with warfarin on discharge. After 6 months of medical treatment and maintenance of stable SR after the third ablation, all medications were ceased and recurrence occurred. Holter monitoring demonstrated paroxysmal AF and frequent atrial extrasystole (AE) with salvos. At this time, transesophageal echocardiography was unremarkable, except for a patent foramen ovale and potentially iatrogenic atrial septal defect. Of note, the LA diameter had reduced to 45 mm.

The fourth ablation procedure was performed on June 10, 2011. During EPS, all PVs were still isolated. After extensive ablation of CFAEs in the LA and RA, the LAA activation recorded on a spiral catheter placed within the LAA became relatively constant, with faster activity (CL 153 ms) compared to the activation within the CS (Figure 1A). PACing within the LAA (CL 130 ms) resulted in AF termination and the patient remained in a stable SR (Figure 1B). Therefore, electrical isolation of the LAA was performed. Mapping demonstrated a small gap at the mitral isthmus line, and further ablation at this site led to completion of the LA isthmus line and to LAA isolation (Figure 2A and B). Afterwards, no further tachycardias were inducible with and without isoproterenol.

Postprocedure monitoring for 2 days showed stable SR with very frequent AEs, which degenerated into a short run of AF during exercise. Therefore, a fifth EPS was performed 3 days after the fourth ablation procedure. The LAA was shown to be still isolated. Frequent AEs with very short coupling intervals were observed, which became shorter with intravenous isoproterenol infusion. These eventually degenerated into AF when the AE coupling interval shortened to 116 ms (Figure 3A) Using the 3.5-mm-tip ablation catheter, the site of earliest atrial activation was identified within the lateral CS (4 o’clock on the mitral annulus) (Figure 3B). Focal ablation at this site with a maximum power output of 20 W eliminated the trigger (Figure 3C). At the end of the procedure, no further AFs/ATs/AEs were inducible with aggressive stimulation and isoproterenol infusion.

The patient was discharged on sotalol 80 mg daily and warfarin. Sotalol was ceased 3 months after the last ablation. Anticoagulation was continued owing to the LAA isolation. During 3 years of regular follow-up with Holter monitoring, no further atrial tachyarrhythmias were documented.

Discussion

In patients with persistent and long-standing persistent AF, mechanisms that initiate and sustain AF remain undefined in individual patients. This is reflected in the single- and multiple-procedure success rates of catheter ablation for the management of AF.5,9 Because of this, additional techniques have been employed to treat atrial tachyarrhythmias, such as atrial lines and ablation of CFAEs, with variable results.5,7,10 In contrast to paroxysmal AF, the pathophysiology seems to be different in persistent AF, with more involvement of the whole atrium.6,11 This is seen during electroanatomic mapping, where diseased myocardium is represented by more extensive areas of low voltage and fractionated potentials.
Figure 1  Left atrial appendage (LAA) activity. A: Electrogram recordings demonstrating rapid firing within the LAA, as seen by the lasso signals. B: Pacing from within the LAA leads to termination of atrial fibrillation.
Figure 2  Left atrial appendage (LAA) isolation. A: Ablation at the posterior mitral isthmus leads to isolation of the LAA. B: Intracardiac electrograms showing LAA isolation. The lasso is placed in the LAA, with 1:1 conduction during the first 3 beats, then no further signal on the spiral catheter during sinus rhythm (entrance block). Red tags = ablation points; white tags = pulmonary vein ostia; pink tags = fractionated potentials; yellow tag = point of isolation of the LAA; AP = anterior-posterior; PA = posterior-anterior; RA = right atrium; LA = left atrium; CS = coronary sinus.
Figure 3  Ablation of focal atrial extrasystoles (AEs) that degenerated into atrial fibrillation. A: Intracardiac electrograms showing recurrent AEs with earliest activation at CS 1,2 (black arrows). Under isoproterenol infusion, the coupling interval became shorter, then degenerated into atrial fibrillation. B: Intracardiac electrograms showing a small, fragmented signal (red arrow) on the distal mapping catheter prior to ablation at the lateral coronary sinus. C: Three-dimensional electroanatomic map of the right atrium, left atrium, and coronary sinus showing large areas of low voltage. Ablation at the lateral coronary sinus (red tags) eliminated the frequent AEs.
During the first 3 procedures in our case, PVI and ablation at the LA anterior wall resulted in conversion of AF to AT, and eventual completion of the mitral isthmus line terminated the tachycardia. During the fourth procedure, a clear substrate with fast activation was demonstrated within the LAA. This substrate was confirmed when the atrial tachyarrhythmia was only be terminated with burst pacing from within the LAA during ongoing AF that was refractory to PVI and CFAE ablation in the LA during the initial 3 procedures. Interestingly, the AE focus from the CS was not initially unmasked after LAA isolation and elimination of the AF substrate, even with intravenous isoproterenol during the fourth procedure. This AE substrate in the CS was seen only during the fifth procedure, which indicates that the AE substrate had temporal variability. This strongly supports multiple substrates for the perpetuation of AF in this patient. Although extensive ablation in this patient led to the identification of several different sources of AF initiation and perpetuation and the elimination of AF, as well as other atrial tachyarrhythmias, one must assess the benefits and risks involved in undertaking such extensive ablation, particularly in young patients. The risk of complications such as tamponade and esophageal fistulae may increase as the amount and duration of lesions increase. In addition, the risk of development of iatrogenic atrial tachyarrhythmias should be taken into consideration after undergoing an extensive ablation strategy. Generally, re-do procedures are postponed 2–3 months, and this is the strategy undertaken in our center. However, in this present case, the second and third redo procedures were performed soon after the initial ablation secondary to the identification of a likely re-entrant AT. On the other hand, such early re-do procedures may have provided the substrate for the multiple complex atrial tachyarrhythmias that were seen subsequently. Waiting out the 3-month blanking period that is usually used post atrial tachyarrhythmia ablations before considering re-do procedures rules out the acute effects of catheter ablation and may reduce the amount of ablation required. Additionally, optimizing medical and lifestyle management plays an important role in the overall management of patients with complex atrial arrhythmias. However, in patients where focal sources can be identified and eliminated, as with our patient during the fourth and fifth procedures, rendering patients arrhythmia-free can significantly improve quality of life and improve long-term atrial and LAA function.

