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Persistent left superior vena cava as an arrhythmogenic source in atrial fibrillation: results from a multicenter experience

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Abstract

Background Persistent left superior vena cava (PLSVC) is one of the most frequently reported congenital anomalies and may be an important source of trigger of atrial fibrillation (AF).

Methods This was a multicenter retrospective experience including 28 patients with PLSVC who were referred for catheter ablation for drug-refractory symptomatic AF. Pulmonary vein and PLSVC isolation were performed (3.5-mm open irrigated tip ablation catheter at maximum power of 20 W, maximum temperature 43 °C with flow rate of 17 ml/min). Clinical outcomes such as complications and long-term freedom from AF were measured.

Results The mean age of the population was 61 ± 8 years, 21% were females, and AF duration was 60 ± 33 months. Sixty-one percent paroxysmal AF (17/28), 25% (7/28) persistent AF, and 14% (4/28) had long-standing persistent AF. There were no major complications that required any intervention. PLSVC isolation was achieved in 96% (27/28). Freedom from AF at 1 year without antiarrhythmic drugs was seen in 75% (21/28) of patients.

Conclusions In PLSVC patients with AF, segmental isolation of PLSVC appears to be feasible and safe and can translate into favorable clinical outcomes.

Keywords Atrial fibrillation · Persistent left superior vena cava syndrome · Radiofrequency ablation · Congenital anomaly

1 Introduction

Catheter ablation is currently a recommended treatment strategy for the management of symptomatic, drug-refractory atrial fibrillation (AF) [1, 2]. Pulmonary vein isolation (PVI) is a commonly accepted end point during AF ablation due to frequent triggers and arrhythmia substrate from the pulmonary veins [3]. Other major thoracic veins including vein of Marshall, superior vena cava, and azygous vein have specific electrical properties in the muscle sleeves at the veno–atrial junction that can trigger AF [4, 5].

Persistent left superior vena cava (PLSVC) has an incidence of 0.3–2% of the general population and 5–9% in patients with congenital heart disease [6, 7]. PLSVC occurs due to the persistence of left superior cardinal vein which regresses in majority of patients to form the ligament of Marshall [8].

PLSVC was previously reported in few case series to be a potential arrhythmogenic source of trigger in the initiation and maintenance of AF [4, 9–11]. While radiofrequency ablation (RFA) of PLSVC for symptomatic AF has been performed, there are high procedural complications reported in some published data [10]. Furthermore, majority of these patients who do not undergo complete PLSVC isolation have recurrence of AF requiring a multiple ablation procedures. The feasibility and safety of complete segmental isolation of the PLSVC and its impact on clinical outcomes requires further study. We report the largest multicenter experience on the safety and feasibility of RFA for AF in patients with PLSVC.

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2 Methods

This was a multicenter retrospective study including 28 patients with PLSVC from five centers who underwent RFA between February 2011 and October 2015 for drug-refractory symptomatic AF. Patient, procedural details and follow-up visits including hospitalizations, EKGs, holter/event monitor recordings, and imaging studies including CT scan, MRI, and echocardiograms were retrieved and analyzed. The Institutional review boards of the respective participating centers approved the study. Clinical outcomes such as complications and long-term freedom from AF at 1 year follow-up were measured.

2.1 Pulmonary vein isolation

The procedure of pulmonary vein isolation (PVI) has been described in detail previously [12]. Periprocedural imaging with either cardiac CT, MRI, or contrast echocardiography was performed in all patients. In brief, PV isolation was achieved using wide antral circumferential ablation (WACA) with a double-transseptal approach. Intracardiac echocardiography (ICE) and fluoroscopy was used to guide transseptal puncture. Two transseptal accesses were acquired using standard needles and sheaths. Left atrium was mapped using a circular mapping catheter (Lasso, Biosense Webster Inc.). Electroanatomical and voltage map was created in all patients. Electrical isolation was accomplished by PVI with 3.5-mm irrigated tip catheter. A maximum of 20–30 W of radiofrequency (RF) energy was used for ablation of the posterior wall of the left atrium at a flow rate of 17 ml/min targeting a maximum temperature of 43 °C. PVI was attempted in all patients undergoing first ablation with an endpoint of entrance and exit block as registered by the Lasso catheter in the respective pulmonary veins. In isoproterenol infusion at 20 μg/min was administered for 20 min to identify additional triggers in all patients. Additional focal or linear ablation was performed in patients who demonstrated ectopy either spontaneously or with isoproterenol.

