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

Chun-Wei Lu

Key Words: Congenital heart disease • Eisenmenger syndrome • Pulmonary arterial hypertension

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 × m⁻² and to avoid the defect closure if the PVRi above 8 Wood units × m⁻² (class of recommendation: IIa; level of evidence: C).7 For patients with borderline hemodynamics (PVRi between 4 to 8 Wood units × 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 vaso-
tors, temporary shunt occlusion and pulmonary arterio-
lar wedge angiography.12-14

For patients of group 2 (PAH with systemic to pul-
monary shunts) and regarded as uncorrectable by de-
fect closure, there are still no evidence-based recom-
mendations at present. The long-term effect of targeted
PAH therapy for this patient group is still unknown. Re-
cently, 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 hemody-
namics (PVRi between 4 to 8 Wood units × m⁻²).
   and outcome of patients with congenital heart disease
   and Eisenmenger syndrome: current advances.

REFERENCES

1. Duffels MG, Engelfriet PM, Berger RM, et al. Pulmonary arterial
   hypertension in congenital heart disease: an epidemiologic per-
   spective from a Dutch registry. Int J Cardiol 2007;120:198-204.
2. Lowe BS, Therrien J, Ionescu-Ittu R, et al. Diagnosis of pulmonary
   hypertension in the congenital heart disease adult population
   prevalence of pulmonary arterial hypertension in adult congeni-
tal heart disease following the updated clinical classification. Int J
   Cardiol 2014;174:299-305.
4. Dai ZG. Insight to pulmonary arterial hypertension associated
   with congenital heart disease (PAH-CHD): classification and
   pharmacological management from a pediatric cardiological
5. Galie N, Hoeper MM, Humbert M, et al. Guidelines for the diag-
nosis and treatment of pulmonary hypertension: The Task Force
   for the Diagnosis and Treatment of Pulmonary Hypertension of
   the European Society of Cardiology (ESC) and the European Re-
spiratory Society (ERS), endorsed by the International Society
   of Heart and Lung Transplantation (ISHLT). Eur Heart J 2009;30:
   2493-537.
6. D’Alto M, Diller GP. Pulmonary hypertension in adults with con-
genital heart disease and Eisenmenger syndrome: current ad-
   for the diagnosis and treatment of pulmonary hypertension: The
   Joint Task Force for the Diagnosis and Treatment of Pulmonary
   Hypertension of the European Society of Cardiology (ESC) and
   the European Respiratory Society (ERS): Endorsed by: Associa-
tion for European Paediatric and Congenital Cardiology (AEPAC),
   International Society for Heart and Lung Transplantation (ISHLT).
   with pulmonary arterial hypertension associated with congenital
   heart disease: a comparison between clinical subgroups. Eur
tients with Eisenmenger syndrome: a multicenter, double-blind,
   randomized, placebo-controlled study. Circulation 2006;114:
   48-54.
   therapy improves functional capacity in Eisenmenger syndrome:
   results of the BREATHE-5 openlabel extension study. Int J Cardiol
   among patients with Eisenmenger syndrome receiving advanced
   therapy for pulmonary arterial hypertension. Circulation 2010;
   121:20-5.
12. Viswanathan S, Kumar RK. Assessment of operability of congeni-
tal cardiac shunts with increased pulmonary vascular resistance.
13. Myers PO, Tissot C, Beghetti M. Assessment of operability of pa-
tients with pulmonary arterial hypertension associated with con-
14. Schwerzmann M, Pfammatter JP. Approaching atrial septal de-
ects in pulmonary hypertension. Expert Rev Cardiovasc Ther
15. Dimopoulos K, Peset A, Gatzoulis MA. Evaluating operability in
   adults with congenital heart disease and the role of pretreat-
ment with targeted pulmonary arterial hypertension therapy. Int
   J Cardiol 2008;129:163-71.
16. Beghetti M, Galiè N, Bonnet D. Can “inoperable” congenital
   heart defects become operable in patients with pulmonary arte-
rial hypertension? Dream or reality? Congenit Heart Dis 2012;
   7:3-11.