**Conclusion**

We demonstrate that in persistent AF, substrates that initiate and perpetuate atrial tachyarrhythmias can be identified in several left and right atrial structures. Isolation of these structures can eliminate the substrates and lead to maintenance of SR.

**References**

1. Haissaguerre M, Jais P, Shah DC, Takahashi A, Hocini M, Quiniou G, Garrigue S, Le Mouroux A, Le Métayer P, Clémenty J. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. N Engl J Med 1998;339:659–666.
2. Ouyang F, Bainsch D, Ernst S, Schumann A, Hachiyi H, Chen M, Chun J, Folk P, Khanedani A, Antz M, Kuck KH. Complete isolation of left atrium surrounding the pulmonary veins: new insights from the double-Lasso technique in paroxysmal atrial fibrillation. Circulation 2004;110:2090–2096.
3. Ouyang F, Antz M, Ernst S, et al. Recovered pulmonary vein conduction as a dominant factor for recurrent atrial tachyarrhythmias after complete circular isolation of the pulmonary veins: lessons from double Lasso technique. Circulation 2005;111:127–135.
4. Calkins H, Kuck KH, Cappato R, et al. 2012 HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design: a report of the Heart Rhythm Society (HRS) Task Force on Catheter and Surgical Ablation of Atrial Fibrillation. Developed in partnership with the European Heart Rhythm Association (EHRA), a registered branch of the European Society of Cardiology (ESC) and the European Cardiac Arrhythmia Society (ECAS); and in collaboration with the American College of Cardiology (ACC), American Heart Association (AHA), the Asia Pacific Heart Rhythm Society (APHRS), and the Society of Thoracic Surgeons (STS). Endorsed by the governing bodies of the American College of Cardiology Foundation, the American Heart Association, the European Cardiac Arrhythmia Society, the European Heart Rhythm Association, the Society of Thoracic Surgeons, the Asia Pacific Heart Rhythm Society, and the Heart Rhythm Society. Heart Rhythm 2012;9(4):619–670.
5. Tilz RR, Rüllig A, Thum AM, Aya A, Wohlmuth P, Metzner A, Mathew S, Yoshiga Y, Wissner E, Kuck KH, Ouyang F. Catheter ablation of long-standing persistent atrial fibrillation: 5-year outcomes of the Hamburg Sequential Ablation Strategy. J Am Coll Cardiol 2012;60:1921–1929. Available from http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?dbfrom=pubmed&cmd=prlinks.
6. Nadermeh K1, McKenzie J, Kosar E, Schwab M, Sunaneewitayakul B, Vasavakul T, Khunnawat C, Ngarmokus T. A new approach for catheter ablation of atrial fibrillation: mapping of the electrophysiologic substrate. J Am Coll Cardiol 2004;43:2044–2053.
7. Oral H, Chugh A, Yoshida K, et al. A randomized assessment of the incremental role of ablation of complex fractionated atrial electrograms after atrial pulmonary vein isolation for long-lasting persistent atrial fibrillation. J Am Coll Cardiol 2009;53:782–789.
8. Narayan SM, Krummen DE, Shivkumar K, Clopton P, Rappel W-J, Miller JM. Treatment of atrial fibrillation by the ablation of localized sources: CONFIRM (Conventional Ablation for Atrial Fibrillation With or Without Focal Impulse and Rotor Modulation) trial. J Am Coll Cardiol 2012;60:628–636.
9. Ouyang F, Tilz R, Chun J, Schmidt B, Wissner E, Zerrn T, Neven K, Köktürk B, Konstantinidou M, Metzner A, Fuenkrianz A, Kuck KH. Long-term results of catheter ablation in paroxysmal atrial fibrillation: lessons from a 5-year follow-up. Circulation 2010;122:2368–2377.
10. Oral H, Chugh A, Good E, et al. Radiofrequency catheter ablation of chronic atrial fibrillation guided by complex electrograms. Circulation 2007;115:2606–2612.
11. Sanders P, Berenfeld O, Hocini M, et al. Spectral analysis identifies sites of high-frequency activity maintaining atrial fibrillation in humans. Circulation 2005;112:789–797.