Anatomy of Congenital Heart Disease Lesions Associated With Pulmonary Arterial Hypertension

Adult congenital heart disease represents a growing population of patients.

Many patients survive to adulthood and lead functional, productive lives. In

fact, there are more adults living with congenital heart disease than pediatric

patients. Many adult patients will have had prior surgical repair as children.

However, some patients present in adulthood with a new diagnosis of congen-

ital heart disease. Furthermore, there are a variety of complications associated

with each individual congenital lesion and specific surgical repair procedure.

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Pulmonary arterial hypertension (PAH) is one of the well-characterized sequelae. It is particularly common with unrepaired large left to right shunt lesions that occur distal to the tricuspid valve. Despite prior cardiac surgery, some patients have residual defects that contribute to the development of PAH. The diagnosis of PAH requires right heart catheterization and is defined as a mean pulmonary artery (PA) pressure greater than 25 mm Hg, with a pulmonary capillary wedge pressure, left atrial pressure, or left ventricular enddiastolic pressure less than 15 mm Hg, and a pulmonary vascular resistance (PVR) greater than 3 Wood units.¹

It is estimated that overall 5%-10% of patients with congenital heart disease and as many as 30% of unrepaired patients have PAH.² When PAH does occur in conjunction with congenital heart disease, it is associated with increased morbidity and mortality.^{2,3} However, the outcome and response to vasodilator therapies is much better for the cohort with congenital heart disease than for all other etiologies of PAH.¹

The pathophysiology leading to the development of PAH in congenital heart disease patients is related to increased pressure and blood flow in association with a left to right shunt lesion. This scenario is common in a large, uncorrected ventricular septal defect (VSD) or patent ductus arteriosus (PDA), and in surgically constructed shunts where the pulmonary vasculature is exposed to aortic systolic pressure. Alternatively, pre-tricuspid valve shunts, which are low-pressure lesions associated with increased volume circulating through the right ventricle (RV) and pulmonary circulation, such as atrial septal defects (ASD) and partial anomalous pulmonary venous return (PAPVR), lead to PAH much less often (Table).

Over time these shunt lesions lead to distinct changes in the pulmonary arterioles with the development of plexiform lesions and subsequent increases in PA pressures and PVR. This often results in right ventricular dysfunction, and in some cases as the PA pressures increase, reversal of shunting from net left to right to net right to left occurs with notable cyanosis and the onset of Eisenmenger syndrome. One rationale for early surgical or percutaneous repair of congenital cardiac disease is to prevent the onset or avoid the progression of PAH.

In this review, we will focus on the anatomy of the various congenital cardiac lesions that are associated with PAH. There are several congenital lesions that produce pulmonary venous hypertension, such as pulmonary veno-occlusive disease, cor triatriatum sinister, mitral valve abnormalities, and other left-sided obstructive lesions (coarctation of the aorta and supra-, sub-, and valvular aortic stenosis), but these lesions produce a different pathophysiology and will not be the focus of this discussion.

A VSD is a common form of congenital heart disease with an estimated prevalence of 3 per 1000 in children and 0.3 per 1000 adults, as some VSDs close sponta-

neously during childhood into adulthood.^{4,5} It is also the most common congenital cardiac lesion associated with PAH in a Dutch registry.⁶ There are multiple types of VSDs depending on their location: membranous or perimembranous, muscular, inlet and outlet varieties (doubly committed or infundibular) (Figure 1). Often more than 1 defect in the ventricular septum is present. Anatomically, a membranous VSD is bordered by the membranous portion of the ventricular septum, the aortic valve, and the tricuspid valve. In some cases, the septal leaflet of the tricuspid valve will cover this defect and form a "windsock" deformity with ventricular systole. Often the windsock is fenestrated with left to right shunting of blood from the left ventricle (LV) to the RV. At times, the septal tricuspid leaflet can fuse with the membranous ventricular septum, leading to closure of the defect and obliteration of shunting.⁵ Muscular VSD, as the name suggests, is surrounded by myocardium and can be located anywhere in the ventricular septum. There are often multiple VSD sites in a given patient. An inlet VSD is bordered by the mitral valve, the tricuspid valve, and the muscular septum. Given this location, it is a part of the spectrum of the atrioventricular (AV) canal or AV septal defect, previously referred to as endocardial cushion defects, and is often associated with trisomy 21 (Down syndrome). The inlet VSD is most commonly associated with PAH, with nearly 40% of such patients developing PAH.⁶ Finally, an outlet VSD, also referred to as an infindibular, doubly committed, or supracristal VSD with it location superior to the crista supraventricularis, is surrounded by ventricular

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CME

Section

Table: Risk for development of PAH with various shunt lesions

Low Risk	Intermediate Risk	High Risk
Secundum ASD	Sinus venosus ASD	Large, unrestricted VSD or PDA
Partial anomalous pulmonary venous return		Cooley-Waterston shunt
Small, restrictive VSD		• Pott's shunt
		Primum ASD
		 AV septal defect

septum, aortic valve, and pulmonic valve. It is important to recognize that any type of VSD may occur either in isolation or with other congenital abnormalities.

