Pulmonary arterial hypertension in adults with atrial septal defect

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Atrial septal defect (ASD) is a congenital heart defect often encountered in the adult population, because many patients are free from overt symptoms for the first few decades and may show limited physical signs. Pulmonary arterial hypertension (PAH) complicating to left-to-right shunting at the atrial level is seen in 6–35% of untreated patients in later adulthood [1–3]. The presence of PAH is associated with older age, female sex, and defect size and causes progressive dyspnea, ascites, edema, presyncope or syncope, functional limitations, persistent right ventricular dilation and significant tricuspid regurgitation after closure of ASD, and increased mid-to-long-term morbidity and mortality [4–8]. Although the exact pathogenesis of PAH in patients with ASD is not clearly defined, it has been postulated that increased pulmonary flow leads to pulmonary endothelial damage with resultant leukocyte activation and release of mediators, ultimately causing vasoconstriction and eventual vascular hypertrophy [9]. The prevalence of Heath–Edwards grade 4 to 6 by histopathology of lung biopsy specimens was observed in 6% of adult patients who underwent surgical ASD closure. Histological changes in the intima and media of the pulmonary vessels can result in luminal narrowing and subsequent development of PAH. PAH can occur in adults with ASD as a result of chronic exposure of the pulmonary vessels to increased blood flow through the shunt.

PAH after ASD closure in adults

Patients with moderate or severe PAH may benefit from substantial reductions in pulmonary artery pressures after ASD closure, although pulmonary artery pressures remain elevated in a sizable population. A reduction in pulmonary arterial systolic pressure >5 mmHg was noted in 34%, 74%, 79%, and 100% of patients with no, mild, moderate, and severe baseline PAH, respectively [7]. Balint et al. [2] showed that systolic pulmonary artery pressure decreased from 58 to 44 mmHg in ASD patients with PAH who have undergone percutaneous closure after a median follow-up of 31 months. The proportion of patients with New York Heart Association functional class III or IV symptoms was reduced by 80% after transcatheter ASD closure [7].

Right ventricular enlargement, persistent PAH, and clinical heart failure development late after percutaneous ASD closure are seen more frequently in elderly patients. ASD closure for patients with PAH may induce further elevation of pulmonary arterial pressure and reduction in cardiac output.

As for arrhythmias, a significant relative risk reduction in the incidence of atrial tachyarrhythmia was noted after ASD closure. However, no reduction in the incidence of atrial tachyarrhythmia was noted after ASD closure in patients with severe PAH.

Evaluation before ASD closure in patients with PAH

ASD closure is associated with an increased post-procedural mortality in elderly patients with PAH. Once severe PAH or Eisenmenger syndrome has developed, ASD closure is problematic due to the increased risk of right ventricular failure and pulmonary hypertensive crisis. For avoidance of such a serious situation, some criteria were used to determine the operability of ASD patients with PAH. Cyanosis from right-to-left shunting at the atrial level is indicative of severe PAH. A hemodynamic study during temporary balloon test occlusion of ASD can be a good indicator of the subsequent evolution of PAH. If a drop in cardiac output or an increase in right ventricular filling pressure occurs with test balloon occlusion, it is indicative of a low likelihood of benefit from ASD closure.

Pulmonary vasodilators for patients with PAH before and after ASD closure

A recent large US-based registry suggested that PAH associated with congenital heart disease is more likely to be responsive to vasodilatory change than other forms of PAH [10]. For ASD patients with severe PAH, successful surgical ASD closure followed by post-operative reduction of pulmonary artery pressure using long-term prostacyclin treatment has been reported. Afterward, many reports indicated that ASD closure is possible in selected patients with severe PAH after advanced therapy with pulmonary vasodilators, i.e. oral bosentan, intravenous epoprostenol, and oral sildenafil [11–14].

Atrial septostomy for patients with PAH after ASD closure

In the presence of severe PAH, ASD would function as a safety valve to unload the right ventricle preserving its function and...
maintaining systemic output, despite the risk of hypoxia and cyanosis [15]. In addition, the natural history of idiopathic PAH may be better if a patent foramen ovale allows a reduction in right heart overextension by right-to-left shunting. For these reasons, percutaneous atrial septostomy is recommended for patients with severe PAH and intractable right heart failure despite maximal PAH-specific agents and inotropes as palliative treatment or bridge to transplantation [16,17]. Atrial septostomy creates a right-to-left interatrial shunt, decreasing right heart filling pressures and improving right heart function and left heart filling. While the created shunt decreases systemic arterial oxygen saturation, it is anticipated that the improved cardiac output will result in overall augmentation of systemic oxygen delivery. Improved cardiac output is considered to be the principal hemodynamic benefit. Kapoor et al. [18] reported hemodynamic and clinical improvement following the atrial septostomy of severe PAH using a unique technique. A major shortcoming of atrial septostomy is relatively high incidence of spontaneous closure or decrease in orifice size that requires repeat septostomy. Consequently, implantation of a fenestrated septostomy device in PAH proved successful in long-term follow-up [19].

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