In patients undergoing redo ablation, pulmonary vein isolation and line of block were assessed by pacing maneuvers using mapping and CS catheters. Ablation was performed in areas of reconnection.

2.2 Complex fractionated atrial electrogram ablation

CFAE was attempted in all patients with persistent and long-standing persistent AF after PVI. The procedure of complex fractionated atrial electrograms (CFAE) has been described in detail previously [13]. The common areas that were targeted included LA posterior wall, septum, roof, left atrial appendage, coronary sinus (CS), and crista terminalis.

2.3 Persistent left superior vena cava ablation

Mapping and identification of the electrical activity of the PLSVC was done in all patients. Isoproterenol infusion at 20 μg/min was administered for 20 min to identify triggers in patients who did not demonstrate spontaneous ectopy. In patient with AF, direct current cardioversion was performed and any early atrial ectopy originating from PLSVC was identified. Using ICE and fluoroscopy guidance, the circular Lasso mapping catheter was placed in the distal PLSVC and gradually pulled back to the coronary sinus ostium (Fig. 1a, b). Double potentials that consist of left atrial far field potentials and a local sharp PLSVC near field potentials were continuously recorded. Premature ectopy with earliest activation in PLSVC was observed during mapping.

Focal ablation was performed in the mid portion of the PLSVC at the level of left pulmonary veins and the body of the coronary sinus targeting all local high-frequency signals. Additional segmental isolation was also performed proximally at the coronary sinus ostium to disconnect various electrical connections (Fig. 1c, d). The power used for ablation in PLSVC was 15–20 W and was restricted to a maximum time of 20 s for each ablation point with a flow rate of 17 ml/min, targeting a maximum temperature of 43 °C. Lateral left atrium endocardial ablation was performed in a few patients at the discretion of the operator. The end point of ablation was electrical PLSVC isolation and ablation of the CS electrograms with disappearance of local near field potentials, identification of dissociated signals, and failure to capture adjacent structures with high-output pacing maneuvers. The ablation catheter was then advanced into the left atrium and exit block was confirmed by pacing with the mapping catheter in the PLSVC. Figures 2 and 3 demonstrates termination of AF and independent firing of the PLSVC after completely disconnecting the electrical circuits. Prior to ablation at the CS ostium, high-amplitude pacing was performed to ensure the ablation site was not close to the phrenic nerve. A coronary angiogram was performed to locate proximity to right coronary artery and left circumflex in a few patients at the discretion of the operator.

2.3.1 Follow-up

Transthoracic echocardiography and chest radiography were routinely performed post procedure to assess complications. All patients were followed post AF ablation at 1, 3, 6, and 12 months. All patients were assessed for clinical symptoms and underwent routine EKGs and 24-h holter monitoring on follow-up. Antiarrhythmic drugs were continued for a minimum of 2–3 months during the blanking period. Any tachycardia documented during the blanking period was not considered recurrence. Oral anticoagulation was continued for a minimum of 3-month post-ablation following which it was discontinued in patients with CHA_2DS_2 VASC < 2.

