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Additional percutaneous transluminal pulmonary angioplasty for residual or recurrent pulmonary hypertension after pulmonary endarterectomy

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ABSTRACT

Background: Pulmonary endarterectomy (PEA) has been the most effective therapy for chronic thromboembolic pulmonary hypertension (CTEPH). However, residual or recurrent pulmonary hypertension often persists after PEA. Recently, catheter-based angioplasty, called percutaneous transluminal pulmonary angioplasty (PTPA) or balloon pulmonary angioplasty, has been developed as a promising strategy for CTEPH. Therefore, the usefulness of PTPA for residual or recurrent pulmonary hypertension after PEA was investigated.
Methods: Thirty-nine patients underwent PEA from January 2000, and a total of 423 consecutive PTPA sessions in 110 patients were performed from January 2009 to May 2014. Of them, 9 patients (23.0% of 39 patients undergoing PEA and 8.2% of 110 patients undergoing PTPA) had undergone previous PEA and additional PTPA.
Results: In these 9 patients, pulmonary vascular resistance (PVR) was 15.6 (7.8–18.9) wood units at baseline, and significantly improved after PEA [5.6 (3.5–6.5) wood units] ($p < 0.05$). However, PVR gradually deteriorated before PTPA [8.1 (6.1–12.3) wood units] compared to after PEA, suggesting that these 9 patients had residual or recurrent pulmonary hypertension after PEA. PTPA was performed at 4.1 (2.7–7.9) years after PEA. Follow-up catheterization at 1.9 (1.3–3.3) years after PTPA revealed significant improvement of PVR [4.2 (2.8–4.8) wood units] ($p < 0.05$).
Conclusions: A hybrid approach combining PEA and additional PTPA may be reasonable for patients with both proximal and very distal lesions not easily approachable by PEA. PTPA could be a promising alternative therapeutic strategy for residual or recurrent pulmonary hypertension after PEA.

1. Introduction

Chronic thromboembolic pulmonary hypertension (CTEPH) treated with conventional medical therapy, such as ambulatory oxygen therapy and anticoagulation, carries a poor prognosis [1–6]. Pulmonary artery vasodilators for pulmonary arterial hypertension, such as prostanoids, phosphodiesterase-5 inhibitors, endothelin receptor antagonists, and stimulators of guanylate cyclase, are palliative [2,7–9]. Pulmonary endarterectomy (PEA) is the only curative strategy with long-term results for CTEPH. Therefore, PEA is established as a first-line treatment for many patients with CTEPH [2,10]. Meanwhile, some patients suffer residual pulmonary hypertension after PEA [10–12]. Residual pulmonary hypertension adversely impacts on quality of life and outcome in many patients. Nevertheless, a therapeutic strategy for residual pulmonary hypertension has not been well established [10–12].

Percutaneous transluminal pulmonary angioplasty (PTPA) has attracted attention as a new, less invasive intervention for patients with CTEPH because it is highly efficacious in relieving symptoms and improving cardiopulmonary hemodynamics [13–23]. Until recently, there have been crucial concerns about reperfusion pulmonary edema in PTPA, but refinement and innovation of PTPA techniques using a specific scoring index, PEPSI, and pressure wire have overcome reperfusion pulmonary edema and pulmonary injury [14,17]. Additionally, there is a high risk associated with re-sternotomy when patients undergo PEA again. Therefore, it is expected that PTPA is suitable for residual pulmonary hypertension after PEA.

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The purposes of this study were: 1) to investigate the clinical characteristics of patients with residual pulmonary hypertension after PEA, and 2) to clarify the efficacy and safety of PTPA in terms of clinical and hemodynamic improvement in patients with residual pulmonary hypertension after PEA. If this approach proves to be effective, PTPA will restructure the current therapeutic strategy for residual pulmonary hypertension after PEA.

2. Methods

2.1. Study patients

A total of 110 patients with CTEPH who underwent 423 consecutive PTPA sessions at Keio University Hospital or Kyorin University Hospital in Japan from January 2009 to May 2014 were included. They were diagnosed as having CTEPH by demonstration of organized pulmonary thromboembolism using contrast-enhanced lung computed tomography, perfusion lung scintigraphy, and pulmonary angiography, and by ruling out collagen vascular disease, pulmonary disease, left heart abnormality, and other systemic diseases by blood tests, pulmonary function tests, and echocardiography.

All patients provided written informed consent, and the performance of PTPA and analysis of clinical data in the present study were approved by the institutional review boards of Kyorin University Hospital and Keio University Hospital. A part of the included patients and data used for analysis in this study were the same as those in our previous reports [13,14,16,17,20].

