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Background

Pulmonary thromboendarterectomy (PTE) is the treatment of choice for patients with chronic thromboembolic pulmonary hypertension (CTEPH) as it can remove the chronic, fibrotic, flow-limiting organized thrombi within the pulmonary arterial bed, addressing the *primum movens* of the disease (1). Despite significant improvement in all haemodynamic parameters, residual pulmonary hypertension (PH) is frequent after PTE, ranging from 17% to 31% (2,3). There is no clear definition of residual PH after PTE, and the actual incidence of this condition has been difficult to quantify. Usually, moderate residual PH is well tolerated by patients and, as shown by data from the United Kingdom cohort, clinically relevant residual PH after PTE mainly occur when the mean pulmonary arterial pressure (mPAP) is greater than 30–35 mmHg (3). The risk of persistent/recurrent PH in the long-term underlines the importance of a systematic patient follow-up, even after PTE. Balloon pulmonary angioplasty (BPA) has been developed as a compassionate procedure for symptomatic patients with CTEPH who are ineligible for surgery or with persistent/recurrent PH after PTE. BPA is not able to remove clots as PTE, but it is able to restore the flow by fragmenting the thrombotic and fibrotic material, resulting in hemodynamic and clinical improvement. Selection of good candidates for BPA, especially after PTE, includes a complete re-assessment of the patient with persistent symptomatic PH after PTE at least four to six months after surgery using high quality imaging techniques such as computed tomography pulmonary angiography (CTPA), selective pulmonary angiography (to provide fine details) and right heart catheterization (RHC) to assess the hemodynamic impairment. However, these imaging techniques are not widely available and require expertise.

Clinical vignette

A sixty-one-year-old male was referred to our centre in September 2020 for exertional dyspnoea and severe right chambers enlargement on the echocardiogram. The patient had been treated with warfarin with sub therapeutic values of international normalized ratio (INR) (self-managed) since the diagnosis of acute pulmonary embolism in 2005. CTPA and non-selective pulmonary angiography showed bilateral perfusion defects suggestive of chronic thromboembolism while RHC confirmed severe pre-capillary PH [right atrial pressure (RAP) 7 mmHg; mPAP 60 mmHg; pulmonary artery wedge pressure (PAWP) 8 mmHg; cardiac index (CI) 3.0 L/min/m²; pulmonary vascular resistance (PVR) 8.4 woods units (WU)].

The case was discussed within a multidisciplinary team (MDT), and the patient was deemed suitable for PTE, which was done on November 2020. Due to haemodynamic impairment sildenafil therapy, 20 mg three times a day (TID) was started as bridging for surgery and withdrawn after PTE. Mild improvement of symptoms after surgery was documented during follow-up outpatient visits.

In February 2021, CTPA and RHC were repeated, as per our centres standard clinical practice for all patients three to six months after PTE. RHC showed the persistence of PH (RAP 8 mmHg; mPAP 51 mmHg; PAWP 10 mmHg; CI 2.5 L/min/m²; PVR 8.0 WU) and CTPA showed continual...
bilateral, multiple sub-segmental perfusion defects (endoluminal webs). Sildenafil therapy was recommenced at 20 mg TID, and the anatomic lesions were deemed suitable for BPA following further MDT discussion.

The patient underwent three BPA sessions during which segments seven and ten (May 2021), segments four and eight (June 2021) of the right lung and segment 10 (November 2021) of the left lung were treated. After these sessions, the patient improved significantly in terms of symptom reduction and hemodynamics, which showed a reduction of PVR from 8.0 to 5.4 WU. Further sessions are planned.

**Technique**

Percutaneous vascular access for BPA was performed via the femoral vein, using long sheaths through which right coronary artery catheters were inserted. Oral anticoagulant therapy with vitamin K antagonist was withdrawn at least five days before the procedure and replaced with low molecular weight heparin (when the INR was <2.0). A biplane angiography catheter laboratory was used to provide simultaneous anterior–posterior and lateral projections, and to avoid excessive exposure to iodized contrast medium. Three-dimensional reconstructions of the pulmonary tree by CTPA were also used to help the operators, two interventional cardiologists, recognize and selectively cannulate the vessels to be treated. In BPA, use of undersized balloons is initially recommended to reduce reperfusion injury and to allow vessels to gradually regain the original size before optimizing results with larger balloons. During the procedure unfractionated heparin was administered, monitoring the activated clotting time (target value 200–250 s).

**Comments and conclusions**

Evidence in the efficacy of BPA after PTE is lacking. Shimura et al. described BPA in nine patients who had undergone PTE but had gradually deteriorated after an initially favourable response (4). Hemodynamics and functional class improved at follow-up and the authors recommend combined PTE and BPA for patients with both proximal and very distal lesions (4). In our experience, between 2015 and 2020, nine patients (mean age 59±11 years; five females) with persistent PH after PTE underwent BPA. After an average of two sessions, we observed a hemodynamic improvement (reduction of mPAP from 44±10 to 38±10 mmHg; reduction of PVR from 6.6±2.2 to 6.3±4.6 WU, P value >0.05). The hemodynamic improvement in this small subset of patients appears less evident in comparison with surgical naïve patients [43 patients (mean age 69±14 years; female 24); reduction of mPAP from 43±14 to 35±11 mmHg (P value <0.05) and reduction of PVR from 7.5±3.5 to 5.2±3.2 WU, P value <0.05, after a median of 3 sessions]. A possible explanation could be that surgically treated vessels have an abnormal compliance and their recoil could be a limiting factor, ending in poor angiographic and haemodynamic results.

We can conclude that the role of BPA after PTE is to treat distal web-like lesions that cannot be reached by the surgeon. Albeit this procedure seems to be able to improve symptoms and hemodynamics, the selection of eligible patients, although mandatory, is not easy, especially after PTE.

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**Footnote**

_Conflicts of Interest:_ The authors have no conflicts of interest to declare.

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**References**

2. Delcroix M, Lang I, Pepke-Zaba J, et al. Long-Term Outcome of Patients With Chronic Thromboembolic Pulmonary Hypertension: Results From an International Prospective Registry. Circulation 2016;133:859-71.