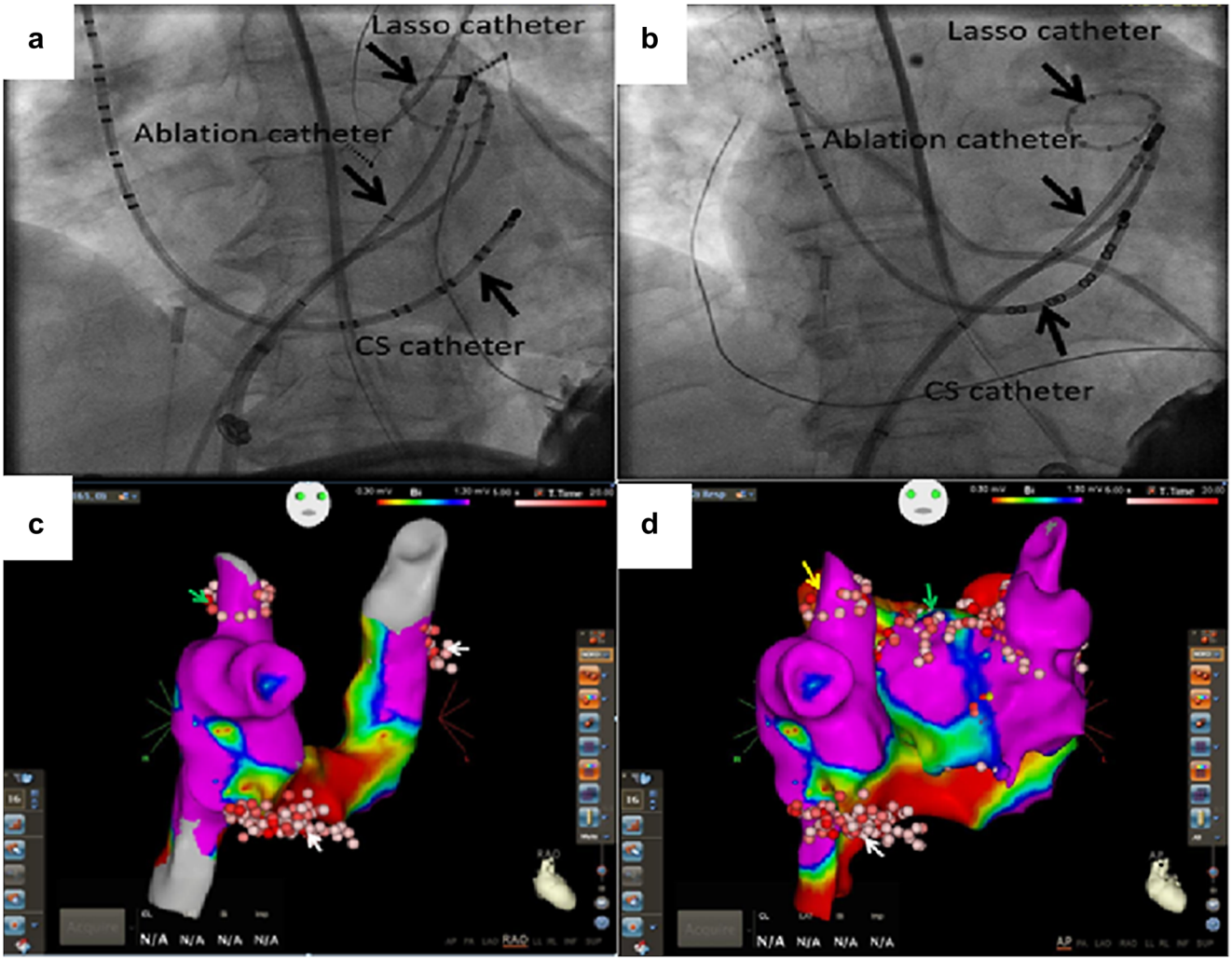

Fig. 1 **a** Fluoroscopy left anterior oblique (LAO) and **b** right anterior oblique (RAO) views demonstrating the Lasso and ablation catheters in the persistent left superior vena cava (PLSVC). Also seen is the coronary sinus (CS) catheter. **c** Carto voltage map in RAO projection demonstrating the right atrium, coronary sinus, and persistent left superior vena cava. Red color demonstrates scar tissue with voltage of < 0.3 mv. Dots represent areas of ablation performed at the superior vena cava (SVC)–right atrium (RA) junction (green arrow), proximal and distal PLSVC (white arrow). **d** Carto voltage map in AP (anterior-posterior) view demonstrating the right and left atrium; red color demonstrates scar tissue with voltage of < 0.3 mv. Dots represent areas of ablation performed at the SVC–RA junction (yellow), roof line (green), and CS and PLSVC (white)

2.3.2 Statistical methods

Categorical variables are represented as *N* (%) and continuous variables are represented as mean ± SD. Outcomes were measured based on recurrence of AF and procedural complications. Statistical analysis was performed using IBM SPSS Statistics version 23.0 (IBM, Armonk, New York).

