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Clinical characteristics of patients with atrial fibrillation suffering from pulmonary vein stenosis after radiofrequency ablation

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Abstract

Objective: Pulmonary vein stenosis (PVS) is a serious complication in patients with atrial fibrillation (AF) receiving radiofrequency catheter ablation (RFCA). We therefore examined these patients' clinical characteristics in relation to PVS occurrence.

Method: We retrospectively analyzed the clinical symptoms, diagnostic procedures, and treatment strategies in patients with AF who developed PVS after RFCA.

Results: Among 205 patients with AF who underwent RFCA, five (2.44%) developed PVS (all men; age 44–64 years; AF history 12–60 months; 2 paroxysmal AF, 3 persistent AF). One patient underwent two RFCA sessions and the others received one. The time to PVS diagnosed by pulmonary vein computed tomography angiography (CTA) was 3 to 21 months. PVS symptoms included dyspnea and hemoptysis. Nine pulmonary veins developed PVS. Single mild PVS occurred in two asymptomatic patients and multiple PVS or single severe PVS in three symptomatic patients who underwent pulmonary vein angiography and stent placement. Symptoms in the three patients significantly improved after stent implantation; however, stent restenosis occurred 1 year later in one case.

Conclusion: PVS is a rare complication of RFCA for AF that can be diagnosed by CTA. Pulmonary vein stent implantation can remarkably improve the symptoms, but stent restenosis may occur.

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Background

Atrial fibrillation (AF) is one of the most common types of arrhythmia and is associated with increased mortality and thromboembolic events.[1] The main treatment strategies for AF currently include radiofrequency catheter ablation (RFCA) and drug therapy. RFCA is the first-line therapy for AF with a success rate of over 80%.[2] However, pulmonary vein stenosis (PVS) is a complication of RFCA, though its occurrence has decreased dramatically from 42.4% in early studies to <5% in studies reported after 2000.[3,4] PVS can cause serious symptoms, including shortness of breath, fatigue, and hemoptysis. Treatments for PVS include anticoagulation, balloon dilatation, stent implantation, and surgical intervention. Of these, stent implantation achieves a good effect, though restenosis may occur in some patients.[5] In this study, we retrospectively summarized the diagnosis and treatment of PVS in five patients with AF who received RFCA.

Methods

Patients

Consecutive patients who received RFCA for symptomatic AF at Xianyang Central Hospital from 1 May 2012 to 30 September 2018 were recruited to our study. Circumferential pulmonary vein isolation was performed in all patients, and other ablation strategies included roofline ablation, mitral isthmus ablation, cavotricuspid isthmus ablation, box ablation, left atrial anterior wall ablation, ablation in the coronary sinus, and matrix modification ablation. Echocardiography and pulmonary vein computed tomography angiography (CTA) were used to detect PVS. Clinical data were collected retrospectively for analysis of the clinical characteristics, diagnosis, and treatment strategies of PVS after RFCA.

Informed consent was obtained from all patients. This study was approved by the clinical research ethics committee of Xianyang Central Hospital (No. 2014-25).

Pulmonary vein angiography and intervention

Pulmonary vein angiography and angioplasty were performed in some patients. Left atrial pressure was measured after puncturing the atrial septum, followed by pulmonary vein angiography. Before stent implantation, a balloon catheter of the appropriate diameter was engaged in each stenotic lesion and bare-metal or drug-eluting stents were placed after dilating the stenosis. Pulmonary vein angiography was performed to examine the effect of residual stenosis after stent implantation.

Follow-up after operation

Patients with PVS were followed up regularly and treated as required. Pulmonary vein CTA and echocardiography were repeated 1, 3, and 12 months after the stenting operation.

Results

Baseline data

A total of 205 patients who underwent RFCA for AF were included in the study, of whom five (2.44%) developed PVS. The characteristics of these five patients are shown in Table 1. Patient 1 underwent a second RFCA because of recurrent AF while the other four received one RFCA. None of the patients had any significant cardiac or pulmonary vein abnormalities before RFCA. Representative electroanatomic maps after ablation in patient 1 and in a patient without stenosis during follow-up are shown in Figure 1 and Figure 2, respectively.

