A CASE FOR EDUCATION

Provocation and ablation of non–pulmonary vein triggers in nonparoxysmal atrial fibrillation: Role of the coronary sinus

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Introduction

Catheter ablation is the most effective rhythm control strategy in patients with atrial fibrillation (AF). An ablation strategy targeting the pulmonary vein (PV) antra may achieve a remarkable long-term arrhythmia control in patients with paroxysmal AF, in whom the PVs are frequently the only source triggering AF. However, other extrapulmonary sources of ectopic triggers may play an important role in initiating atrial tachyarrhythmia paroxysms.1 As a result, an ablation strategy targeting those foci, which are harbored in specific regions within the atria and some thoracic veins (eg, left atrial posterior wall [PW], interatrial septum [IAS], crista terminalis [CT], left atrial appendage [LAA], superior vena cava [SVC], coronary sinus [CS]), has been demonstrated to significantly improve outcomes in nonparoxysmal AF patients.2–5 From a pathophysiological standpoint, as arrhythmia persists, progressive functional and structural changes occur in the atria and sites other than the PVs become more prone to trigger AF. Herein, we describe an explanatory case on the importance of seeking and ablating non-PV triggers in nonparoxysmal AF.

Case report

A 57-year-old male patient with a history of hypertension, hyperlipidemia, severe obstructive sleep apnea on continuous positive airway pressure, nonischemic dilated cardiomyopathy (ejection fraction: 35%–40%), and persistent AF with multiple failed electrical cardioversions was referred to our institution for consultation 8 months following radiofrequency (RF) catheter ablation (RFCA). He had experienced AF relapse 4 months post-procedure and 2 further electrical cardioversions had been attempted, with early arrhythmia recurrence thereafter. During the previous procedure, the PVs and the PW had been targeted for ablation. The patient reported to be severely symptomatic for dyspnea with marked limitation of physical activity while in AF. He was deemed a good candidate for repeat RFCA.

Antiarrhythmic therapy (flecainide 150 mg twice per day) was discontinued 1 week prior to ablation.

The patient presented to the electrophysiology laboratory in AF. The procedure was conducted under general anesthesia and uninterrupted oral anticoagulation (rivaroxaban 20 mg/day).1 A 7F 20-pole linear catheter was advanced via the right internal jugular vein, with electrodes spanning from the SVC and CT to the CS. After left atrial instrumentation was achieved by double transseptal puncture under fluoroscopic and intracardiac echocardiography guidance, a circular mapping catheter (CMC; Lasso 20 mm/10 electrodes, Biosense Webster, Irvine, CA) was placed in all 4 PV antra and along the PW of the left atrium. Voltage mapping revealed severe LA scarring (Figure 1). The left and right PVs remained electrically silent from the previous procedure. The PW and the roof were reisolated using an electrogram-based ablation: all potentials recorded by the CMC were targeted for ablation, in order to

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achieve complete absence of electrical activity. Short-duration RF lesions were delivered to the PW/roof using a power of up to 45 W. A temperature probe was continuously moved along the esophagus to align the sensor with the ablation electrode; additionally, power and contact force titration allowed to avoid any esophageal damage. RF lesions were extended to involve the floor of the left atrium above the endocardial aspect of the CS, as well as the anterior roof and the mid-septal areas. The patient remained in AF despite ablation and isolation of the PW and roof.

Owing to the history of early AF recurrence post-ablation, the presence of persistent PV isolation, a significant atrial remodeling, and risk factors associated with a higher prevalence of non-PV triggers (eg, sleep apnea, hypertension, heart failure), the LAA was empirically targeted for ablation (Figure 2). Once the CMC was positioned at the level of the LAA ostium, high-power short-duration RF lesions (45–47 W for up to 15 s) were applied in order to target the earliest activation sites. Further energy delivery to the LAA terminated AF, restoring sinus rhythm (Figure 3). LAA isolation was successfully completed in sinus rhythm.
Subsequently, a pharmacologic challenge test with high-dose isoproterenol infusion (20 μg/min for 12 min) was started in order to check for PW reconnection, as well as elicit other latent non-PV triggers. Mapping of non-PV triggers during the pharmacologic test was performed following our standard institutional protocol, which includes multiple catheters positioned with the following setup: (1) the 10-pole CMC in the left superior PV recording the far-field LAA activity; (2) the 20-pole linear catheter recording the SVC, CT, and CS activity; (3) the ablation catheter in the right superior PV recording the far-field IAS.

Following isoproterenol infusion, there was no evidence of PV reconnection and the PW remained silent. A focal atrial tachycardia (cycle length 280 ms) was seen with earliest activation in the proximal electrodes of the distal 20-pole catheter (Figure 4) within the CS.

Additional RF energy was delivered epicardially to the CS, starting from the segment corresponding to the earliest activation recorded by the linear catheter. While ablating the CS, the atrial tachycardia terminated with restoration of sinus rhythm (Figure 5). Further ablation was performed inside the CS (epicardial CS ablation), as well as from the left atrium (endocardial CS ablation), until complete isolation was observed (Figure 6). Isolation was achieved via elimination of all potentials along the CS. The ablation catheter was moved every 5–10 seconds (maximum power 40 W) and impedance was continuously monitored to reduce the risk of steam pops. Continuous PR interval and esophageal temperature...
monitoring was performed, in order to prevent any significant damage to the esophagus or the conduction system.