3 Results

3.1 Patient demographics

A total of 28 patients with symptomatic drug-refractory AF who underwent catheter ablation was included in the study. Sixty-one percent paroxysmal AF (17/28), 25% (7/28) persistent AF, and 14% (4/28) had long-standing persistent AF. The mean age was 61 ± 8 years, 21% (6/28) were females and AF duration was 60 ± 33 months. One patient had received a prior aortic valve and extended root replacement due to a bicuspid aortic valve with severe regurgitation and coarctation. The mean LA size was 4.4 ± 0.8 cm and left ventricular ejection fraction was 58 ± 13%. Mean CHA2DS2-VASC score was 1.7 ± 1.2 and HAS-BLED score was 1.3 ± 1.1. Thirty-nine percent (11/28) underwent previous PVI for AF at other centers among which two patients underwent focal PLSVC and coronary sinus ablation (not complete segmental isolation). Table 1 demonstrates the other baseline patient characteristics. Although, only 46% of patients were on AAD just prior to the procedure, majority [98% (25/28)] had a prior history of failed AAD.

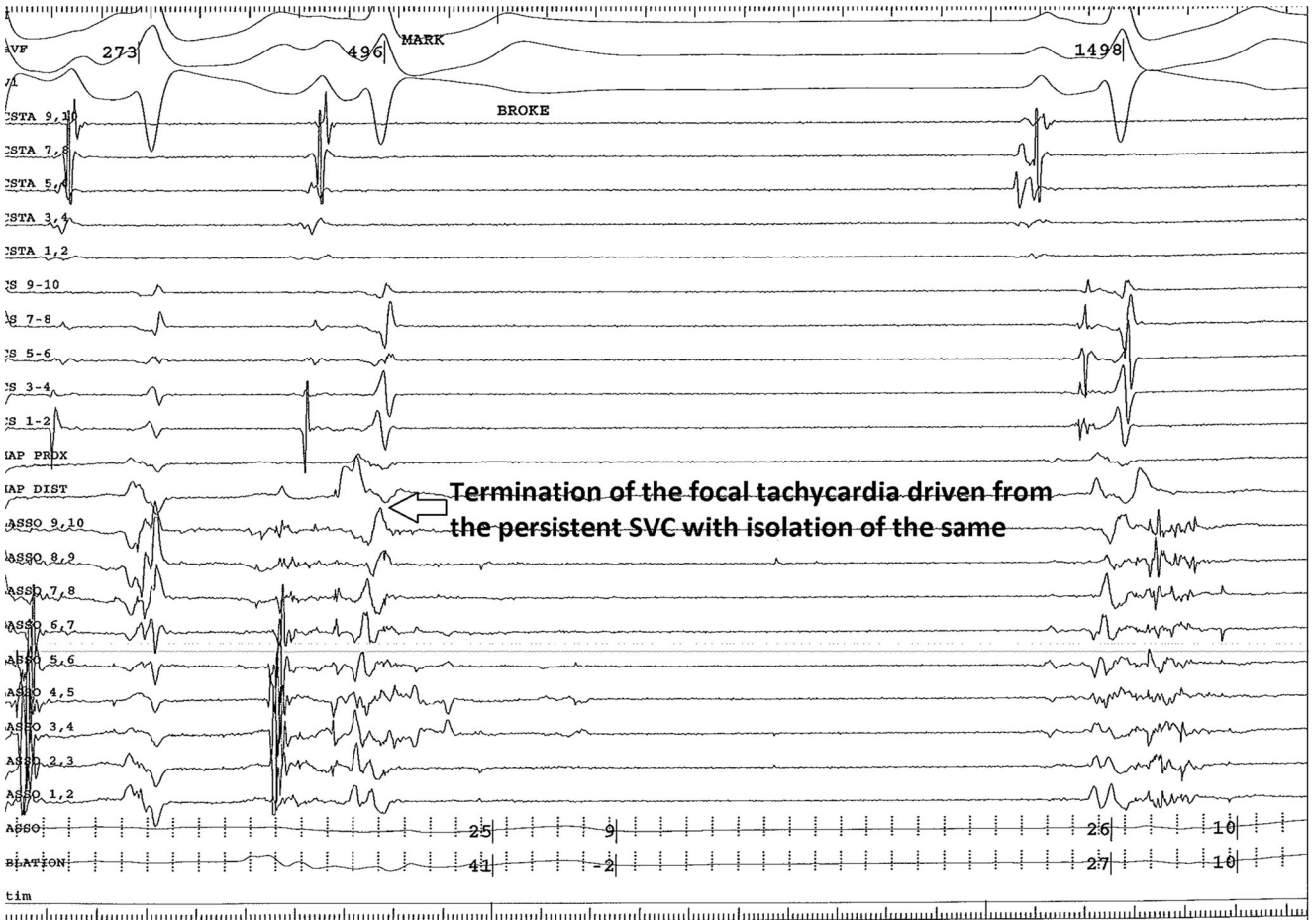

Fig. 2 Electrograms demonstrating termination of atrial fibrillation on complete isolation of persistent left superior vena cava (PLSVC)

3.2 Procedural characteristics

Table 2 demonstrates the procedural characteristics. All patients included in the study underwent RFA (radiofrequency ablation) under general anesthesia. About 61% (17/28) presented with sinus rhythm and only 7% (2/28) with paroxysmal AF presented with atrial arrhythmia including atrial tachycardia and flutter. PLSVC was identified on periprocedural CT scan in 86% (24/28), MRI 7% (2/28), and echocardiogram with left venous contrast administration in 7% (2/28). The site of insertion of PLSVC was the left atrium in 