2.2. Parameters studied

Clinical parameters including New York Heart Association (NYHA) functional class reflecting subjective symptoms, hemodynamics obtained by right heart catheterization, arterial oxygen saturation, mixed venous oxygen saturation, and B-type natriuretic peptide (BNP) were examined at the following four time points: 1) baseline (before PEA), 2) after PEA, 3) before PTPA, and 4) at follow-up, 6 to 12 months after the final PTPA session.

Right atrial pressure (RAP), pulmonary arterial pressure (PAP), and pulmonary arterial wedge pressure (PAWP) were measured by right heart catheterization. Cardiac output (CO) was determined by the Fick technique using assumed oxygen consumption. Pulmonary vascular resistance (PVR) was calculated by subtracting PAWP from mean PAP and dividing by CO. Plasma BNP level and 6-minute-walk-distance (6MWD) were measured at the time of right heart catheterization.

2.3. Definition of residual pulmonary hypertension and criteria for additional PTPA

The hemodynamic criteria for residual pulmonary hypertension were: 1) mean PAP of 25 mm Hg or greater and 2) PVR of 3.75 wood units (300 dyn/s/cm^{-5}) or greater, at more than 3 months after PEA, according to a previous report [24].

Therefore, patients were selected as potential candidates for additional PTPA based on fulfillment of all the following criteria: 1) the hemodynamic criteria mentioned above, 2) NYHA functional class II or worse, and 3) the patient understood the procedures of PTPA and possible complications, and gave informed consent of their own free will.

Meanwhile, patients who had active infectious disease and/or serious complications such as hepatic disease, kidney disease, hemorrhagic tendency, or poorly-controlled diabetes mellitus or hypertension, or were unable to lie on the treatment table during the procedure because of mental disorders, were excluded from additional PTPA.

2.4. PTPA procedures

PTPA was performed as described in our previous reports [13–20]. In brief, warfarin was stopped 3 days before the procedure and replaced by heparin, with a goal of activated clotting time during the procedure of 250–300 s. A catheter was inserted via the right jugular vein, because most patients had an anti-embolic filter in the inferior vena cava. A balloon wedge pressure catheter was inserted into the main pulmonary artery tract and replaced by a long Spring Guide Wire, before insertion of an 8-French long metallic sheath into the main pulmonary artery tract. A 7-French guide catheter was then inserted through the long sheath, and a 0.014 inch guide wire was passed through the target lesion. The target lesions were dilated with a 1.2 to 9.0 mm monorail or an over-the-wire balloon catheter according to the vessel diameter. The balloons were inflated by hand with an inflation device for 15–30 s until they were fully expanded. Selection of target vessels for PTPA was performed according to the methods described in our previous reports [13,14,16,17,20].

2.5. Statistical analysis

All data are presented as median (25th to 75th percentile). Hemodynamic parameters and BNP at baseline, after PEA, before PTPA, and at follow-up after PTPA were compared in each paired time-point by Chi square test and Dunn's multiple comparison test, as appropriate. A value of $p < 0.05$ was considered statistically significant.

3. Results

3.1. Performance of PTPA

In our institutions, 39 patients underwent PEA since January 2000. Of these, 9 (23%) patients subsequently underwent PTPA based on the hemodynamic criteria for residual pulmonary hypertension. These 9 patients represented 8.2% of the total population of 110 patients who underwent PTPA in our institutions from January 2009 to May 2014.

The baseline characteristics are detailed in Table 1. In the 9 patients included in this study, the time from PEA to PTPA was 4.1 (2.7–7.9) years, and that from PTPA to the follow-up catheter after PTPA was 1.9 (1.3–3.3) years, and therefore that from PEA to follow-up after PTPA was 7.4 (4.7–9.6) years.

Regarding the distribution of Jamieson classification, 3 patients were type I, 2 were type II and 4 were type III. The number of PTPA sessions performed per patient was 5.0 (3.0–7.0).

Fig. 1 shows representative angiographic findings during the PTPA procedure. In our experience, the characteristic lesions treated by PTPA in patients with residual or recurrent pulmonary hypertension after PEA were a sudden narrowing distal to the end of the endarterectomy segment with maintained patency.

Table 1
Baseline characteristics of patients at baseline (before PEA).

	Patients (n = 9)
Age, years old	55.1 (44.9–61.7)
Gender, female/male, n	7/2
NYHA functional class, I/II/III/IV, n	0/0/6/3
Systolic PAP, mm Hg	83.0 (67.0–93.0)
Mean PAP, mm Hg	52.0 (39.0–56.5)
CO, L/min	3.3 (2.8–4.2)
PVR, wood units	15.6 (7.8–18.8)
BNP, pg/mL (n = 8)	197.0 (78.1–372.8)

Values are n or median (25th to 75th percentile).
PEA, pulmonary endarterectomy; NYHA, New York Heart Association; PAP, pulmonary arterial pressure; PVR, pulmonary vascular resistance; CO, cardiac output; PVR, pulmonary vascular resistance; BNP, B-type natriuretic peptide.