Characteristics of PVS patients

Sinus rhythm was observed in all patients after RFCA when PVS was diagnosed 3 to 21 months after RFCA by CTA. Patients 1 and 4 had no discomfort but the others were symptomatic with dyspnea or hemoptysis. Patients 2 and 5 had moderate and severe pulmonary hypertension, with pulmonary artery systolic pressures of 105 and 59 mmHg, respectively, on echocardiography. Pulmonary vein CTA confirmed stenosis of >70% in nine vessels, with six vessels close to occlusion. A single PVS was detected in patients 4 and 5, respectively, and multiple PVS in the others (Table 1).

Pulmonary vein angiography and intervention

Pulmonary vein angiography was performed in three of the five patients with PVS. Patients 1 (Figure 3), 2 (Figure 4), and 5 (Figure 5) were implanted with two, two, and one stents, respectively. The stents used ranged from 4 to 8 mm diameter and 1 to 29 mm long (Table 2).

Intraoperative complications

No serious complications occurred during stent placement. Patient 1 suffered from transient ST segment elevation in the inferior leads, hemoptysis, and hypotension lasting <5 minutes. Subsequent electrocardiography and myocardial enzyme testing show no evidence of myocardial infarction.

Hemoptysis also occurred in patient 2 immediately after pulmonary vein dilation. Three pulmonary veins in patient 2 were almost occluded, with a pulmonary artery pressure of 105 mmHg. Hemoptysis was alleviated 3 minutes after trachea hemorrhage by bronchoscopy and respiration was assisted with a noninvasive ventilator. Stents were implanted in the left and right superior pulmonary vein. The hemoptysis gradually disappeared after implantation, and the pulmonary artery pressure decreased to 40 to 60 mmHg.

Follow-up results

All five patients were followed up for 1 year and received standard anticoagulant therapy with warfarin or novel oral anticoagulants, clopidogrel, and atorvastatin to achieve a target international normalized ratio (INR) of 1.5 to 2.5. Symptoms were relieved in all patients, and all patients were asymptomatic and with no restenosis at CTA examinations 1 and 3 months after stent implantation. However, stent restenosis and thrombosis were detected in patient 1 in the left inferior pulmonary vein 1 year after stent implantation. The time in therapeutic range (TTR) on warfarin was <70% and the warfarin dosage was subsequently increased. The INR was 2 to 3. CTA showed 70% stenosis in the left superior pulmonary vein and left inferior pulmonary vein in patient 3 at 1 year after RFCA. Patient 4 had no symptoms during the follow-up period, and patients 3 and 4 received no further interventions.

Table 1. Clinical data for patients with pulmonary vein stenosis after radiofrequency ablation of atrial fibrillation.

Patient no.	Sex	Age, years	AF duration, months	Type of AF	LAD, mm	LVEF, %	PAP before RFCA, mmHg	Ablation method	TFS after RFCA, months	Symptoms	Pulmonary vein	Degree of stenosis, %	DPV, mm	PAP after PVS, mmHg
1	M	59	12	Paroxysmal	46	72	30	CPVI + FPL	14	No	LS	95	1.4	30
											LI	100	0	
											RS	0	14	
											RI	0	9.7	
2	M	64	24	Paroxysmal	40	57	31	CPVI + FPL	7	Cough, hemoptysis	LS	95	5.4	105
											LI	0	27	
											RS	95	2.8	
											RI	100	0	
3	M	50	60	Persistent	46	73	40	CPVI + FPL	6	Dyspnea	LS	70	6	39
											LI	70	9	
											RS	0	18	
											RI	0	15	
4	M	44	48	Persistent	43	61	26	CPVI + LA	3	No symptoms	LS	75	4	29
5	M	62	24	Persistent	43	70	30	CPVI + LA	21	Dyspnea, hypoxemia	LS	100	0	59
											LI	0	14.1	
											RS	0	21.2	
											RI	0	16.9	

AF, atrial fibrillation; PAP, pulmonary artery pressure; LAD, left atrial dimension; LVEF, left ventricular ejection fraction; RFCA, radiofrequency catheter ablation; PVS, pulmonary vein stenosis; M, male; NA, not available; CPVI, circumferential pulmonary vein isolation; LS, left superior; LI, left inferior; RS, right superior; RI, right inferior; DPV, diameter of pulmonary vein; FPL, focal pulmonary lesions; LA, linear ablation; TFS, time to first symptoms.