11% (3/28) and 89% (25/28) on the CS. A mapping system was used in all cases; 79% (22/28) with Carto (Biosense Webster), 18% (5/28) Ensite-Velocity (St. Jude Medical), and 4% (1/28) Rhythmia (Boston Scientific). Ectopy was spontaneously triggered from PLSVC in 11% (3/28) patients while isoproterenol triggered ectopy in the rest 89% (25/28) patients. Ectopy from PLSVC was repetitive and initiated sustained AF in 50% (14/28) patient. Electrical PLSVC isolation was attempted in all patients that involved extensive circumferential ablation in the mid-PLSVC, the body, and coronary sinus ostium but successful isolation was achieved in 96% (27/28). In 11% (3/28), no ablation was performed on the superior aspect of the coronary sinus ostium due to risk of AV block but extensive ablation was performed in the mid-PLSVC and body of the coronary sinus from which isolation was achieved in two patients. Lateral LA endocardial ablation was performed in 18% (5/28) of which four patients (14%, 4/28) developed mitral isthmus block. Isolation of PLSVC resulted in acute termination of AF in 35% (10/28) patients (Fig. 2). Dissociative firing of the PLSVC was observed in 18% (5/28) of patients (Fig. 3).

In the 39% (11/28) who underwent prior PVI (paroxysmal AF, 4 and persistent/long-standing persistent, 7), there was no evidence of pulmonary vein reconnection in all patients with paroxysmal AF and in three patients with persistent AF. Spontaneous or isoproterenol triggered ectopy were identified in the PLSVC in all patients who subsequently underwent complete isolation that resulted in termination of AF.

CFAE ablation was attempted in all patients with persistent and long-standing persistent AF but only performed in 45% (5/11) of patients in whom they were considered to be significant.

