Chronic thromboembolic pulmonary hypertension (CTEPH) is characterised by stenosis and obstruction of pulmonary arteries with non-resolving organised thromboemboli combined with a variable microvasculopathy. This can lead to elevated pulmonary vascular resistance (PVR), severe pulmonary hypertension (PH), right heart failure, and finally, death [1,2]. Pulmonary endarterectomy (PEA) remains the standard treatment if patients with CTEPH who are judged to be operable [2].

Balloon pulmonary angioplasty (BPA), an endovascular procedure to dilate stenotic or obstructed pulmonary arteries, has emerged as an alternative treatment option for patients with non-operable CTEPH (Fig. 1). The first case series, reported by Feinstein et al. in 2001, demonstrated a reduction in mean pulmonary artery pressure (mPAP) of 9 mmHg, but also reported that its mortality rate was 5.6% [3]. With refinements in the technique, several reports, mainly from Japan, have succeeded in improving the efficacy and safety of BPA. These studies, mostly published since 2012, reported an overall reduction in mPAP of 21 mmHg from baseline and a mortality rate of 1.5% after averaged 4 angioplasty sessions in each patient [4]. The most common complication of BPA is lung injury which is characterized by lung opacities on chest X-ray or computed tomography resulting in hypoxia or hemoptyis (Fig. 2). The underlying cause of lung injury is distal vascular injury provoked by either iatrogenic wire injury, overdilation by the balloon or high reperfusion pressure in some cases [5]. Severe hemodynamic compromise is an important risk factor for lung injury during BPA [6]. Recent approaches with undersized balloons may reduce or prevent vessel injury, but it would be less effective in each individual segment. In order to resolve this paradox, the highly expert centers are increasing the number of targeted lesions, segments and lobes per session. There might be no limitation of treatment area, because high perfusion injury or balloon injury may be prevented with undersized balloon. Secondary dilatation with an appropriate balloon size for the same lesions which had been approached with undersized balloon in previous sessions can normalize pulmonary blood flow [5]. Moreover, difficult and high-risk lesions such as total occlusion have been treated aggressively at the highly experienced centers (those with more than 100 BPA sessions being performed per year) [5,6]. Thus, with not only accumulation of experience but also refinements in technique, severe and fatal complications would be minimised without sacrificing the efficacy of BPA.

Almost normal hemodynamics achieved by BPA have been maintained up to 3.5 years after BPA [7]. Moreover, these hemodynamic improvements translate into excellent survival rates for patients who undergo BPA. In the aforementioned study, the 1-, 3-, and 5-year survival rates were 98.7%, 98.0%, and 95.5% from 170 patients studied [7], which is markedly better than expected for inoperable CTEPH patients. These high survival rates are also comparable with those of operated CTEPH patients in the international prospective CTEPH registry (n = 404) where 1-, and 3-year survival were 93% and 89% [8]. The efficacy and safety of BPA for non-operable cases were equivalent to those achieved using PEA for operable cases [9]. However, these reports never propose that BPA could replace the role of PEA. Patients with surgically accessible lesions and others with surgically inaccessible lesions should have different phenotypes. Even though there might be slight overlap in the indication, almost all patients with CTEPH can be treated mechanically either with PEA or BPA, and it would lead to a notable improvement in their prognosis.

Furthermore, ‘hybrid therapy’ combining PEA and BPA must be one possible treatment strategy, because some patients may have both proximal fibrotic lesions and also distal surgically inaccessible lesions, or other patients may have residual/persistent PH after PEA which is observed in 15–18% of the patients [8]. A Japanese BPA team reported that additional BPA for residual PH after PEA improved hemodynamics significantly with mPAP decreasing from median 43 to 26 mmHg, and PVR median from 8.1 to 4.2 Wood units after average 5 sessions of procedures in 9 patients studied [10]. Although the hemodynamics were almost normalized after PEA, additional BPA for symptomatic patients (> NYHA 2) achieved further improvement of exercise capacity and symptoms compared to patients treated only by PEA in a study of 20 patients [11]. On the other hand, although persistent severe PH after incomplete PEA carries a risk of death, the benefit of ‘rescue BPA’ for persistent severe PH after failed PEA is questionable [12]. Although PEA should be considered as the first choice for operable patients, hybrid therapy with initial unilateral BPA to the lung with distal lesions and secondary PEA to the other lung with proximal lesions for severe hemodynamic patients might be appealing, because antecedent BPA could improve a very high PVR, which is a risk factor of perioperative mortality [13]. We have experienced several successful cases who underwent BPA first and then secondary PEA without any complications.

Until recently, many reports on the efficacy and safety of BPA had been published mainly from Japan. However, with accumulation of evidence, attempts to treat non-operative CTEPH patients with BPA has spread to several countries outside Japan, even to countries where BPA was initially viewed with skepticism [14,15]. Currently, the hemodynamics improvements in these countries appear to be inferior compared to the results of Japanese BPA registry. This could
be due to the accumulation of operator experience, or patient phenotypes also may differ such as the gender ratio or proportion with a history of acute pulmonary embolism \[1\]. More work is still needed to better understand these differences.

The management of non-operable CTEPH patients has recently evolved dramatically with the availability of BPA. BPA should be considered as an established treatment strategy for non-operable patients; the recent 2018 World Symposium on pulmonary hypertension in Nice proposed and recommended PH targeted medical therapy and BPA for inoperable cases at the expert centers which are characterized by high volume and multidisciplinary team of experts including an experienced thoracic surgeon, chest physician, BPA interventionist and radiologist \[2\]. In the near future, the respective position of PH targeted medical therapy (riociguat; only approved for non-operable CTEPH) and BPA for these patients may be clarified by the ongoing RACE trial (Clinical Trials. Gov NCT02634203).

Large-scale prospective investigation by international BPA registry (Clinical Trials. Gov NCT 03245268) with specialized PH centers would provide further information regarding the safety, efficacy, and the best treatment strategy for patients with non-operable CTEPH.

**Disclosure of interest**

The authors declare that they have no competing interest.

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Received 11 March 2019
Received in revised form 1st April 2019
Accepted 2 April 2019
Available online 17 April 2019