Discussion

Pulmonary veins are an important source of ectopic discharge in AF patients. Although various strategies such as segmental pulmonary vein isolation, and circumferential pulmonary vein, linear, fragmentation, and matrix modification ablation techniques have significantly improved the success rate of ablation, ablation itself may cause rare severe complications, including PVS, atrial-esophageal fistula, cardiac tamponade, and phrenic nerve lesions.[6,7] PVS may be associated with a poor and even fatal prognosis in the absence of reasonable treatment. Balloon dilatation and stent implantation are often used to resolve PVS. In our study, the incidence of PVS was 2.44%, which is in accord with other recent reports that reported incidences ranging from <2% to 8%.[8] Similar to some studies in patients who underwent pulmonary vein intervention,[9] most (7/9) affected pulmonary veins in the current study were on the left side. Pürerfellner et al.[10] explained that the ostia of the left pulmonary veins might be more difficult to define and that the right inferior pulmonary vein was sometimes difficult to reach and ablate.

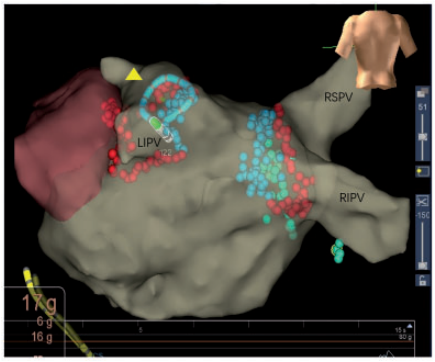

Figure 1. Three-dimensional model of left atrium of patient 1 during the second ablation indicated severe stenosis of left superior pulmonary vein (yellow triangle). LIPV, left inferior pulmonary vein; RSPV, right superior pulmonary vein; RIPV, right inferior pulmonary vein.

Patients with mild to moderate stenosis of a single pulmonary vein often have no symptoms, while those with severe stenosis of a single pulmonary vein or multiple PVS usually have severe symptoms. The severity of the symptoms is accordingly associated with the number of pulmonary veins affected, lesion severity, and the presence and extent of collateral circulation in the affected lung lobe. Most patients presented with dyspnea as the first symptom while hemoptysis was uncommon in a previous study.[4] In the current study, three of the five

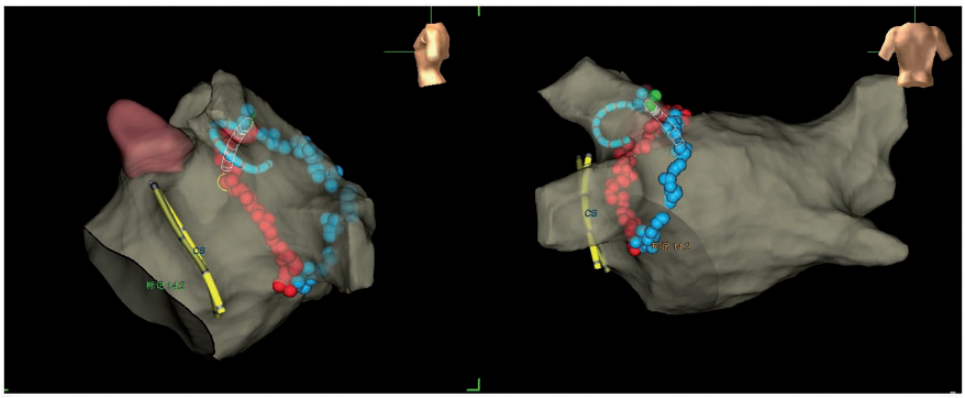

Figure 2. Electroanatomic map after ablation for atrial fibrillation in a patient without pulmonary vein stenosis during follow-up.