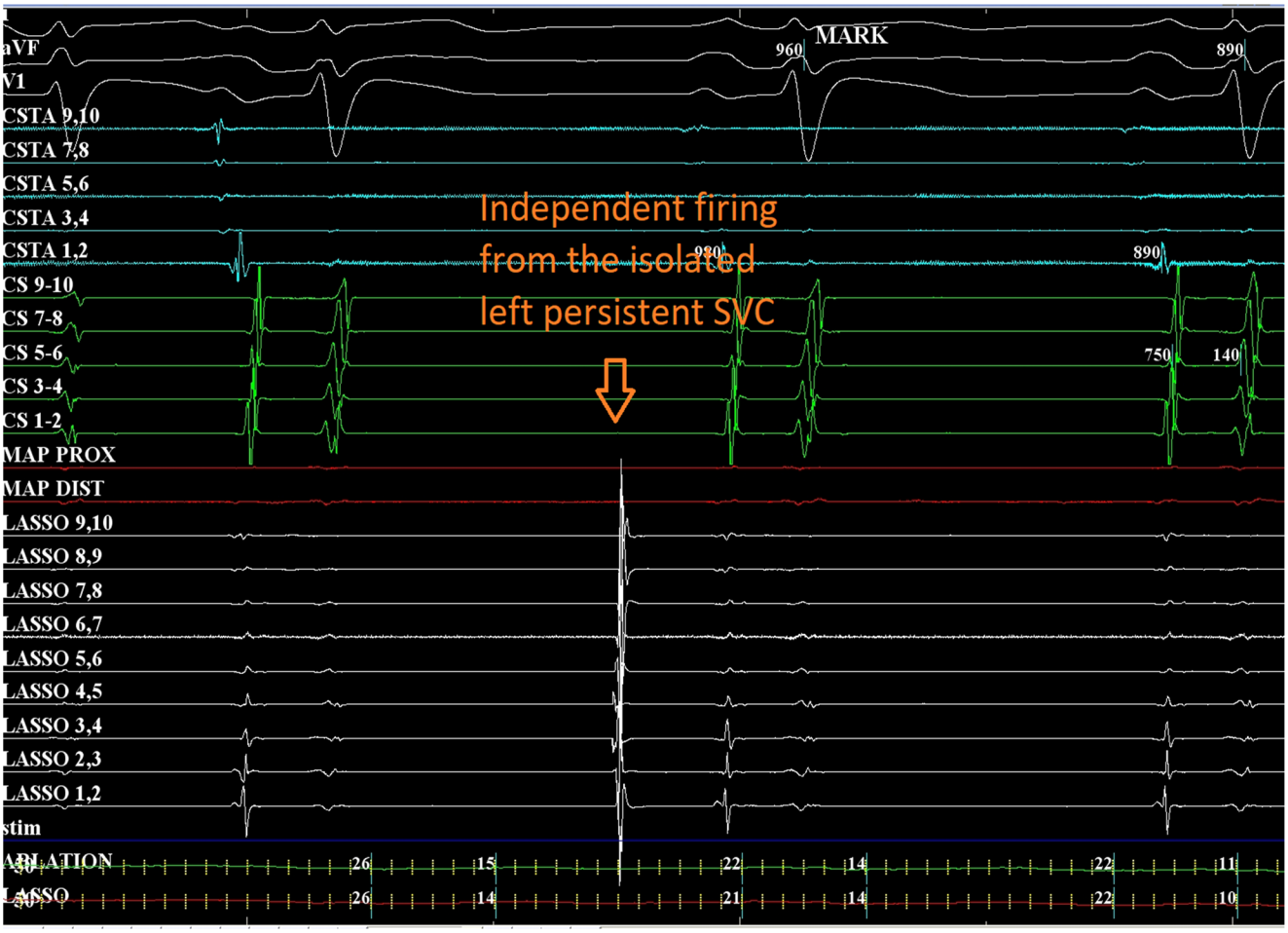

Fig. 3 Electrogram demonstrating independent firing from persistent left superior vena cava (PLSVC) on the Lasso mapping catheter following complete isolation of PLSVC from the CS. Lasso catheter is positioned distally in the PLSVC while CS catheter is more proximal in relationship to the Lasso. Coronary sinus (CS) catheter and surface EKG demonstrating sinus rhythm

3.3 Clinical outcomes

3.3.1 Complications

Total complications occurred in 14% (4/28) (Table 3). They were all minor complications not requiring any intervention. One patient developed a small pericardial effusion due to a steam pop while ablating near the left inferior pulmonary vein. Three patients had small groin hematomas all of which were observed and managed conservatively. No patients developed coronary sinus dissection, coronary damage, phrenic nerve palsy, or stroke/TIA.

3.3.2 Arrhythmia recurrence

Freedom from AF/AT at 1 year was seen in 75% (21/28) without antiarrhythmic drugs. In patients who underwent prior ablation elsewhere, freedom from AF/AT at 1 year was seen in 72.7% (8/11). Seventy-five percent (3/4) patients with paroxysmal AF who underwent prior PVI remained free from AF/AT at 1-year follow-up with complete segmental isolation of PLSVC. Of the seven patients who underwent prior PVI for persistent and long-standing persistent AF, 71% (5/7) remained free of AF at 1-year follow-up.

