Percutaneous Transluminal Pulmonary Angioplasty for Distal-Type Chronic Thromboembolic Pulmonary Hypertension

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hronic thromboembolic pulmonary hypertension (CTEPH) is a life-threatening condition characterized by a pulmonary vascular bed that is obstructed or obliterated with the organized thrombi, promoting increased pulmonary vascular resistance (PVR), progressive pulmonary hypertension (PH) and right heart failure. In a prospective study following survivors of acute pulmonary embolism, 3.8% of patients developed CTEPH within 2 years. However, up to 40% of patients with CTEPH have not had a clinically apparent acute pulmonary embolic episode. Survival without intervention is poor and proportional to the degree of PH and right ventricular dysfunction at the time of diagnosis. In one study, the 5-year survival rate in patients with CTEPH was 30% when the mean pulmonary artery pressure (PAP) was greater than 40 mmHg and 10% when it was greater than 50 mmHg.

Pulmonary endarterectomy (PEA) is recommended as the only curative treatment of choice for eligible patients with CTEPH and should be considered as the first treatment option whenever possible. However, only a proportion of patients fulfill the criteria for surgical intervention. Current basic criteria for the application of PEA include: (1) NYHA functional class III or IV symptoms; (2) a preoperative PVR greater than 300 dyne·s⁻¹·cm⁻⁵; (3) surgically accessible thrombus in the main, lobar or proximal segmental pulmonary arteries; and (4) no severe comorbidities. In particular, the location and extent of the proximal thromboembolic obstruction are the most critical determinants of operability. Patients with inaccessible thromboembolic pathology in distal pulmonary arterial regions are generally considered inoperable.

Medical treatment has been attempted in such cases of inoperable distal-type CTEPH and post-PEA residual PH with a distal lesion. Patients with CTEPH should receive lifelong anticoagulation to prevent recurrence of thromboembolic events, but conventional medical treatments, such as diuretics, digitalis, and chronic oxygen therapy, show low efficacy in the treatment of CTEPH because they do not affect the underlying disease processes. Over the past decade, several novel therapies have been developed for pulmonary arterial hypertension, including prostacyclin analogs, endothelin-receptor antagonists, and phosphodiesterase-5 inhibitors. However, direct evidence of the efficacy of these novel drugs from clinical trials in CTEPH patients is limited to date. In the largest and only randomized controlled trial with CTEPH patients (BENEFIT [Bosentan Effects in iNopErable Forms of chronic Thromboembolic pulmonary hypertension]), which involved 1,157 patients (bosentan 577, placebo 580), approximately 30% of whom had undergone previous PEA, treatment with bosentan significantly reduced PVR and NT-proBNP levels at week 16, but the 6-min walk distance remained unchanged, and there was no treatment effect on time to clinical worsening.

Percutaneous transluminal pulmonary angioplasty (PTPA) has the potential to improve not only the patient’s hemodynamic data but also exercise capacity and prognosis, and can be applied to those patients for whom PEA is not an option because of distal surgically inaccessible lesions or residual PH after PEA.

Feinstein et al reported that PTPA reduced mean PAP (42±12 to 33±10) and improve both the NYHA functional class (3.3 to 1.8, P<0.001) and 6-min walk distance (209 to 497 yards, P<0.0001) in 18 patients with CTEPH; however, 11 patients developed reperfusion pulmonary edema and required mechanical ventilation.

In this issue of the Journal, Sugimura et al demonstrate the efficacy and safety of PTPA in 12 patients with distal-type CTEPH. PTPA in a step-wise manner (5±2 procedures in 14±7 lesions) significantly improved hemodynamic data such as mean PAP (43±9.5 to 24.8±4.9 mmHg, P<0.01) and PVR (672±236 to 310±73 dyne·s⁻¹·cm⁻⁵, P<0.01), WHO functional class, and 6-min walk distance (340±112 to 441±76 m, P<0.05). All 7 patients treated with intravenous epoprostenol could be tapered off safely without deterioration after PTPA. Hemoptyisis occurred in half of the patients but could be treated with oxygen supply and non-invasive positive pressure ventilation without intubation only. Significant improvement of prognosis was observed in the PTPA patients compared with 39 historical controls with distal-type CTEPH. In this article, optical coherence tomography was used as a new imaging modality to estimate the target lesions, and it may be suitable for detecting the detail of these structures before and after PTPA, which pulmonary angiography and enhanced CT cannot demonstrate because all the webs and bands in the pulmonary arteries are comprised of thin fibrous tissues.
A troublesome complication associated with PTPA is reperfusion pulmonary edema, which almost always occurs within 48 h after vessel dilation. Feinstein et al reported that the development of reperfusion pulmonary edema correlated with a pre-PTPA mean PAP >35 mmHg (P<0.04; odds ratio, 4.8), but it did not correlate with the patient’s age, cardiac index, or the size of the dilated pulmonary artery segment. One patient died of right ventricular failure 1 week after PTPA, despite mechanical ventilator support and administration of inhaled nitric oxide. To minimize the hazard of complications, the number of target lesions should be limited per procedure (Sugimura et al: up to 2 lobes, Feinstein et al: up to 3 lobes) and PTPA should be performed in a staged fashion over multiple procedures. In addition, the maximal balloon size should be less than or equal to the surrounding vessel size to avoid vessel rupture.

Although PTPA might be a promising alternative treatment in selected patients who have inoperable disease because of distal surgically inaccessible disease or persistent or recurrent PH after PEA, experience with this technique in CTEPH patients is currently very limited worldwide and there are a number of unanswered questions such as the frequency of recurrence and longer prognosis after PTPA, appropriate techniques to avoid complications and the significance of medical therapy to stabilize hemodynamics and right cardiac function before the procedure. More reliable data from larger clinical trials are required to establish this technique. Until the establishment of its feasibility, efficacy and safety, the performance of this technique should be limited to institutions with special expertise in pulmonary vascular diseases and cardiopulmonary catheterization, because of the risk of potentially lethal complications.

References