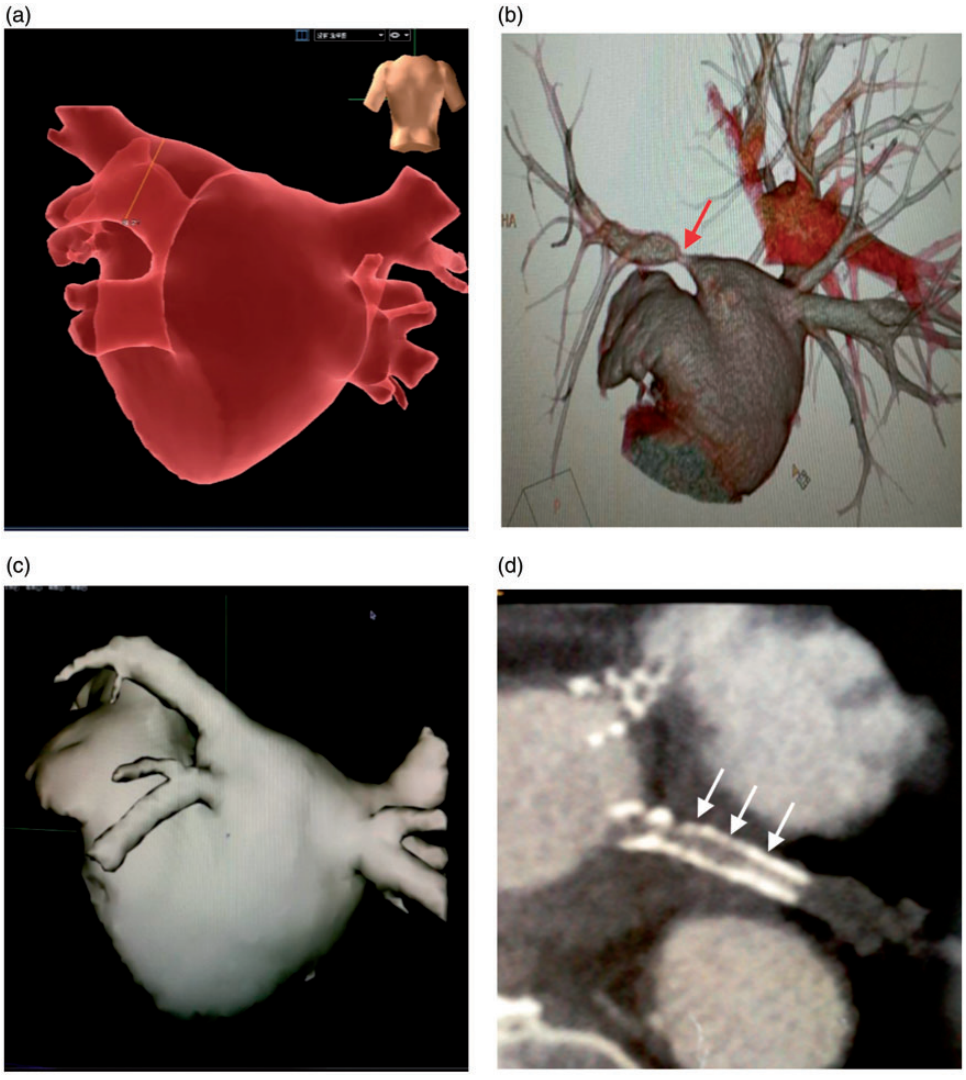

Figure 3. Normal pulmonary vein before radiofrequency ablation in patient 1 (a), severe stenosis in left superior and left inferior pulmonary veins after ablation (b), stent implantation in the left superior and left inferior pulmonary veins (c), and restenosis 1 year after stent implantation (d). Red arrow indicates severe stenosis in left superior pulmonary vein after ablation; white arrows indicate restenosis after stent implantation.

patients showed dyspnea and two had hemoptysis. These symptoms might be associated with the presence of pulmonary hypertension, which reflected the severity of PVS.

Notably, the clinical symptoms of PVS are similar to those of some respiratory diseases, and the condition can thus be easily misdiagnosed. Clinicians should therefore evaluate the possibility of PVS in patients with dyspnea, chest pain, and hemoptysis and a history of AF ablation. Various diagnostic methods have been used to detect PVS. Percutaneous

