

The Role of Catheter-Based and Surgical Treatments in Patients With Congenital Heart Disease and Pulmonary Hypertension

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This manuscript is intended to provide a brief overview of the indications for and outcomes of surgical and transcatheter interventions for congenital heart disease and pulmonary hypertension (PH). Pulmonary hypertension is frequently encountered in children and adults with congenital heart disease and is most commonly related to large “central” shunts, ie, those occurring at the ventricular or great arterial level (Figure 1). If uncorrected early in infancy or childhood, large central shunts result in increased pulmonary blood flow, left heart volume overload, PH, and heart failure. If the child survives this initial period of volume overload and heart failure, they will very likely develop effacement of the normal pulmonary arterial architecture and severe elevations in pulmonary arterial resistance, eventually resulting in cyanosis and Eisenmenger syndrome.¹

Pre-tricuspid valve shunts, ie, those at the atrial and/or venous level, are typically not associated with severe PH in infancy and childhood, although progressive PH with age often occurs. Indications for surgical or transcatheter closure include evidence of right heart volume overload, arrhythmias, mild to moderate PH, and decreased functional capacity (Table 1).² Doppler echocardiography is indispensable as a cost-effective tool for the noninvasive evaluation of hemodynamics and shunt fractions.^{3,4} Invasive cardiac catheterization is reserved for the subset of patients in whom inadequate acoustic windows limit the utility of transthoracic echocardiography or those in whom pulmonary vascular resistance or chamber pressures must be measured directly. Cross-sectional imaging techniques using computed tomography or magnetic resonance imaging are also widely used in the noninvasive assessment of anatomy and function.⁵

SURGICAL INTERVENTIONS

Operative interventions to palliate or repair the congenital lesions were originally devised to address physiologic issues, specifically to increase or diminish the supply of blood to the pulmonary circulation. The early era of congenital cardiac surgery is marked by giant leaps forward in the physiologic treatment of lesions. For example, patients with pulmonary atresia or single ventricle defects under-

went placement of an arterio-pulmonary shunt, a wave of surgical innovation initiated by the famed Blalock-Taussig shunt, a subclavian to pulmonary artery connection supplying a controlled volume of arterial blood to the pulmonary arterial circulation (Figure 2).⁶ Residual hemodynamic defects are often present in operated patients and are a major cause of progressive deterioration that may not become evident for decades after surgery. Residual hemodynamic defects may be amenable to further surgery or transcatheter intervention. Reoperations in adults with congenital heart disease are common and provide particular challenges.⁷ The risks of reoperation are often greater than for the primary procedures, requiring careful entry into the chest with extensive dissection of scar tissue and longer cardiopulmonary bypass times and greater use of blood products.⁸ Careful preopera-

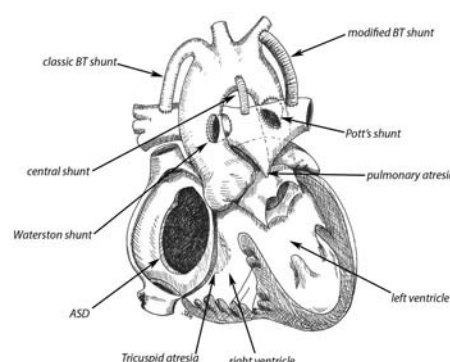


Figure 2: Tricuspid atresia and pulmonary atresia. Surgical arterio-pulmonary shunts placed to increase pulmonary blood flow. The classic BT (Blalock-Taussig), Waterston, and Pott's shunts are of historical importance and may be present in adults, but are no longer in clinical use for a variety of reasons, including difficulty in controlling pulmonary blood flow and the development of PH. The central and modified BT shunts are made of synthetic materials and are used in the current surgical era.

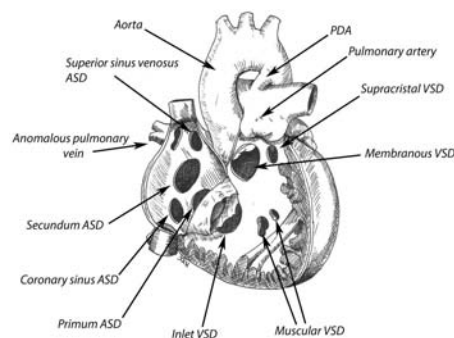


Figure 1: Types and locations of congenital cardiac defects.