4 Discussion

4.1 Major findings

This is the largest retrospective multicenter experience on the feasibility and safety of PLSVC isolation during catheter ablation for AF. The major findings of the study are as follows: (1) Spontaneous or isoproterenol induced triggers were identified from PLSVC in all patients. (2) Isolation of PLSVC may require both circumferential ablation of mid-PLSVC at the level of left pulmonary veins, the body of the coronary sinus targeting all local high-frequency signals, and segmental isolation of the proximal coronary sinus ostium to disconnect various electrical connections. (3) Segmental isolation of PLSVC was safely

Table 1 Baseline characteristics of the study patients ($N = 28$). *LVEF* left ventricular ejection fraction, *LA* left atrial size, *COPD* chronic obstructive pulmonary disease, *BMI* body mass index

Characteristics	$N = 28$
Age (years) (mean ± SD)	61.1 ± 8.0
BMI (kg/m^2) (mean ± SD)	29.5 ± 4.1
Female	6 (21%)
Caucasian	26 (93%)
Type of AF	
• Paroxysmal	17 (61%)
• Persistent	7 (25%)
• Long-standing persistent	4 (14%)
Duration of AF (months) (mean ± SD)	60 ± 33.7
Previous AF ablation (%)	11 (39%)
CHA2DS2-VASC (mean ± SD)	1.7 ± 1.2
HAS-BLED (mean ± SD)	1.3 ± 1.1
Congestive heart failure	4 (14%)
Coronary artery disease	3 (11%)
Stroke/TIA	2 (7%)
Obstructive sleep apnea	7 (25%)
Chronic kidney disease	2 (7%)
COPD	3 (11%)
Valvular heart disease	5 (18%)
Medications just prior to the procedure	
• Aspirin	15 (65%)
• Beta-blocker	12 (43%)
• Calcium channel blocker	7 (25%)
Antiarrhythmics	3 (46%)
LVEF (mean ± SD)	58 ± 13
LA size (cm) (mean ± SD)	4.4 ± 0.8

Table 2 Procedural characteristics. *PVI* pulmonary vein isolation, *CFAE* common fractionated atrial electrogram, *CTI* cavotricuspid isthmus, *SVC* superior vena cava, *RA* right atrium, *ACT* activated clotting time, *PLSVC* persistent left superior vena cava

Procedural characteristics	$N = 28$
Type of AF ablation	
• PVI	24 (86%)
• CFAE	5 (18%)
• SVC–RA junction	2 (7%)
• Linear ablation	12 (43%)
• Linear lesions (mean ± SD)	1.3 ± 1.6
• PLSVC isolation	27 (96%)
Electrical cardioversions (mean ± SD)	0.44 ± 0.5
ACT (mean ± SD) (sec.)	317 ± 22
Fluoroscopy time (min.) (mean ± SD)	30.6 ± 9.8
Procedure time in (min.) (mean ± SD)	253 ± 35

Table 3 Clinical outcomes of AF ablation

Clinical outcomes	$N = 28$
Total complications	4 (14%)
• Small pericardial effusion	1 (3%)
• Pericardial tamponade	0
• Groin hematoma	3 (11%)
• TIA/Stroke within 30 days	0
• Coronary sinus dissection	0
1-year freedom from AF	21 (75%)

performed without major complications. (4) Electrical isolation of PLSVC may be associated with long-term freedom from AF in a large percentage (75%) of patients at 1-year follow-up.

The role of PLSVC in the initiation and maintenance of AF was first identified by Hsu et al. [9] in five patients undergoing AF ablation. They further circumferentially isolated the proximal PLSVC to terminate AF using RFA [9]. Since then, a few other small case series have been published that have demonstrated the PLSVC as an arrhythmogenic source in AF [10, 11, 14]. Elayi et al. [11] reported a small series of six patients with history of prior RFA for symptomatic drug-refractory AF in which 4/6 had no evidence of pulmonary vein reconnections and ablation of the PLSVC resulted in long-term freedom from AF. This study highlighted the need of locating unusual sources of AF trigger such as PLSVC and performing extensive ablation at several locations to disconnect various electrical connections to completely isolate the anatomical structure in patients undergoing catheter ablation procedures for AF [11].

