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CASE REPORT

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Drug-Coated Balloon Venoplasty to Treat Iatrogenic Pulmonary Vein Stenosis

Mohammed Salih, MD, Modar Alom, MD, Ahmed Kazem, MD, Brian DeVille, MD, Srinivasa Potluri, MD

ABSTRACT

Pulmonary vein stenosis (PVS) is a condition that has seen a decrease in incidence in recent years. Whereas balloon angioplasty and stenting are both acceptable treatment options for PVS, they are limited by the high rate of restenosis. This research paper presents 4 cases of severe symptomatic PVS that were successfully treated with the use of drug-coated balloons, resulting in positive outcomes. **(Level of Difficulty: Advanced.)** (J Am Coll Cardiol Case Rep 2023;24:102019) © 2023 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Pulmonary vein stenosis (PVS) can have several underlying causes, including congenital anomalies, compression from adjacent pathologies, or iatrogenic causes, such as following atrial fibrillation (AF) ablation. The diagnosis of PVS can be difficult, even in patients with relevant histories, due to the ambiguity of symptoms and the absence of standardized screening protocols. In cases of suspected PVS, consensus from all the global societies recommend cardiac magnetic resonance imaging or computed tomography (CT) as the diagnostic tests of choice.[1]

Interventions, such as percutaneous transluminal angioplasty (PTA) or stenting, are indicated when PVS is severe (>75% stenosis).[2] However, restenosis rates after these procedures can be as high as 50%, often requiring reintervention.[3] The use of drug-coated balloons (DCBs) in the treatment of PVS has not been extensively described in the published data, but it may offer a promising treatment strategy.

LEARNING OBJECTIVES

- To raise attention about the importance of PVS diagnosis after AF ablation.
- To highlight the role of DCB as a potential treatment strategy for PVS with a low restenosis rate.

CASE 1

A 36-year-old male patient with a history of AF status post ablation 8 months prior, as well as subsequent PVS status post left superior pulmonary vein stent placement, presented to the office for shortness of breath, chest pain, and hemoptysis. Work-up included an echocardiogram that was unrevealing. CT of the heart then revealed a moderate degree of in-stent restenosis within the left superior pulmonary vein (LSPV); however, severe stenosis in the proximal segment of the left inferior pulmonary vein (LIPV). After discussion by the interventional and electrophysiological teams, we decided to proceed with PTA.

The patient underwent successful angioplasty of the left upper and lower pulmonary veins using a 7 mm × 40 mm and 6 mm × 40 mm DCBs with simultaneous kissing to accommodate the size of the

From Baylor, Scott, and White, Baylor University Medical Center/The Heart Hospital Plano, Plano, Texas, USA.
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ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

CT = computed tomography

DCB = drug-coated balloon

LIPV = left inferior pulmonary vein

LSPV = left superior pulmonary vein

PTA = percutaneous transluminal angioplasty

PVS = pulmonary vein stenosis

pulmonary veins for the LIPV and LSPV, respectively, through right femoral vein access.

On serial follow-up visits, the patient reported resolution of his symptoms, and CT imaging 5 years after the procedure showed no evidence of restenosis (**Figures 1A and 1B**, Videos 1 to 4).

CASE 2

A 52-year-old male with a history of AF status post AF ablation 9 months prior, presented to the office for shortness of breath and hemoptysis, as well as recurrent pleural effusion. Further evaluation using CT heart imaging revealed 99% stenosis of the LIPV. The patient underwent successful angioplasty of the LIPV using a 7 mm × 40 mm DCB and subsequently experienced resolution of his symptoms. On serial follow-up visits, the patient remained symptom-free and resolved of pleural effusions. Follow up CT angiography of the chest 6 months post procedure showed patent LIPV (**Figures 2A and 2B**, Videos 5 and 6).

CASE 3

An 81-year-old female with a history of AF, status post 2 AF ablations as well as a left atrial occlusion device implantation and pulmonary hypertension presented to the office, 5 months after her second ablation with shortness of breath and cough. Work-up showed occlusion of the LSPV, as revealed by CT heart imaging. She underwent angioplasty using a 5 mm × 40 mm DCB with significant improvement in her symptoms. On follow-up visit 3 years post procedure, she reported no recurrence of symptoms and CT imaging 2 years post procedure revealed no evidence of restenosis (**Figures 3A and 3B**, Videos 7 and 8).