tive planning should include an in-depth understanding of the underlying cardiovascular anatomy and the alterations caused by previous surgical intervention. Computed tomography or magnetic resonance angiography may be utilized to determine the anatomic relationships and quantify the proximity of the heart to the sternum; sternal entry is particularly risky when a high pressure ventricle, great artery, or conduit lies immediately posterior to the sternum. In patients with complex congenital heart disease, specifically those with cyanotic lesions, definitive “correction” may not be possible until the anatomy and physiology have been opti-

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Table 1: Indications for intervention in congenital shunt defects. Right ventricular enlargement (RVE), right atrial enlargement (RAE), pulmonary artery pressure (PAP), pulmonary vascular resistance (PVR), supraventricular tachycardia (SVT), dyspnea on exertion (DOE), left atrial enlargement (LAE), left ventricular enlargement (LVE), aortic regurgitation (AR), patent ductus arteriosus (PDA), pulmonary blood flow (Qp), systemic blood flow (Qs)

Defect	Indications for Intervention
Secundum ASD	Qp:Qs >1.5:1 RVE, RAE Mild-Mod Pulmonary HTN: PAP <2/3 systemic PVR <2/3 systemic Paradoxical Embolism SVT/DOE
Patent Foramen Ovale	Paradoxical Embolism (not prevented by antiplatelet/antithrombotic Rx)
Ventricular Septal Defect	Qp:Qs >1.5:1 LAE, LVE Mild-Mod Pulmonary HTN: PAP <2/3 systemic PVR <2/3 systemic DOE AR
Patent Ductus Arteriosus	Qp:Qs >1.5:1 Mild-Mod Pulmonary HTN: PAP <2/3 systemic PVR <2/3 systemic LAE, LVE SVT/DOE Any PDA?

mized by 1 or more “palliative” procedures. In patients with known PH, modulation of pulmonary arterial resistance with inhaled nitric oxide or parenteral prostacyclin therapy is indicated in the perioperative period. The decrease in systemic arterial resistance and systemic blood pressure encountered with prostacyclin therapy can be counteracted with

selective alpha 1 agonists or vasopressin in hypotensive patients.

Heart and heart-lung (block) transplantation are ultimate therapeutic options in patients who continue to deteriorate with optimal medical therapy and have no other good reparative surgical or interventional options. Compared with adult recipients, patients with adult congenital

heart disease experience higher post-heart transplantation mortality and retransplantation.⁹ Patients with Eisenmenger syndrome may be offered lung transplantation with repair of the cardiac defect or heart-lung transplantation. The success of either approach in these patients has been limited.¹⁰ Given the advancements in the management of PH and the limited success of these operations, mainly the sickest patients who fail to stabilize or improve on pulmonary arterial vasodilator therapy are considered candidates. The potential roles of ventricular assist devices and the total artificial heart in congenital patients are currently being investigated with promising early results.^{11,12}

TRANSCATHETER INTERVENTIONS

Major advances in percutaneous transcatheter interventions have been made over the past 25 years in the field of congenital heart disease.¹³ Improvements in device, imaging, and catheterization technologies and procedural techniques have brought interventional cardiology to the forefront as a therapeutic intervention that may delay or obviate surgery. Adult congenital cardiac catheterizations today are often performed solely for reparative or palliative transcatheter interventions.^{13,14} Interventional catheterization has largely replaced surgery as the treatment of choice for a number of congenital cardiovascular conditions, including secundum atrial septal defect (ASD) (Figures 3 and 6), patent ductus arteriosus (Figure 5), and ventricular septal defect (VSD) closure (Figure 4).^{13,15} Careful patient selection and imaging are imperative to the safety and success of transcatheter procedures.

SPECIFIC LESIONS

Atrial Septal Defect

Atrial septal defects are commonly encountered and occur in one-third of adults with congenital heart disease. Various types exist: secundum ASD is the most common, accounting for 75% of defects.¹⁶ Ostium primum defects, often accompanied by endocardial cushion defects and inlet-type VSDs, occur in 20% of cases. Sinus venosus defects (usually superior)