There are several reasons for the arrhythmogenicity of PLSVC. The sinus horns and common cardinal veins have pacemaker function during embryogenesis, which is later taken over by the sinoatrial node of the right heart. Persistence of remnant pacemaker tissue in the left superior cardinal vein that persists into PLSVC, results in ectopic triggers and source of arrhythmia substrate that contributes to initiation and maintenance of AF [15]. Furthermore, overlapping muscle sleeves into the PLSVC has been demonstrated to be a source of abnormal triggers and electrical potentials [16, 17].

Prior reports have reported mixed results regarding ablation of PLSVC, with one study demonstrating more complications and less success [10] compared with the others [9, 11, 14]. The major reported complications included phrenic nerve palsy and pericardial tamponade requiring intervention. Our large multicenter study results support the earlier published case series that RFA including isolation of PLSVC with pulmonary veins are safe with low complications and are associated with long-term freedom from AF in both paroxysmal and persistent AF. Our results have significant clinical implications regarding ablation approach in patients with PLSVC, especially in an era of technological advancement with the use of ICE and contact force sensing catheters.

Isolation of PLSVC may require several areas of ablation in the mid-PLSVC at the level of left pulmonary veins, the body of the coronary sinus targeting all local high-frequency signals and segmental isolation of the proximal coronary sinus ostium to disconnect various electrical connections. There are several important considerations with isolation of a PLSVC and the dilated coronary sinus. First is recognizing the anatomic location of the compact AV node along the superior aspect of the coronary sinus ostium. With a PLSVC, this relationship can be distorted and shortened, especially when the coronary sinus is dilated. As such, ablation in the proximal coronary sinus can be associated with a higher risk of AV block. We used low power of 15–20 W and short duration (20 s) of ablation lesions during ablation in PLSVC and coronary sinus to minimize risk of AV block. Second, in 10–20% of patients with a PLSVC, venous drainage is into the left atrium [18]. We report similar findings in our series. However, this can be an important source of right-to-left shunting, paradoxical emboli, and arrhythmogenesis due to the functional shunt. Peripheral contrast administration from the left with echocardiogram can rule out this possibility in patients who do not undergo periprocedural imaging. With ablation distal in the coronary sinus, particularly when anatomically distorted, the location of the left-sided phrenic nerve should be identified and then ablation in that area should be avoided. Finally, when the coronary sinus is severely dilated and the PLSVC is not, this can suggest coronary sinus atresia, which has implications on transseptal catheterization and catheter insertion [19].

4.2 Limitations

This is a retrospective study with several inherent limitations. The major limitation being this was not a comparative study so the impact of PLSVC isolation remains unclear. It is only an impression that PLSVC isolation may be of relevance but it cannot be clarified in this study as no control group was identified. The results were pooled from five centers and multiple operators with some differences in extent of ablation performed. However, PLSVC was an identified trigger spontaneously or with isoproterenol in all patients in whom successful isolation of PLSVC resulted in excellent long-term clinical outcomes. Furthermore, the extent of ablation performed was largely similar in all patients. It is not clear if only electrical isolation of PLSVC without PVI can yield the same results as we are unable to perform a comparative analysis between clinical outcomes in patients who had 100% PLSVC triggers who received isolation vs. those patients with no PLSVC triggers, vs. those with PLSVC triggers but did not receive isolation. However, PVI remains the standard approach in AF ablation. The results cannot be applied to other methods of ablation such as cryoablation, laser ablation, etc. We also cannot rule out asymptomatic subclinical AF recurrence in our patients as none of them had a cardiac implantable electronic device. Even if there were, it would have been brief and asymptomatic and would not affect the way we manage our patients as those with CHA2DS2VASC ≥ 2 were continued on oral anticoagulation. We cannot rule out the possibility of having greater recurrence of arrhythmia on longer follow-up. The role of supplementary ablation remains controversial and needs further investigation in ablation technology and patient selection.

5 Conclusion

In patients with atrial fibrillation and persistent left superior vena cava, segmental isolation of persistent SVC appears to be feasible and safe and can be associated with long-term freedom from AF.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The manuscript has not been submitted or is under consideration elsewhere in any other Journal. Consent to submit has been received explicitly from all co-authors.

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