CASE 4

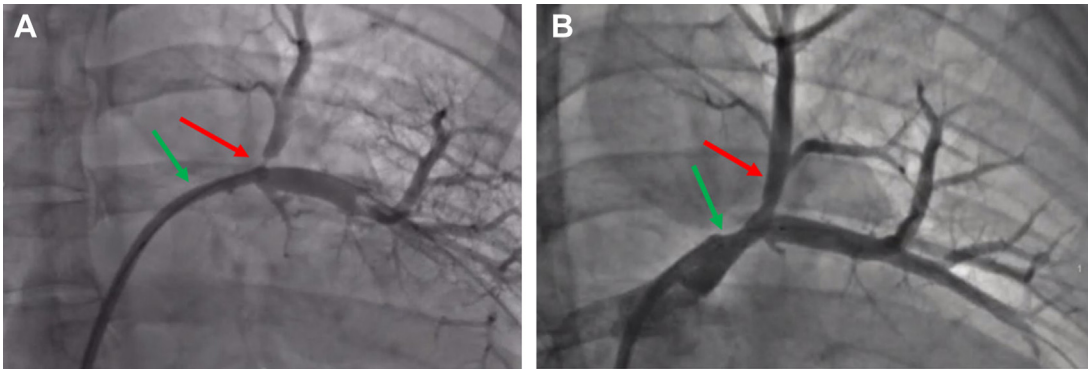
A 73-year-old male with a history of transcatheter aortic valve replacement and AF status post 4 previous ablations and thoracoscopic surgical maze procedure presented to the office for worsening shortness of breath 4 months after his last ablation. Work-up with a CT of the heart confirmed occlusion of the branch of LSPV. The patient underwent pulmonary angioplasty using 5 mm × 40 mm and 4 mm × 40 mm DCBs simultaneously in the main branch and side branch with an excellent result and no recurrence of symptoms on 3-year follow-up. CT angiography of the chest was done 1 month after the procedure and showed no evidence of significant LSPV stenosis (**Figures 4A and 4B**, Videos 9 and 10).

DISCUSSION

PVS has seen a decline in frequency in recent years, with an incidence of up to 4%. It can have variable underlying etiologies, but it is most commonly iatrogenic following AF ablation.

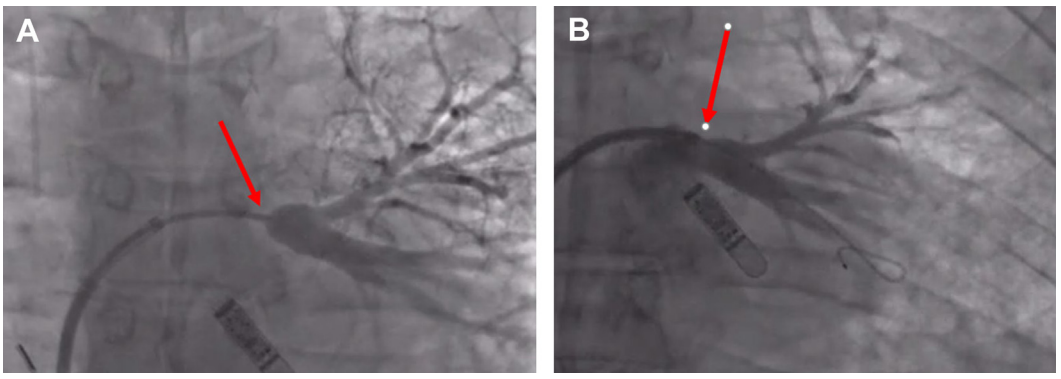
Symptoms of PVS include cough, fatigue, shortness of breath, hemoptysis, parenchymal lung disease,

FIGURE 1 Case 1: Pre- and Post-Intervention Venogram



(A) Preintervention angiographic image showing left superior and left inferior pulmonary veins (confluent in common vein) severe stenosis. The green arrow is pointing toward the narrowing in the common left pulmonary vein. The red arrow is pointing toward the narrowing in the left superior pulmonary vein. (B) Postintervention angiographic image showing restoration of flow in the left pulmonary veins. The green arrow demonstrates resolution of stenosis in the left common pulmonary vein. The red arrow demonstrates resolution of stenosis in the left superior pulmonary vein.

