

Intravascular ultrasound-guided drug-coated balloon venoplasty for in-stent restenosis in pulmonary veins stenosis: a case report

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Background

Pulmonary veins stenosis (PVS) after atrial fibrillation radiofrequency ablation is an uncommon complication. When it occurs, percutaneous treatment is the preferred approach. There is a lack of standardized procedures, and when stenting restenosis is relatively common.

Case summary

We present a young patient with recurrence of PVS after first percutaneous treatment. The recurrence of haemoptysis and dyspnoea after treatment in PVS allowed the diagnosis of significant stenosis again in our patient. In the Heart Team, we opted for a new percutaneous treatment, using intravascular ultrasound (IVUS) to optimize the final result.

Discussion

Nowadays, percutaneous approach is preferred and among percutaneous treatments for PVS, stenting has shown better results than balloon angioplasty (BA). Despite this, experience in in-stent restenosis is limited, and there is a lack of adequate and specific material for its approach. In this case, we present the possible role of the IVUS and the drug-coated BA in this entity.

Keywords

IVUS • In-stent restenosis • Drug-coated balloon • Pulmonary vein • Atrial fibrillation • Case report

Learning points

- Restenosis is a common complication of the percutaneous treatment for radiofrequency ablation-related pulmonary vein stenosis.
- Intravascular ultrasound-guided procedures, both the index procedure and subsequent restenosis, may decrease restenosis risk.
- Drug-coated balloon angioplasty could be a good strategy when restenosis occurs in order to avoid metallic multilayering.

Introduction

Pulmonary vein stenosis (PVS) is estimated to complicate between 0.3% and 3.4% of atrial fibrillation (AF) ablation procedures.¹ Better

results have been described with stenting vs. balloon angioplasty (BA) alone for the treatment of this complication. Unfortunately, pulmonary veins restenosis (PVR) after percutaneous treatment of radiofrequency-related stenosis is a common complication. The

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mechanism of PVR is poorly understood, and the reason for this lack of benefit from stenting during a second intervention is unclear. We present a case of in-stent restenosis (ISR) successfully treated with intravascular ultrasound (IVUS)-guided drug-coated BA and especially, highlighting the role that the use of IVUS may play in the management of this complication.

Timeline

May 2016	Atrial fibrillation diagnosed.
March 2017	Pulmonary veins radiofrequency ablation.
May 2017	Haemoptysis and dyspnoea of new appearance.
July 2017	Pulmonary veins stenosis (PVS) diagnosed.
August 2017	Percutaneous treatment of PVS.
November– December 2017	Haemoptysis and dyspnoea of new appearance.
May 2018	In-stent restenosis in pulmonary veins and intravascular ultrasound-guided drug-coated balloon angioplasty.
May 2019	One-year follow-up. No symptoms.
Nov 2020	No Symptoms. Sinusal rhythm.

Case presentation

A 67-year-old woman with AF underwent pulmonary veins radiofrequency ablation in March 2017. Four months after index procedure, she was admitted with progressive dyspnoea and PVS was diagnosed using computed tomography (CT). Percutaneous treatment with BA and stent implantation was performed. Balloon-expandable cobalt-chromium stents Omnilink Elite[®] 10 mm × 19 mm on left superior pulmonary vein (LSPV), 8 mm × 19 mm on left inferior pulmonary vein (LIPV), and 7 mm × 16 mm on right inferior pulmonary vein (RIPV) were used.

Twenty months later, she started again with progressive dyspnoea and cough. The CT confirmed severe ISR of all treated veins, and new severe stenosis in right superior pulmonary vein (RSPV). A new percutaneous approach was decided by our Heart Team. Through the right femoral vein and transeptal access (Agilis[™] sheath and BRK-1[™] needle, St. Jude Medical, MN, USA) with SafeSept[®] wire (PressureProducts, CA, USA), a significant increased pressure gradient (20–30 mmHg on average) between pulmonary veins and left atrium was demonstrated. Intravascular ultrasound (Opticross[™], Boston Scientific, MA, USA) showed severe ISR of RIPV [minimum stenotic area (MSA) 4.72 mm²], LSPV (MSA 21.4 mm²), LIPV (MSA 5.72 mm²), and severe *de novo* stenosis in RSPV was proved (Figure 1, Videos 1–3, and Supplementary material online, Videos S1 and S2).

With CT measures and IVUS assessment, drug-coated balloon (DCB) angioplasty was performed successfully (Table 1) with no residual gradient and good luminal result (RIPV MSA after treatment 62.3 mm², LSPV MSA after treatment 21.7 mm², and LIPV MSA after treatment 18.1 mm²).

Clopidogrel 75 mg and edoxaban 60 mg daily for 3 months was used empirically. At 1-year follow-up, she has not presented new symptoms and until nowadays the patient remains in sinusal rhythm.