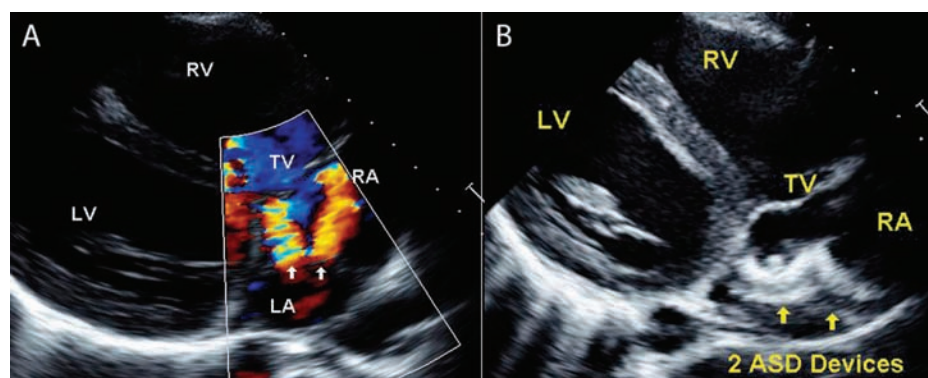


Figure 3: A) Transthoracic echo with color Doppler, modified parasternal long-axis view demonstrating a complex secundum type atrial septal defect (ASD) (vertical white arrows) that has multiple fenestrations and a left to right shunt. The right atrium (RA) and right ventricle (RV) are dilated. B) Post-transcatheter ASD closure with 2 Amplatzer septal Occluder devices. Left ventricle (LV), tricuspid valve (TV).

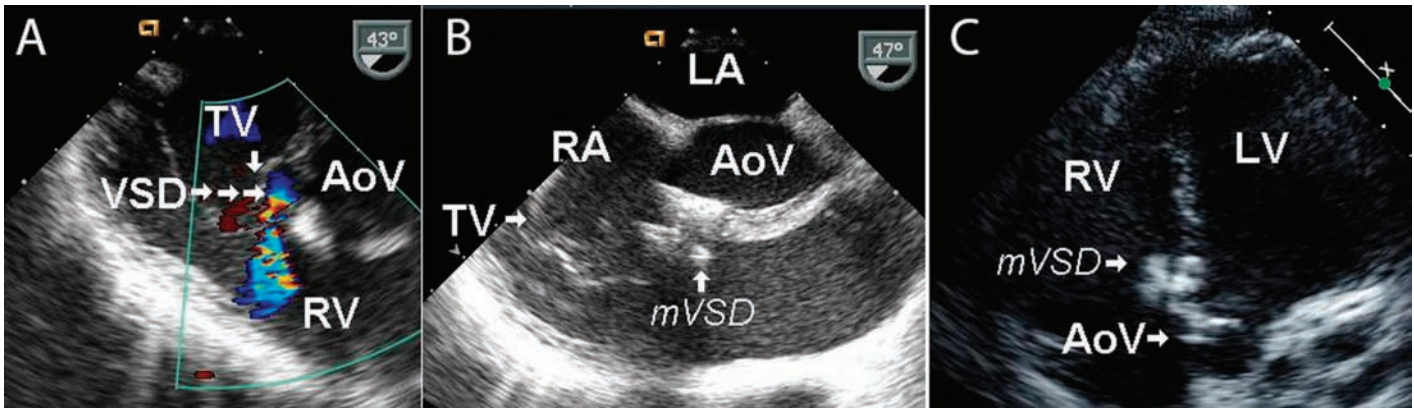


Figure 4: A) Transesophageal echo with color Doppler demonstrating a membranous ventricular septal defect (VSD) with left to right shunt and partial closure by the septal leaflet of the tricuspid valve (TV). B) Following placement of Amplatzer muscular VSD (mVSD) transcatheter device occlusion. C) Transthoracic echo, apical 4-chamber view demonstrating the mVSD device straddling the membranous septum below the aortic valve (AoV). Right ventricle (RV), right atrium (RA).

occur in 5% of patients; the rarest type is the coronary sinus ASD (Figure 1).

Atrial septal defects often go unrecognized for the first 2 decades because of the indolent clinical course and benign findings on physical examination. Initial diagnosis in adulthood is common and survival into adulthood is the rule. However, life expectancy is not normal in the unrepaired patient, with mortality increasing by 6% per year after age 40.^{17,18} Progressive symptoms of dyspnea on exertion and palpitations frequently occur in adulthood and are caused by increasing right-sided chamber enlargement, PH, right ventricular failure, tricuspid regurgitation, and atrial arrhythmias. The degree of left to right shunt may increase with age as left ventricular compliance decreases and systemic arterial resistance increases after the fourth decade. Paradoxical embolism may occur.