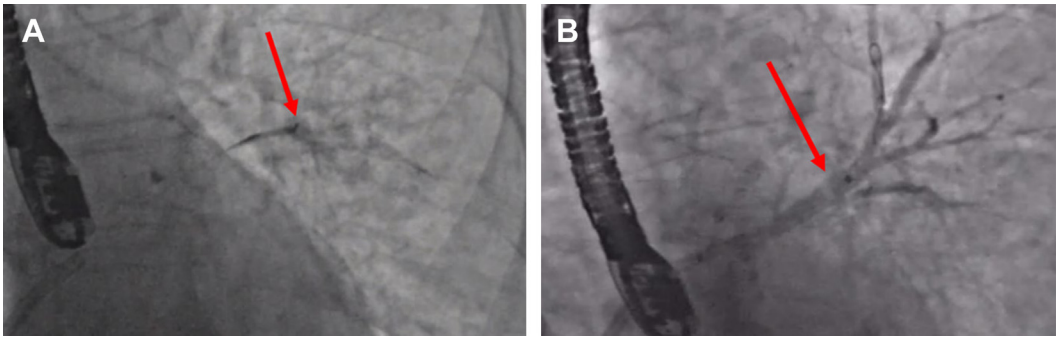
FIGURE 2 Case 2: Pre- and Post-Intervention Venogram



(A) Preintervention angiographic image highlighting left inferior pulmonary vein stenosis. The red arrow is pointing to the stenotic segment in the left inferior pulmonary vein. (B) Postintervention image showing flow restoration with good angiographic results. The red arrow demonstrates resolution of stenosis in the left inferior pulmonary vein.

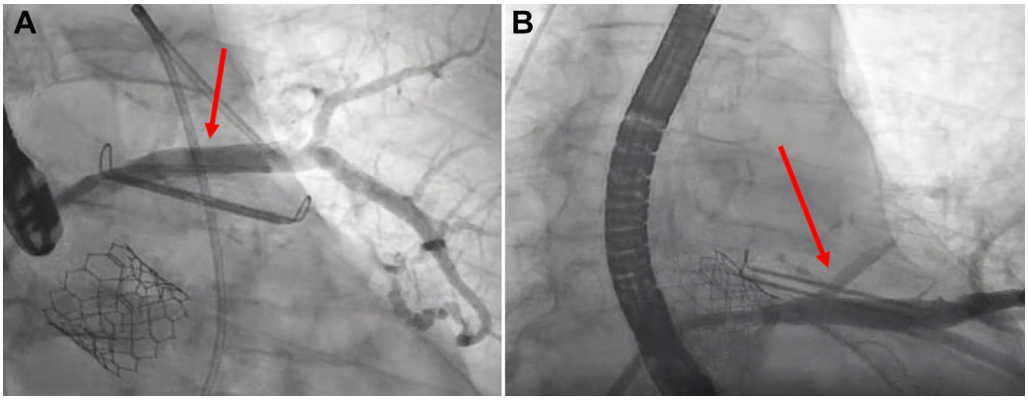
which can mimic airway disease, pleural effusion, and chest pain and tend to occur 3 months or more after the ablation. The severity of the symptoms can range from mild to severe, highlighting the importance of prompt diagnosis and plan for treatment to improve patients' symptoms and quality of life. All of the patients in our cohort had presenting symptoms of cough and dyspnea (Table 1). The pathophysiology of PVS after ablation is not fully understood, but it is thought be related to fibrosis and scarring of the pulmonary vein through intimal thickening, proliferation of elastic laminae, and endocardial contraction.[4] PVS is more common after radiofrequency ablation than with cryoablation.[3] Treatment of symptomatic patients usually involves PTA, with or without stenting, although the procedure is limited by the development of restenosis, with rates as high as 40%. A recent analysis, which included 340 patients, suggested that stenting may be superior to PTA due to a longer patency rate and lower restenosis rate.[5] Whereas DCBs have been widely used in peripheral vascular intervention and some coronary artery interventions, limited data are available for their use in PVS. DCBs use balloons coated with paclitaxel, which has an antiproliferative effect on fibroblasts and smooth muscle cells, leading to apoptosis of these cells. The paclitaxel in DCBs typically washes out quickly from the vessel lumen but

FIGURE 3 Case 3: Pre- and Post-Intervention Venogram



(A) Preintervention angiographic image showing occlusion of the left superior pulmonary vein. The red arrow is pointing to the occluded left superior pulmonary vein. (B) Postintervention image showing flow restoration with good angiographic results. The red arrow is pointing toward the recanalized left superior pulmonary vein.