Discussion

Pulmonary vein stenosis is an uncommon but potentially deadly complication after radiofrequency ablation of AF. The incidence varies from 0.3% to 3.4%¹ and symptoms development depends on the number of veins affected and the stenosis severity. Cough, dyspnoea, and haemoptysis are the more common symptoms.

Nowadays, due to the high surgical risk, percutaneous approach is preferred and among percutaneous treatments, stenting has shown better results than BA. Recently, Suntharos et al.² published long-term outcomes (17 ± 1.98 months) of 205 patients with PVS treated by percutaneous approach between 2000 and 2016, with less restenosis rates in stented patients vs. BA [15% vs. 73%, *P* < 0.01, hazard ratio (HR) 5.7]. Despite the correct treatment, PVR occurs in one-third of cases with worse prognosis and higher likelihood for subsequent recurrent restenosis.^{3,4} Pathophysiology is not well known, but the hypothesis is that periadventitial inflammation and collagen deposition cause reactive hyperplasia and fibrosis.

Widmer et al.¹ reviewed risk factors for PVR, finding higher rates in patients with more than one previous procedure (HR: 1.91; 95% 1.07–3.41; *P* = 0.01). Among intraprocedural factors, BA vs. stenting [HR: 2.77; 95% confidence interval (CI): 1.72–4.45; *P* < 0.001] and higher post-procedure pressure gradients, are the stronger predictors for PVR. Moreover, lower PVR rates have been demonstrated with higher pressure BA (HR: 0.87; 95% CI 0.78–0.98; *P* = 0.02). These intraprocedural risk factors suggest that, as in coronary angioplasty, previous vessel or plaque preparation is highly recommended. Although there are no standardized procedures for PVR percutaneous treatment, an increased risk of complications in patients treated with higher atmospheres deployment have not been described.

Taking into consideration these points, it could be suggested that a careful planification of the index procedure may significantly reduce the risk of related complications. Fender et al.⁶ had already proposed an algorithm to guide management for recurrent stenosis recommending BA predilation for ISR. In addition to these recommendations, it seems reasonable to add IVUS assessment to the management of pulmonary veins ISR. The IVUS may be a useful tool, both in the index procedure and if restenosis occurs, helping to choose the appropriate devices according to vein diameter and stenosis, and also for assessment of the stent apposition and expansion.

Our case was based on the good results of previous *in vitro* experiences of DCB on PV myofibroblasts inhibition,⁷ and it suggests that like in coronary ISR, DCB may have a role for PVR treatment to avoid metallic multilayer. There are a lack of large enough drug-eluting stent so bare-metal stents (BMS) have been the device of choice in pulmonary veins. It can be affirmed that, as in coronary devices, DCB angioplasty could be an alternative to a second metal layer for BMS ISR in pulmonary veins.⁸ Even though previous experience with DCB and myofibroblasts inhibition have shown good results in PVR,^{9,10} to our best knowledge, this is the first case with success percutaneous approach using DCB and IVUS in PVR.