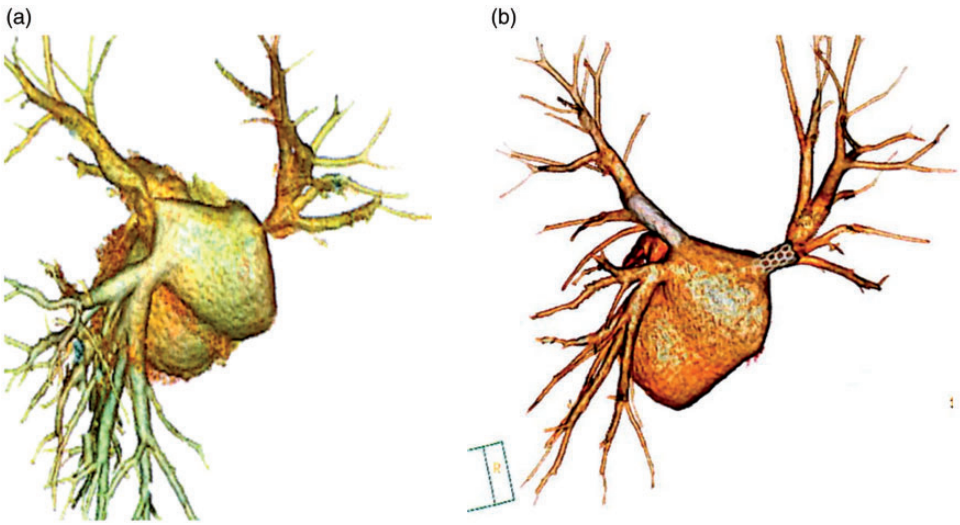

Figure 4. Severe stenosis in left superior and right superior pulmonary veins 7 months after RFCA in patient 2 (a) and left superior and right superior pulmonary veins after stent implantation (b).

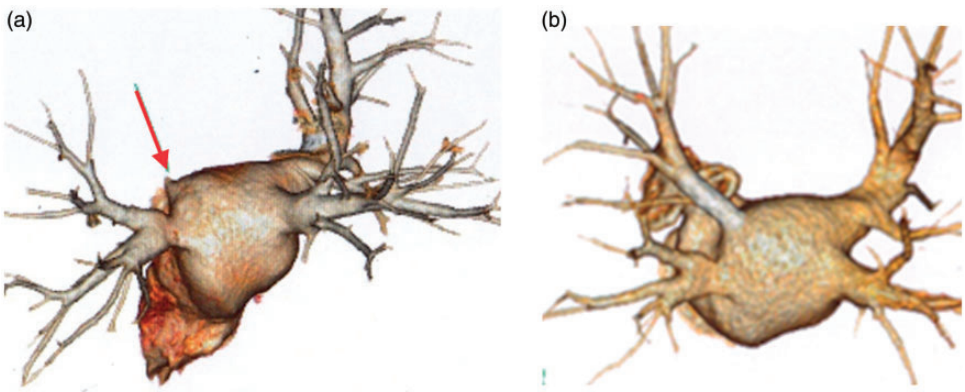

Figure 5. Severe stenosis in left superior and right superior pulmonary veins 7 months after radiofrequency ablation in patient 5 (a) and left superior and right superior pulmonary veins after stent implantation (b). Red arrow indicates close to occlusion of left superior pulmonary vein after ablation.

pulmonary vein angiography is currently the gold standard for the diagnosis of PVS in terms of determining the location and the degree of stenosis. Immediate angiography after RFCA can assess the occurrence of acute PVS; however, delayed PVS may occur in some patients after RFCA. The diagnostic values of blood gas analysis and pulmonary function tests may not be specific for early PVS, but are sensitive in some patients. CTA can clearly show the location and extent of PVS, and is thus the first-line noninvasive method for evaluating and diagnosing PVS.[11] Pulmonary ventilation perfusion scans (V/Q) can show the blood flow distribution and

Table 2. Interventions for pulmonary vein stenosis.

Patient no.	Pulmonary angiography	Location of stent	Diameter of stent	Length of stent	Complications during intervention	Anticoagulant drugs
1	Yes	LSPV	8	24	Hemoptysis, ST elevation	Antiplatelet + warfarin
		LIPV	4	24		
2	Yes	LSPV	8	29	Hemoptysis, Hypoxemia	Antiplatelet + NOAC
		RSPV	7	18		
3	No	NA	NA	NA	NA	Warfarin
4	No	NA	NA	NA	NA	Warfarin
5	Yes	LSPV	8	29	No symptoms	Antiplatelet + NOAC

LSPV, left superior pulmonary vein; LIPV, left inferior pulmonary vein; RSPV, right superior pulmonary vein; RIPV, right inferior pulmonary vein; NA, not available; NOAC, novel oral anticoagulants.

ventilation perfusion ratio, thus contributing to a better understanding of the pathophysiology of the stenosis and its progression.[12] A V/Q scan shows a perfusion mismatch when the degree of narrowing reaches 65% to 75%. However, the PVS images may mimic pulmonary embolism on V/Q scan, leading to misdiagnosis and mismanagement.[13] Transesophageal echocardiography can clearly visualize the superior pulmonary veins, but diffusion images are often shown in the inferior pulmonary veins.[14] Percutaneous pulmonary vein angiography can be performed to confirm a suspected PVS diagnosis.