Subsequently, the LAA regained conduction and was successfully reisolated (Figure 7). Dissociated firing was documented from the LAA once isolation was achieved.

The CMC was then placed in the SVC, which was electrically silent. A total of 63 minutes of RF energy lesions were delivered. The procedure was uncomplicated and the patient was discharged home the following day. An event recorder was provided for the first 6 months, which did not document any episode of atrial tachyarrhythmia. The patient remained asymptomatic and arrhythmia-free after 8 months of follow-up.

Discussion

Our case demonstrates the importance of non-PV trigger detection and ablation in patients with nonparoxysmal AF. The prevalence of non-PV triggers has been reported to be higher in specific subpopulations.1–5 Female sex, older age, and nonparoxysmal AF, as well as other comorbidities and cardiovascular conditions (eg, obesity, sleep apnea, heart failure, hypertrophic cardiomyopathy), have been consistently associated with a higher likelihood of extrapulmonary triggers initiating AF.

PV isolation might be insufficient to maintain sinus rhythm in these subsets of patients who frequently have different mechanisms initiating AF. Therefore, identification and ablation of non-PV sites clustering AF triggers becomes critical to improve long-term success rate. In our case, given the clinical history of persistent AF, obstructive sleep apnea, and reduced ejection fraction, a pharmacologic test with high-dose isoproterenol should have been performed and non-PV triggers ablated, if induced, at the time of the first procedure.

The role of the LAA in initiating and sustaining atrial tachyarrhythmias has been demonstrated in several clinical studies.3,5

In 2010, our group reported a prevalence of triggers from this site in 27% of patients with documented persistent PV

Figure 5  A: Radiofrequency applications to the proximal coronary sinus interrupted the atrial tachycardia. B: Fluoro image (anteroposterior) showing the ablation point (red star) where sinus rhythm was restored.

Figure 6  Complete isolation of the coronary sinus (CS) (B) was achieved with further ablation inside the CS (A; epicardial ablation), as well as from the left atrium (C; endocardial ablation). Red arrow: temperature probe.
isolation undergoing redo AF ablation. Subsequently, the BELIEF (Effect of Empirical Left Atrial Appendage Isolation on Long-term Procedure Outcome in Patients With Persistent or Longstanding Persistent Atrial Fibrillation Undergoing Catheter Ablation) randomized trial showed that empirical electrical isolation of the LAA improves long-term freedom from atrial tachyarrhythmias in long-standing persistent AF.

Of note, LAA electrical isolation is associated with a not negligible risk of thromboembolic events, which may occur if anticoagulation is interrupted or suboptimal. Therefore, adequate patient education and oral anticoagulation management and monitoring are of utmost importance to prevent complications.

The present case also highlights the arrhythmogenic role of the CS in atrial tachyarrhythmia recurrence.

From an anatomical standpoint, the length of the CS ranges between 3 and 5.5 cm and depends on the site of drainage of the posterolateral vein. Another anatomical landmark is the valve of Vieussens, which can be found in approximately 80%–90% of the hearts and represents the junction between the CS and the great cardiac vein. Similar to the PVs, the CS is surrounded by muscular sleeves that may generate rapid electrical activity. The muscular wall of the CS often ends when the great cardiac vein begins; however, sleeves may extend over the vein for 1 cm or more in some cases.

In an elegant study by Wit and colleagues on a canine model, electrical stimulation of the CS triggered sustained rhythmic activity, even after separation from the atria, and norepinephrine increased resting potentials and caused the development of delayed afterhyperpolarization and afterdepolarization.

As the muscular wall surrounds the CS and creates a connection with the left atrium, electrical isolation has to be achieved by targeting this structure from both the endocardium and the epicardium.

Several anatomical and preclinical studies demonstrated that the CS forms an important electrical connection between the atria. Its musculature is anatomically continuous with the left atrium in the proximal portion and with the right atrium at the ostium. As the role of impulse propagation between the atria in sustaining AF is known, results from surgical procedures demonstrated successful elimination of AF by targeting the muscular sleeves surrounding the CS. As such, CS isolation may significantly contribute to the success of AF ablation in 2 different ways. On one side, ablation of the CS muscular sleeves with abolition of all electrical potentials eliminates an important source of rapid repetitive electrical activity that may be involved in AF initiation. On the other side, CS isolation may interrupt an important electrical connection between the atria and avoid the development of unstable re-entry, thereby preventing AF perpetuation.

In a series of 45 paroxysmal and persistent AF patients, RFCA targeting the CS led to significant prolongation of the fibrillatory cycle length and terminated AF in approximately 35%.

Similar observations were reported in a population of paroxysmal AF patients, in whom electrical disconnection of the CS from the left atrium significantly reduced the likelihood of AF reinducibility and resulted in an 80% freedom from atrial tachyarrhythmias at 199 ± 35 days of follow-up.

**Conclusions**

Detection and elimination of non-PV triggers is of utmost importance to improve RFCA success rate. Special consideration should be given to patients with nonparoxysmal AF, as well as with comorbidities associated with a higher

**Figure 7** A: Left atrial appendage (LAA) reconnection with delayed activation was documented via the circular mapping catheter positioned at the level of the LAA ostium. B: The LAA was subsequently reisolated.
prevalence of extrapulmonary triggers. Among them, PV antrum isolation alone may result in early arrhythmia recurrence with low success rate. The CS is the most common site harboring AF triggers; its isolation may eliminate an important source of rapid repetitive electrical activity and prevent AF perpetuation.

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