Surgical repair has been performed for over 40 years and has been efficacious and safe provided the pulmonary arterial resistance is not severely elevated.^{16,19} Several studies have shown improvement in functional capacity, reduced arrhythmia risk, and reduced incidence of PH after surgical or transcatheter closure, including in those with small defects (<1 cm), older patients, and asymptomatic individuals.²⁰⁻²³ Predictors of increased surgical mortality include: older age at operation, advanced heart failure (NYHA III or IV), Qp:Qs >2.5:1, pulmonary artery systolic pressure >40 mm Hg, and

increased pulmonary arterial resistance.²⁴ The exclusion of patients with severe PH from defect closure may eventually be obviated by pulmonary artery vasodilator therapy with prostaglandins, endothelin blockers, and phosphodiesterase type 5 (PDE-5) inhibitors that may reduce pulmonary arterial pressure and resistance permitting shunt closure in these patients.^{25,26} Severe PH in patients with ASD probably represents the coincidence of idiopathic PH or PH secondary to another process (eg, scleroderma) and ASD.¹ Unlike patients with large unoperated nonrestrictive central shunts (eg, VSD) who experience PH from birth and develop pulmonary vascular disease within the first few years, patients with

large ASD of similar shunt magnitude do not necessarily develop severe PH and right to left shunting or the onset of PH is delayed into late adulthood. That being said, a large ASD may contribute to the development of PH, but may not be the sole cause of the underlying pulmonary vascular disease in a cyanotic patient. Patients with trisomy 21 (Down syndrome) may develop accelerated pulmonary vascular disease in the presence of ASD (primum or secundum).

Transcatheter device closure of secundum type ASD was first performed in 1976 by King and Mills.²⁷ Advancements in biocompatible materials, device design, and catheterization technology have led to the availability of a variety of occlusion

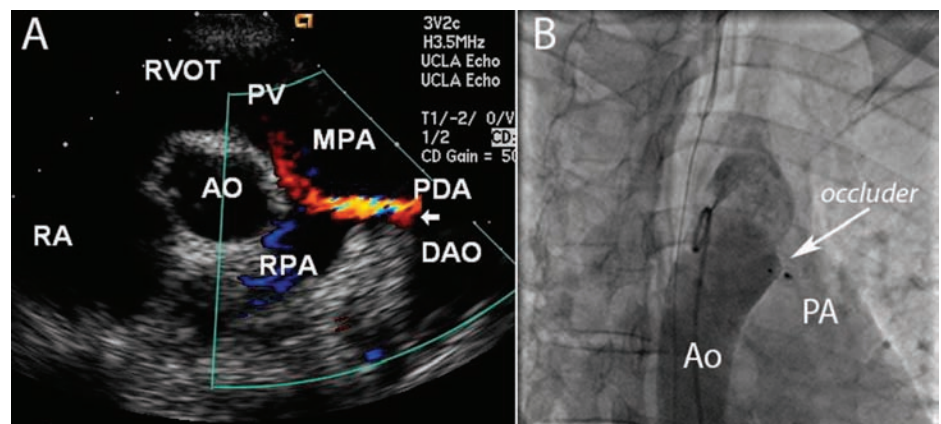


Figure 5: A) Transthoracic echo with color Doppler, parasternal short axis view, demonstrating continuous left to right shunting from the descending aorta (DAO) to the main pulmonary artery (MPA) via a patent ductus arteriosus (PDA). B) Aortic cineangiogram, right anterior oblique view following transcatheter device closure of the PDA, no residual shunting is seen. Right atrium (RA), right ventricle (RV), right pulmonary artery (RPA).