FIGURE 4 Case 4: Pre- and Post-Intervention Venogram



(A) Preintervention angiographic image showing occlusion of the left superior pulmonary vein. The red arrow is pointing to the occluded segment of the LSPV. (B) Postintervention image showing flow restoration with good angiographic results. The red arrow is pointing toward the recanalized left superior pulmonary vein.

maintains a high concentration within the deeper smooth muscles and fibroblasts by diffusion through the vessel wall.[6] This mechanism of action makes DCBs a potential treatment option for PVS.[7] This is especially important in cases where the anatomy presents challenges for stenting, such as when the distance to bifurcation is short or when there is very ostial disease that may require extending a stent into the atrium. The appropriate sizing of DCBs for PVS has not been clearly established, but previous research has suggested that larger pulmonary vein sizes may have better long-term patency with DCB use.[5] Previously, the sizes of DCBs were a limitation; however, in the current era, different sizes of DCBs are available. In our series, we used DCBs with sizes ranging from 4 mm × 40 mm to 7 mm × 40 mm (Table 2), and all patients experienced good outcomes with resolution of symptoms at an average follow-up of 3.5 years. All patients did well post procedure and were discharged the same day. Three of 4 patients were placed on clopidogrel for 3 months and oral anticoagulation for life, whereas the fourth patient was placed on Plavix for 3 months and aspirin 81 mg for life because this patient had a left atrial occlusion device. Overall, the use of DCBs in our series had a success rate of 100% and was associated with good outcomes and symptom resolution at long-term follow-up. Our case series supports the feasibility of DCB use in PVS. Given the limited data, further studies are needed to validate this approach and fill the knowledge gap regarding its use in such cases.

CONCLUSIONS

PVS following AF ablation is becoming increasingly rare, with incidence rates decreasing dramatically from 42.4% in 1999 to 0.5%-4% in recent years. When PVS becomes severe and causes symptoms, intervention is usually required. PTA and stenting are acceptable options, but they are limited by the high

TABLE 1 Patient Characteristics, Pulmonary Veins Involved and Diagnostic Modality

Cases	Age at Presentation, y	Sex	PV Involved	Ablation Type	Symptoms at Presentation	Diagnostic Imaging
1	30	Male	LIPV LSPV	RFA	Fatigue, SOB, hemoptysis, and cough	CTA pulmonary vein protocol
2	52	Male	LIPV	RFA	SOB and cough	CTA pulmonary vein protocol
3	81	Female	LSPV	RFA	SOB and cough	CTA pulmonary vein protocol
4	73	Male	LSPV	RFA	SOB and cough	CTA pulmonary vein protocol

CTA = computed tomography angiography; LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary vein; RFA = radiofrequency ablation; SOB = shortness of breath.

TABLE 2 Procedure Characteristics

Cases	Procedure State	Site Treated	Treatment Type	Balloon Size	Procedure Success	Therapy Afterward
1	Elective	LIPV	DCB	DCB 7 mm × 40 mm for the LIPV, and 4 mm × 40 mm for the LSPV	Yes	None
2	Elective	LIPV	DCB	DCB 7 mm × 40 mm	Yes	None
3	Elective	LIPV	DCB	DCB 5 mm × 40 mm	Yes	None
4	Elective	LSPV	DCB	DCB 4 mm × 40 mm and 5 mm × 60 mm	Yes	None

DCB = drug-coated balloon; other abbreviations as in Table 1.

risk of restenosis (72% for PTA vs 33% for stenting at 25-month follow-up).[8] Intervention with the use of DCBs may provide a promising alternative treatment for PVS, as demonstrated in our case series and in previous, limited reported cases. Further research is necessary to assess the effectiveness of DCBs in the treatment of PVS.

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ADDRESS FOR CORRESPONDENCE: Dr Srinivasa Potluri, Department of Cardiology, Cardiac Catheterization Laboratory, Interventional Cardiology Fellowship, Baylor, Scott, and White, The Heart Hospital Plano, 1100 Allied Drive, Plano, Texas 75093, USA. E-mail: srinivasa.potluri@bswhealth.org. @Potluri70.

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APPENDIX For supplemental videos, please see the online version of this paper.