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The Challenges in Managing Pulmonary Arterial Hypertension Associated with Congenital Heart Disease

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Pulmonary arterial hypertension (PAH) is a common complication in congenital heart disease (CHD). The development of PAH may be associated with increased mortality and morbidity in patients with CHD.[1,2] A recent nationwide study from the Netherlands reported that the prevalence of PAH was 3.2% in an adult CHD population.[3] In the current issue, the article by Dr. Dai provides a comprehensive review focusing on the contemporary knowledge about classification and medical treatment for PAH associated with CHD (PAH-CHD).[4] According to the 2009 European Society of Cardiology (ESC) guidelines on the management of PAH, PAH-CHD was subdivided into 4 clinical groups: (1) Eisenmenger syndrome; (2) PAH associated with systemic-to-pulmonary shunts; (3) PAH with small defects; and (4) PAH after surgical repair.[5] This classification is very efficacious for the purpose of choosing proper management strategies for PAH-CHD patients. For patients in group 3 (PAH with small defects) and group 4 (PAH after repair), the treatment principles are similar to idiopathic PAH with the exception of use of calcium channel blockers and anticoagulation.[6] Closing the defects of patients in group 3 and group 1 (Eisenmenger syndrome) are contraindicated.[7] In a recent study on the different clinical groups of PAH-CHD, the worst survival was observed in patients with PAH after defect repair or with small defects, as compared with patients with Eisenmenger syndrome or those with systemic-to-pulmonary shunts.[8] For patients in group 1 (Eisenmenger syndrome), targeted medical therapy such as bosentan may be beneficial in improving the clinical symptoms and long-term survival.[9-11] The treatment algorithms for patients of PAH-CHD group 1, group 3 and group 4 were well summarized recently by D'Alto et al.[6]

The current greatest challenge is the treatment decision on the group 2 (PAH with systemic to pulmonary shunts) patients. Closure of the cardiac defect before the development of irreversible pulmonary vascular disease may provide a chance of recovery in PAH-CHD with left to right shunts. However, on the contrary, the patients who develop or have persistent PAH after shunt closure have a worse prognosis than patients with uncorrected PAH-CHD.[8] Therefore, in patients with large systemic to pulmonary shunts presenting at an older age, careful evaluation of the operability before the shunt closure is extremely important. In recently proposed 2015 ESC guidelines for the diagnosis and treatment of pulmonary hypertension, closure of the defect is recommended if the pulmonary vascular resistance index (PVRi) below 4 Wood units $\times$ m^2 and to avoid the defect closure if the PVRi above 8 Wood units $\times$ m^2 (class of recommendation: IIa; level of evidence: C).[7] For patients with borderline hemodynamics (PVRi between 4 to 8 Wood units $\times$ m^2), although there is a lack of evidence-based recommendations at present, a personalized, patient-specific approach to evaluate the operability in tertiary centers is preferable. In addition to the baseline pulmonary flow and resistance calculations by cardiac catheterization, the evaluations may include clinical non-invasive assessment (cyanosis during rest or exercise, symptoms and signs of left heart failure, cardiac enlargement and pulmonary vascularity by the chest X-ray, left or right ventricular hypertrophy by electrocardiography) and invasive catheterization with reversibility test using pulmonary vasodila-

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tors, temporary shunt occlusion and pulmonary arteriolar wedge angiography.[12-14]

For patients of group 2 (PAH with systemic to pulmonary shunts) and regarded as uncorrectable by defect closure, there are still no evidence-based recommendations at present. The long-term effect of targeted PAH therapy for this patient group is still unknown. Recently, the concept of using of PAH therapy for these inoperable patients to reduce PVR and increase their chances of successful defect closure ("treat-to-close" strategy) had been raised.[15,16] However, this concept is still not supported by available data.[7]

TAKE HOME POINTS

1. The management strategies are different among the 4 clinical groups of PAH-CHD: (1) Eisenmenger syndrome; (2) PAH associated with systemic-to-pulmonary shunts; (3) PAH with small defects; and (4) PAH after surgical repair.
2. For patients in group 1, targeted medical therapy such as bosentan may be beneficial in improving the clinical symptoms and long term survival.
3. For patients in group 3 and group 4, the treatment principles are similar to idiopathic PAH.
4. Defect closure is contraindicated for those patients in group 1 and group 3.
5. A careful evaluation of the patient's operability before the shunt closure should be performed in the group 2 patients, especial in those with borderline hemodynamics (PVRi between 4 to 8 Wood units $\times$ m^2).

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