The size of a VSD (small vs large) is clinically often estimated, especially in children, by the ratio of the diameter of the VSD to the diameter of the aortic annulus.⁷ Defects that are less than or equal to 25% of the diameter of the aortic annulus (usually less than 1 cm) are designated as small, restrictive defects. In general, the smaller size limits flow and left to right shunt magnitude. In this scenario, the development of PAH is much less likely. Conversely, a large defect is defined as having a diameter greater than 75% of the diameter of the aortic annulus (usually greater than 1 cm). Given the larger defect and lack of restriction to flow, the pulmonary arterial bed is exposed to a greater degree of systemic LV systolic pressure, and the subsequent development of PAH is much more common.

Atrial septal defects are another common form of congenital heart disease. However, PAH develops less commonly (10%) with this lesion than in posttricuspid valve shunt lesions in which the pulmonary vascular bed is exposed to higher pressures as well as the increased shunt volume.8 Five subtypes of ASD have been described: secundum (75%), primum (15%), and superior sinus venosus (10%) are the most common. Less common are the unroofed coronary sinus and the inferior sinus venosus defect (Figure 2).9 A secundum ASD is characterized by a defect in the fossa ovalis region (generally central region) of the atrial septum. The primum ASD involves the inferior



Figure 1: Anatomic locations of VSD subtypes.

aspect of the atrial septum near the atrioventricular valves. If a concomitant inlet VSD is present, then the defect is classified as an AV septal defect (see previous section on VSD subtypes). In addition, the primum ASD is often associated with an abnormality in the anterior mitral valve leaflet termed a cleft mitral valve, which is associated with varying degrees of mitral regurgitation. The sinus venosus ASD is divided into 2 anatomic subtypes: a superior sinus venosus defect and an inferior sinus venosus defect. The superior sinus venosus ASD involves a defect in the superior aspect of the atrial septum at the junction of the roof of the atria and the entrance of the superior vena cava into the right atrium (RA). A superior sinus venosus ASD is associated with greater than 90% of cases with PAPVR of the right upper pulmonary vein, which aberrantly drains into the RA instead of the left atrium. The inferior sinus venosus ASD is defined by a defect in the interatrial septum inferiorly near the junction with inferior vena cava.

Partial anomalous pulmonary venous return functions as a low-pressure, pretricuspid valve shunt lesion, which serves to volume load the RV and pulmonary circulation in a similar manner to an ASD. It is also a rare lesion, with autopsy studies demonstrating an incidence of 0.6%-0.8%.^{17,18} Likewise, in addition to the previously discussed association of superior sinus venosus ASD and right upper pulmonary vein anomalous return, there is an association in 5%-10% of cases of secundum ASD with PAPVR.¹⁹ Anomalous pulmonary venous return also occurs at an increased frequency in patients with Turner syndrome.

There are multiple variations of PAPVR in terms of the anatomic location of the vein and number of veins involved and location of anomalous venous attachment/drainage. Anomalous veins may drain into the right atrium, left innominate vein, coronary sinus, superior vena cava, or the inferior vena cava (Scimitar syndrome) (Figure 3). Given that PAPVR is an uncommon lesion, an accurate population level estimate of association with PAH is not available. However, multiple case reports have been pub-



Figure 2: Anatomic locations of ASD subtypes.

lished describing PAH due to PAPVR in the absence of other congenital anomalies. The pathophysiology is similar to an isolated ASD, and thus a small percentage of patients with this pathology may develop PAH.

A PDA is another post-tricuspid valve, high-pressure to low-pressure shunt lesion that may lead to subsequent PAH. An essential component of fetal circulation and physiology, the ductus arteriosus usually closes during the first few days after birth. However, in some individuals the ductus does not close and persists as a congenital PDA. This represents 5%-10% of all congenital abnormalities.¹⁰ From an anatomic perspective, the fetal ductus arteriosus and persistent PDA are a funnel-like connection from the thoracic aorta to the main pulmonary artery. The development of PAH is related to the size of the PDA and the amount of shunt. In some series, the PDA accounts for 20% of cases of congenital heart disease-related PAH.¹¹

An aortopulmonary (AP) window is a rare congenital abnormality that is similar to a PDA, but differs in anatomic location. It is an anatomic connection between the ascending aorta and the main PA, and is usually large and unrestricted in terms of allowing high-pressure systemic flow into the pulmonary vasculature. This facilitates and accelerates the development of PAH and often progression to Eisenmenger syndrome if not surgically corrected at an early age.