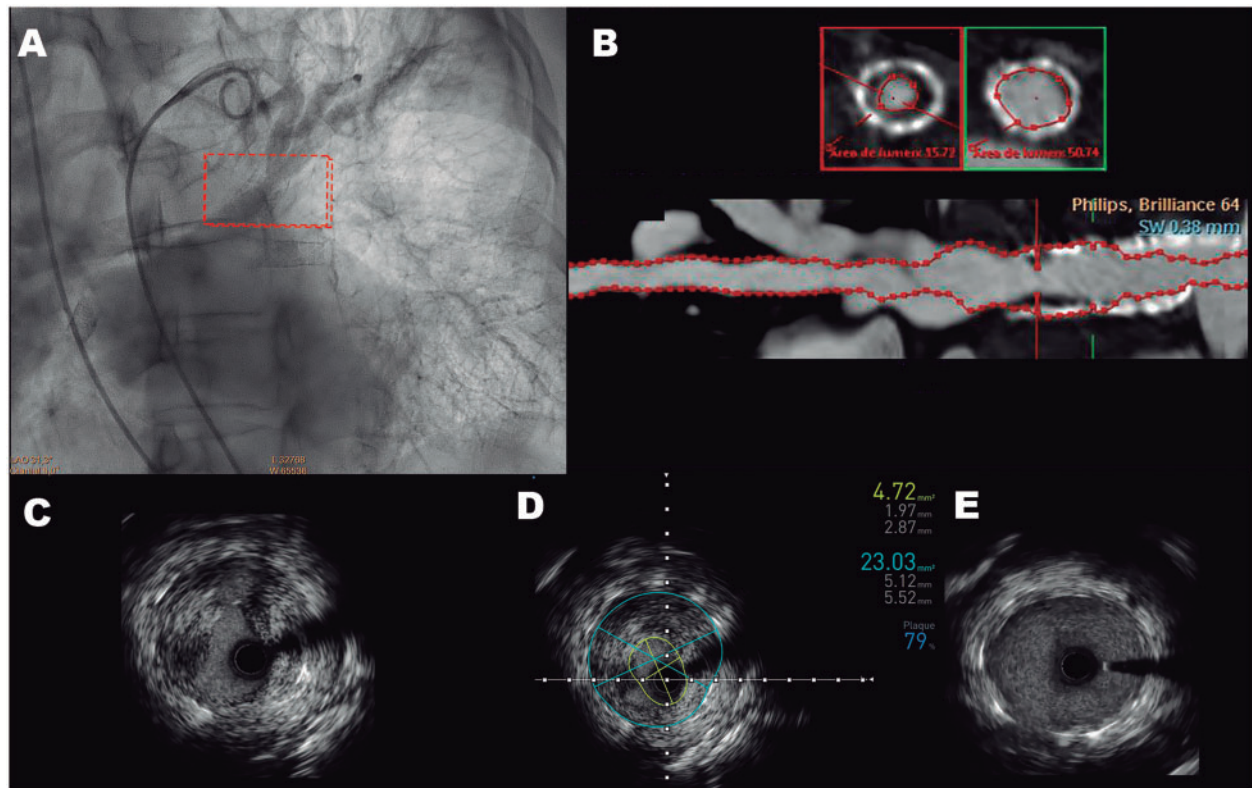


Figure 1 Central composition with left superior pulmonary vein treatment. (A) Angiography of the left superior pulmonary vein with severe in-stent stenosis (red box) using a pigtail catheter in the pulmonary artery. (B) Longitudinal computed tomography reconstruction of the left superior pulmonary vein showing the involvement between the affected distal end (red box) and proximal (green box). (C and D) Intravascular ultrasound image of left superior pulmonary vein before treatment of severe in-stent stenosis. (E) Intravascular ultrasound image of left superior pulmonary vein without stenosis after treatment.

Table 1. Device type, localization, measures, inflation pressure and hemodynamic gradient pre/post.

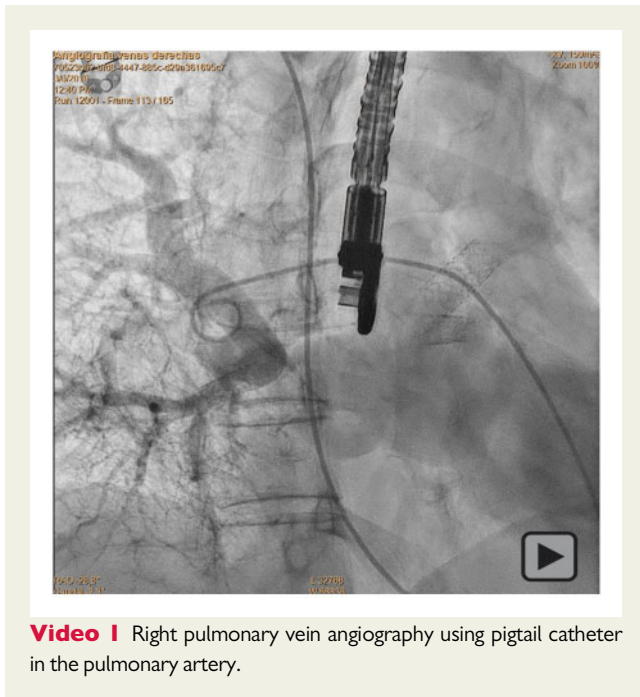
Vein	Device	Size (mm)	Inflation pressure (atm)	Pre/post gradient (mmHg)
LSPV	Pantera Lux TM (Biotronik, Berlin, Germany)	4 × 15	8	13/6
LIPV	Ranger TM (Boston Scientific, Massachusetts, USA)	8 × 30	6	20/3
RSPV	Pantera Lux TM (Biotronik, Berlin, Germany)	4.0/4.0 × 15	8/8	
RSPV*	Mustang TM (Boston Scientific, Massachusetts, USA)	10 × 40	8	20/4
RIPV	Ranger TM (Boston Scientific, Massachusetts, USA)	7 × 30	6	18/3

*In RSPV two drug coated balloons were inflated in parallel due to the lack of appropriate size coated balloon, finally a peripheral regular balloon angioplasty was realized.

