Chronic thromboembolic pulmonary hypertension (CTEPH) is a distinct disease entity of pulmonary hypertension (PH) with a mean pulmonary arterial pressure (PAP) greater than 25 mmHg and is classified into central- and distal-types. 

Central-type CTEPH is diagnosed when PH persists for more than 6 months after acute pulmonary embolism associated with thrombotic obstruction of the large pulmonary artery (PA).

Although pulmonary thromboendarterectomy is an established treatment for central-type CTEPH, it is limited to only central-type CTEPH and is not feasible for distal-type CTEPH. Thus, distal-type CTEPH remains a fatal condition because of the lack of effective treatment.

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Although it has been reported that balloon pulmonary angioplasty may be useful for distal-type CTEPH, the interventional procedure is complicated by pulmonary hemorrhage and edema, right ventricular failure, and even death. Thus, a safer and more effective therapeutic strategy with an appropriate imaging method needs to be developed.

Optical coherence tomography (OCT) is an interferometer-based imaging modality that produces a 2-D image of optical scattering from the internal tissue microstructure with a high resolution of approximately 10–20 μm, 10-fold higher than that of intravascular ultrasound. We recently demonstrated that OCT is useful for observing PA lesions in distal-type CTEPH. In the present study, in order to develop an effective and safe treatment for distal-type CTEPH, we examined our modified method of percutaneous transluminal pulmonary angioplasty (PTPA) combined with OCT evaluation.
PTPA for Distal-Type CTEPH

After right heart catheterization, we performed PTPA with a continuous infusion of heparin (400–600 U/h), using a highly maneuverable, soft-tipped 0.035-inch wire to enter the distally stenosed or occluded PA, and 2–7-mm balloons to dilate the target lesions to 50–75% of the vessel diameter after oral administration of hydrocortisone (500 mg). We selected those PA segments for balloon dilation with signs of intravascular webs, filling defects, or complete occlusion. Before and after inflation, we performed 3 imaging evaluations (PA angiography and intravascular ultrasound in all patients and OCT in half of them) in order to assess the effectiveness and safety of PTPA. The PTPA procedure was limited maximally to up to 2 lobes in 1 procedure. After catheterization, the patients were observed for 1 day for possible development of reperfusion pulmonary edema. Catheterization was repeated at an interval of 4–8 weeks after PTPA in all patients, and additional PTPA was repeated until the mean PAP became less than 30 mmHg.

**Statistical Analysis**

All statistical analyses were performed using GraphPad Prism 5.0E (GraphPad Software, La Jolla, CA, USA). Differences among groups were assessed using 1-way ANOVA followed by Fisher’s protected least significant difference test. P<0.05 was considered to be statistically significant.

**Results**

Conventional pulmonary vasodilator therapy significantly improved plasma levels of brain natriuretic peptide and the cardiac index, but did not decrease PAP, pulmonary vascular resistance (PVR) or right atrial pressure (RAP) (Table). We performed PTPA in a step-wise manner (5±2 procedures for 14±7 lesions), which resulted in significant additional improvement of mean PAP and PVR (Table). OCT examination revealed that PTPA destroyed the typical flaps and webs in the PA and shifted them to the PA’s walls (Figure A–F). Pulmonary angiography also showed that PTPA enlarged the lumen diameter (55±77% increase), although some severe occlusions by thrombus were resistant to PTPA. Furthermore, PTPA significantly improved the WHO-FC, RAP and 6-min walk distance (Table). Importantly, all 7 patients treated with intravenous epoprostenol were successfully tapered off to oral beraprost without any hemodynamic worsening (Table).
Figure. Effects of percutaneous transluminal pulmonary angioplasty (PTPA) in patients with distal-type chronic thromboembolic pulmonary hypertension (CTEPH). (A–F) OCT findings of typical flaps and webs in 3 patients with distal-type CTEPH before (A,C,E) and after PTPA (B,D,F). (G) Kaplan-Meier curves of the PTPA group and historical control group. OCT, optical coherence tomography.
Discussion

The novel findings of the present study are that PTPA, when performed in a step-wise manner, markedly improves pulmonary hemodynamics and long-term prognosis in patients with distal-type CTEPH with no major complications, and that OCT is useful for evaluating the effectiveness of PTPA.

PTPA has been considered as an alternative therapy only in selected patients who are inoperable because of distal lesions or recurrent PH after surgery, although the experience with this procedure is extremely limited. It has already been reported that PTPA improves symptoms, exercise tolerance and PAP; however, a safer procedure needs to be developed. The fundamental difference between the previous report and the present study was that we used smaller sized balloons for fewer lobes per procedure, resulting in less severe complications as compared with the previous report.

The present results indicate that PTPA combined with conventional vasodilator treatment is quite effective in improving pulmonary hemodynamics in patients with distal-type CTEPH, suggesting that PTPA is a promising new therapy for the disorder. Importantly, we were able to taper off intravenous epoprostenol without any hemodynamic worsening in all patients having intravenous therapy, which is important to improve their quality of life as well as the healthcare cost. Furthermore, the present study demonstrates that the PTPA therapy markedly improves the long-term prognosis of patients with distal-type CTEPH. Although the prognosis of patients with non-surgical CTEPH has been improved with recent progress in medical treatment, we consider that additional PTPA can further improve their quality of life and long-term prognosis.

In conclusion, the present study demonstrates that PTPA combined with conventional vasodilator treatment is quite effective in improving the pulmonary hemodynamics and long-term prognosis in patients with distal-type CTEPH, although the procedure should be performed in a step-wise manner by specialists in PH centers to prevent major complications.

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Disclosures

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