Truncus arteriosus is a rare type of con-

genital heart disease characterized by a common great vessel originating from the heart and the PAs and coronaries arising from the ascending vessel. There are 2 classification systems, the system of Collett and Edwards¹² and the Van Praagh and Van Praagh¹³ system used to describe the relationship between the aorta and the PA. A VSD is essentially universal. This form of congenital heart disease is always diagnosed shortly after birth and unrepaired leads to severe PAH and Eisenmenger physiology. In adults with prior surgical repair for truncus arteriosus, residual shunt may exist and lead to PAH.

Double-outlet right ventricle (DORV) is another rare expression of congenital heart disease characterized by the origin of both great vessels from the morphologic RV, along with a VSD to allow oxygenated systemic blood from the LV, albeit mixed with venous return in most cases, to reach the aorta. Double-outlet right ventricle represents a broad spectrum of anatomy and pathophysiology depending on the location of the VSD in relation to the great vessels (subaortic, subpulmonic, doubly committed, or remote).¹⁴ Furthermore, the clinical presentation may vary from that of an isolated VSD, to transposition with a VSD, to tetralogy of Fallot-like, to single-ventricle physiology in the case of a remote VSD.



Figure 3: Anatomic variants of partial anomalous pulmonary venous return.

The subaortic subtype of DORV is most common, accounting for approximately 50% of cases.¹⁴ The subaortic DORV subtype also has the strongest association with development of PAH given pathophysiology similar to a large VSD. Pulmonary arterial hypertension may also occur in the unrepaired subpulmonic DORV subtype if there is not RV outflow or pulmonary valve level obstruction to minimize pulmonary blood flow. In one recent series from a database of patients with adult congenital heart disease, 17% of patients with the diagnosis of DORV were noted to have PAH.⁶

Some patients with congenital heart disease have had a surgical shunt to increase flow into the pulmonary circuit when the congenital abnormality prevented adequate pulmonary perfusion. These are generally palliative shunts as a bridge to complete surgical repair. As such, surgical shunts would often be ligated or taken down at the time of subsequent cardiac surgery. However, it is not uncommon to encounter an adult patient with a patent surgical shunt. Through the 1960s and 1970s, as surgical experience with congenital heart defects grew, it was discovered that these palliative high-flow, high-pressure shunts that delivered systemic blood flow to the lungs commonly resulted in PAH.

The first surgical shunt, referred to as a Blalock-Taussig (BT) shunt, was performed in 1944.²⁰ The BT shunt was constructed from connection of the right subclavian artery to the right PA (Figure 4). The original BT shunt evolved through several modifications, including use of the left side and a synthetic conduit (modified Blalock shunt) to connect the subclavian artery to the PA, which preserved the subclavian artery and circulation to the upper extremity along with control over flow to the lung via diameter of the conduit.

Subsequently, Dr Willis Potts performed a surgical procedure connecting the descending thoracic aorta to the left PA, which became known as a Potts shunt (Figure 4).²⁰ In a similar manner, Dr David Waterston devised a surgery whereby an anastomosis between the posterior aspect of the ascending aorta and the right PA was created (Figure 4).²⁰ This is commonly known as a Cooley-Waterston shunt. Less frequently used as a palliative shunt was the central shunt, or a surgically created equivalent of the congenital AP window, in which an anastomosis was made between the ascending aorta and the main PA. The Potts and Waterston surgical shunts have a much stronger propensity to produce PAH than the Blalock shunts due to less restrictive flow into the PA from the aorta. For that reason, they were abandoned in favor of the Blalock approach.

Eisenmenger syndrome is the end-stage result of long-standing PAH. It has a prevalence of approximately 8%-10% in patients with congenital heart disease.²¹ The pathophysiology involves the progression of irreversible PVR to the point at which PA pressures are greater than systemic aortic pressures and a shunt lesion that was originally left to right reverses in direction of blood flow right to left. With the onset of right to left shunting, cyanosis is apparent. In cases of a PDA, differential cyanosis may be observed due to the anatomic location of the shunt with cyanotic lower extremities and normal appearing upper extremities. Moreover, Eisenmenger syndrome is associated with a variety of other end-organ system complications. Once PA systolic pressure and/or PVR is greater than two thirds of systemic values, and certainly when Eisenmenger syndrome with right to left shunting is present, surgical intervention to correct the underlying cardiac pathology is generally contraindicated.

In conclusion, several anatomic forms of congenital heart disease can lead to PAH. In particular, pressure and volume loading left to right shunt lesions (posttricuspid valve) in contradistinction to only volume loading left to right shunt lesion (pre-tricuspid valve) are much more likely to cause PAH. From an epidemiologic perspective, unrepaired VSD and PDA are 2 of the more common lesions that will be complicated by pulmonary hypertension. The management of patients with congenital heart disease is complex, and pulmonary hypertension experts should work closely with cardiologists who have specialized training in adult congenital heart disease in order to optimize outcomes for patients with PAH related to congenital heart disease.

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Figure 4: Anatomic locations of surgical palliative shunts.

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