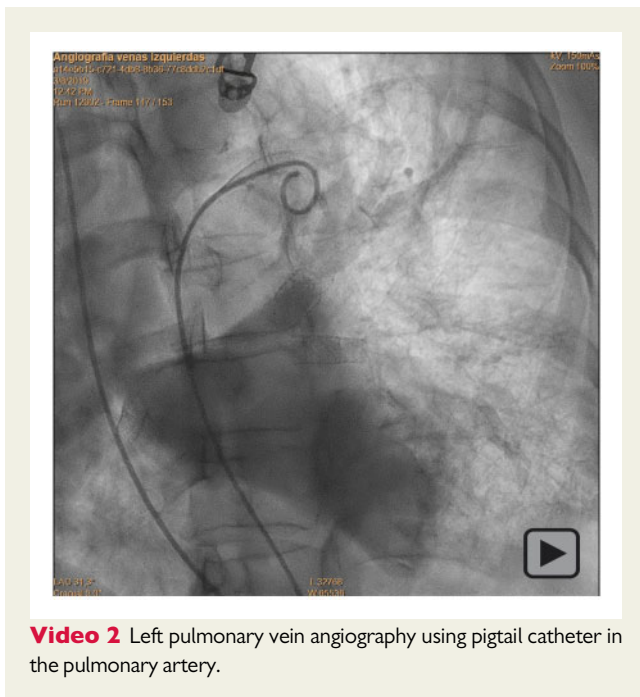
Follow-up after radiofrequency ablation of AF is neither standardized nor protocolized in most hospitals. Asymptomatic patients generally do not require imaging tests and clinical follow-up seems to be sufficient. In patients who develop symptoms suggestive of restenosis, the use of different imaging tests has been reported. In the longest series published after percutaneous treatment,⁵ it seems that CT could be the gold-standard test for follow-up because it provides anatomical information that allows diagnosis and planning future treatment. Although timing is not standardized, it seems prudent to

perform a first study at least at 6 months after treatment, spacing them according to clinical follow-up. The role of transthoracic echocardiography may be limited, but transthoracic echocardiography may show indirect data of increased pressures in the right cavities, or an established pulmonary hypertension. Despite this, the use of imaging tests should be standardized in the coming years in order to achieve a correct follow-up of these patients.

Finally, the antithrombotic regimen after PV angioplasty and stenting has been extrapolated from the experience with other coronary



Video 1 Right pulmonary vein angiography using pigtail catheter in the pulmonary artery.

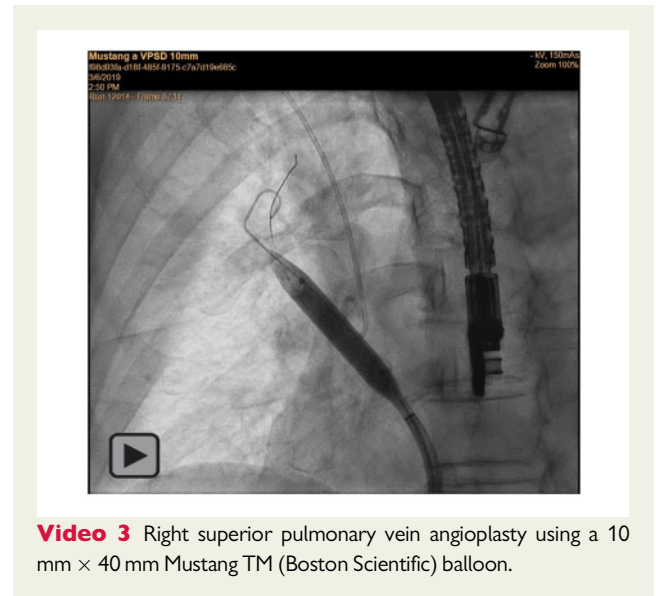


Video 2 Left pulmonary vein angiography using pigtail catheter in the pulmonary artery.

and intracardiac devices, without specific studies on this question. In our case, we decided to treat the patient with clopidogrel and edoxaban during the first 6 months after the procedure, maintaining only anticoagulation after that period.

Conclusion

Recurrent PVS following a successful percutaneous intervention is common. The use of IVUS for stenting index procedure and to guide



Video 3 Right superior pulmonary vein angioplasty using a 10 mm × 40 mm Mustang TM (Boston Scientific) balloon.

DCB angioplasty when restenosis occurs, seems to be an effective and safe strategy avoiding metallic multilayering in PV.

Lead author biography



Juan J. Portero-Portaz received his medical degree from the University of Castilla La-Mancha, Spain. Currently, he is doing a fellowship in haemodynamics and interventional cardiology at the General University Hospital of Albacete, Spain.

Supplementary material

[Supplementary material](#) is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as [Supplementary data](#).

Consent: The author/s confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: The authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements) or non-financial interest (such as personal or professional relationships, affiliations, knowledge, or beliefs) in the subject matter or materials discussed in this manuscript.

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