Chronic thromboembolic pulmonary hypertension (CTEPH) is a life-threatening condition characterized by the pulmonary vascular bed obstructed by organized thrombi, which leads to progressive right-sided heart failure and a poor prognosis if left untreated. Pulmonary endarterectomy (PEA) has been recommended as the only curative treatment of choice for eligible patients with CTEPH and should be considered as the first treatment option whenever possible. Successful PEA can dramatically improve the patient’s hemodynamics and prognosis. However, only a proportion of patients fulfill the criteria for PEA and medical treatment has been attempted in cases of inoperable distal-type CTEPH and of post-PEA residual PH with a distal lesion. The principal medical treatment for CTEPH consists of life-long anticoagulant therapy, oxygen supply and a pulmonary vasodilator such as the soluble guanylate cyclase agonist, riociguat. Recently, Japanese investigators have refined balloon pulmonary angioplasty (BPA) by using smaller balloons, by cautiously limiting the number of balloon inflations and by the use of intravascular imaging. And they have demonstrated significant improvement in both the hemodynamic and exercise capacity after BPA. BPA is rapidly gaining attention worldwide as an effective treatment option for distal-type CTEPH.

In patients with CTEPH, persistent pressure overload induces progressive right ventricular (RV) remodeling, including myocardial hypertrophy, ventricular dilatation, tricuspid regurgitation and early diastolic ventricular septal bowing. These morphologic changes result in RV dysfunction and subsequent RV failure, which are the most common causes of death in CTEPH patients. And it is well known that RV pressure overload affects left ventricular (LV) function by not only limiting LV preload but also the abnormal pressure interaction via the interventricular septum and the pericardium, known as ventricular interdependence, which results in impaired LV filling, a decrease in LV stroke volume, and ultimately low cardiac output (Figure). Therefore, improvement in RV function is one of the most important treatment goals for CTEPH patients. PEA has been shown to restore RV function and RV remodeling by an acute reduction in RV afterload on echocardiography and magnetic resonance imaging (MRI). BPA also improves RV volume, RV systolic function, RV dyssynchrony and interventricular septal bowing assessed by echocardiography and cardiac MRI. However, the effect of BPA...
on LV function remains to be elucidated.

In this issue of the Journal, Sato et al.\(^{14}\) demonstrate that BPA improved not only RV function but also LV function and pulmonary flow estimated by cardiac MRI in CTEPH patients. Their retrospective study enrolled 30 consecutive patients with inoperable CTEPH because of the distal location of thrombi, surgical inaccessibility, high age and comorbidities. After BPA, WHO functional class and serum B-type natriuretic peptide concentration decreased and 6-min walk distance increased significantly. In addition, vasodilator drugs for PH could be partially decreased and all 7 patients treated with continuous epoprostenol infusion were successfully tapered off. Hemodynamic parameters such as mean pulmonary arterial pressure (MPAP: 40.8±23.2 vs. 23.2±4.9 mmHg, P<0.01), cardiac index (CI: 2.19±0.64 vs. 2.50±0.57 L⋅min\(^{-1}\)⋅m\(^{-2}\), P<0.01) and pulmonary vascular resistance (PVR: 7.50±2.43 vs. 9.79±2.92 Wood units, P<0.01), significantly improved after BPA. Cardiac MRI before and 9.0±8.7 months after BPA revealed significant improvements among both RV parameters, including RV end-diastolic volume index, RV end-systolic volume index, RV ejection fraction and RV mass index, and LV parameters including LV end-diastolic volume index (LVEDVI: 72.1±14.0 vs. 81.6±18.6 ml/m\(^{2}\), P<0.01) and LV stroke volume index (5.70±2.43 vs. 9.79±2.92 ml/m\(^{2}\), P<0.01). Among 22 patients who regained pulmonary arterial flow before and after BPA, the average velocity was significantly increased (7.50±2.43 vs. 9.79±2.92 cm/s, P<0.01).

In a recent report, Fukui et al.\(^{8}\) demonstrated the effect of BPA on advanced RV remodeling and dysfunction relative to hemodynamic parameter improvements in inoperable CTEPH patients. However, they showed that BPA did not significantly affect LV volumes or function. As the authors describe in the current report,\(^{14}\) incomplete hemodynamic improvement and short duration from final BPA to cardiac MRI assessment may be reasons for the discrepancy in the effects of BPA on LV remodeling. As another possible reason, the patients enrolled in Fukui’s study had longer average disease duration (60 months) than patients in the present study (20.5 months). Leftward ventricular septal bowing with LV compression in combination with low LV preload and underfilling has been shown to cause LV diastolic filling impairment in CTEPH patients.\(^{10}\) Chronic LV unloading leads to atrophic remodeling with LV diastolic and systolic dysfunction.\(^{16}\) Har dizyenka et al demonstrated that RV failure in CTEPH patients is associated with a reduction in LV free-wall mass, which is reversible after PEA.\(^{16}\) Hemodynamic parameter such as MPAP, CI and PVR before BPA were almost same between the 2 studies, but LVEDVI, LVESVI and LV mass index were smaller than in the present study. Such atrophic LV remodeling associated with disease duration may also influence the discrepancy in LV function after BPA between the 2 studies.

This study might be an important contribution to our understanding of the efficacy of BPA for biventricular function. Further studies on the influence of BPA on the long-term prognosis of inoperable CTEPH are anticipated in the future.

References