Observation, rather than excessive intervention, is recommended in patients with mild to moderate single PVS, and symptoms in some of these patients may be improved by anticoagulant agents. However, interventional therapy is recommended in patients with obvious symptoms, severe PVS, or multiple lesions. Single balloon dilation and stent implantation can dilate the pulmonary veins and improve symptoms, but the long-term effects remain unclear. Furthermore, attention should be paid to the potential complications of interventional therapy. Early complications including transient ST elevation, detached thrombus, pulmonary vein laceration, hemothorax, stent displacement, and acute pericardial tamponade due to a ruptured left atrial entrance of the pulmonary vein,[4,15] while late complications include restenosis, stent thrombosis, and thromboembolism. The incidence of restenosis after interventional therapy is 30% to 50%,[5] and may be caused by neointimal hyperplasia, fibrosis, and stent thrombosis. Qureshi et al.[9] reported a 47% restenosis rate at 11 months after intervention, and Neumann et al.[16] reported a rate of in-stent restenosis of 23% after 4 years of follow-up in patients with stent sizes $\leq$10 mm. In our study, stents were implanted in three patients. Stenosis was significantly improved after implantation and the patients' clinical symptoms were effectively alleviated. However, the left inferior pulmonary vein showed restenosis 1 year after implantation in one patient. A smaller diameter of the pulmonary vein is associated with a higher rate of restenosis after stent implantation,[17] and drug-coated stents or no intervention are recommended for pulmonary veins with a diameter $<$5 mm. The combination of anticoagulants, antiplatelets, and statins can help to reduce the restenosis rate, and should be continued for at least 1 year.

The ablation site and pulmonary vein diameter are risk factors for PVS. Arentz et al.[18] found that distal ablations inside smaller pulmonary veins were associated

with a higher risk of stenosis than ablation at the ostium, while the diameters of pulmonary veins with stenosis were significantly smaller than those without stenosis. PVS is a progressive process with a prolonged follow-up time. In animal experiments, PVS was shown to involve progressive intimal hyperplasia, gradual replacement of necrotic myocardium by collagen, vasoconstriction, and elastic proliferation.[19] In our study, there was no clear difference in procedural parameters between patients with PVS and those without, and the occurrence of PVS was likely to have been caused by technical factors, such as inaccurate location of the pulmonary vein ostium and ablation inside the pulmonary vein.

In the current study, we performed transesophageal echocardiography to evaluate pulmonary artery pressure after RFCA and to indicate the probability of PVS. Pulmonary artery pressure should thus be evaluated routinely after RFCA and pulmonary vein CTA is recommended in patients with suspected PVS.

Several factors have contributed to the recent decline in the incidence of PVS. First, a wide area of circumferential ablation can improve the ablation efficacy. Second, the use of cryoablation in pulmonary vein isolation is related to less damage. Third, multiple imaging techniques can be used to accurately locate the pulmonary vein ostial anatomy, including intracardiac echo and preprocedural CT combined with electroanatomical mapping. Bertaglia et al.[20] found no severe PVS in patients undergoing intracardiac echo-guided RFCA. Martinek et al.[21] compared the efficacy and safety of sophisticated imaging with electroanatomical mapping and showed that CT combined with electroanatomical mapping significantly improved the success of RFCA (85.1% vs 67.9%; $P = 0.018$) and decreased the occurrence of PVS (0 vs 3, $P = 0.098$). In general, the current opinion is that prevention of PVS is more important than its treatment.

This study was limited by the fact that it was a single-center study with a small sample size and a short follow-up duration.

Conclusion

The incidence of PVS in the current study was 2.44%. Patients with PVS presented with dyspnea and hemoptysis, though patients with mild to moderate stenosis often had no obvious discomfort. Patients should thus be evaluated regularly after RFCA. Anticoagulant therapy may be effective in patients with no or mild symptoms, while early intervention could significantly improve hemodynamics and relieve symptoms in patients with severe PVS.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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