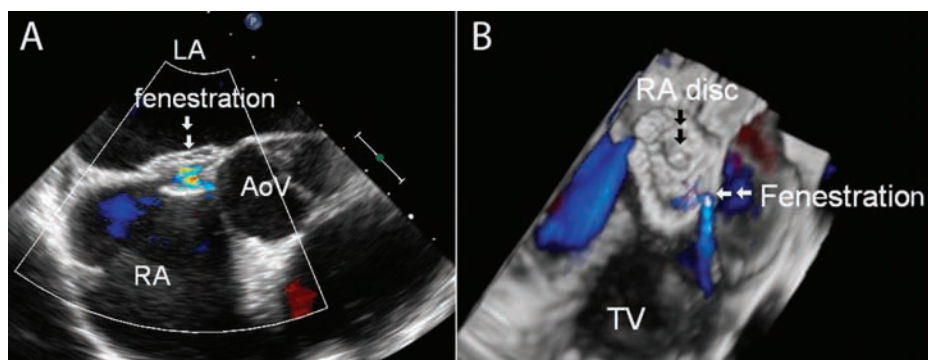


Figure 6: A) Transesophageal echo with color Doppler demonstrating a restrictive residual shunt through a fenestrated Amplatzer septal occluder. B) 3-D color Doppler viewed from the right atrium (RA) demonstrating residual shunting through a fenestration. Tricuspid valve (TV), left atrium (LA), aortic valve (AoV).

devices (Figures 3 and 6).^{28,29} Transcatheter device closure compares favorably with surgical closure in terms of long-term outcome and is associated with shorter hospital stays and fewer post-procedural complications.^{30,31} Appropriate patient selection is imperative and may be accomplished via a variety of noninvasive and/or invasive imaging methods.³²⁻³⁵ Transcatheter device closure techniques have supplanted surgery at many institutions as the method of choice for ASD closure in properly selected patients; complications are rare. Short-term complications have included device embolization, aortic root or atrial wall perforation, and cardiac tamponade.¹⁵ Mid- and long-term complications include thrombus formation, device erosion into the aortic root, atrial dysrhythmias, and infective endocarditis. The use of platelet inhibitors for at least 6 months following device closure is recommended to decrease the risk of device thrombosis.³⁶ The long-term outcomes of device closure using the Amplatzer septal are equivalent to long-term surgical results.^{31,37} Older patients with abnormal left ventricular compliance or restrictive physiology may have a significant increase in left heart filling pressure following ASD closure. Balloon test occlusion of the ASD with simultaneous measurement of pulmonary artery occlusion pressure or direct measurement of left ventricular diastolic or left atrial pressure may be revealing. Manual fenestration of commercially available devices allows for a

small “pop-off” for decompression (Figure 6).³⁸

Ventricular Septal Defect

Isolated VSD is the most commonly encountered form of congenital heart disease in the pediatric population; most are small and close spontaneously. The spectrum of isolated residual VSD encountered in the adult patient usually consists of:

- 1) Small restrictive defects or defects that have closed partially with time. The pulmonary vascular resistance is not significantly elevated and the left to right shunt magnitude is mild ($Q_p:Q_s \leq 1.5:1$).
- 2) Large nonrestrictive defects in cyanotic patients who have developed Eisenmenger syndrome, with systemic pulmonary vascular resistance and shunt reversal (right to left).
- 3) Patients with moderately restrictive defects ($Q_p:Q_s \geq 1.6:1$ and $\leq 2:1$) who have not undergone closure for some reason. These patients often have mild to moderate PH.
- 4) Patients who have had their defects closed in childhood. These patients may have VSD patch leaks.

Small restrictive defects of the muscular or membranous septum may be watched conservatively without need for operative intervention. Six percent of patients with small supracristal or perimembranous defects may develop aortic valve prolapse

and resultant aortic regurgitation that may be progressive.^{39,40} The prolapsing aortic valve cusp (usually the right coronary cusp) may partially or completely close the VSD. Aortic valve repair or replacement may be necessary in patients with aortic regurgitation who develop exertional symptoms or progressive left ventricular dilation.^{41,42} In a long-term follow-up registry, the overall survival rate was 87% for all patients with unoperated VSD at 25 years.⁴³ For patients with small defects ($Q_p:Q_s < 1.5$ and low pulmonary artery pressure), the survival rate was 96%; patients with moderate and large defects fare worse, with 25-year survival of 86% and 61%, respectively. Those with cyanosis (Eisenmenger's complex) had a much lower 25-year survival of 41.7%.

In patients with large nonrestrictive VSD, pulmonary vascular disease begins at birth or soon afterwards with abnormal vascular remodeling; eventually, if the defect is not repaired, the pulmonary arterial resistance exceeds the systemic arterial resistance resulting in right to left shunting and cyanosis, the condition known as Eisenmenger syndrome.⁴⁴ Early attempts at surgical closure of central shunts in patients with Eisenmenger syndrome were met with an unacceptably high risk of mortality and the practice was quickly abandoned. Thereafter, the condition was deemed “irreversible”; however, this common wisdom is now being challenged. There is ample evidence that pulmonary vasodilators result in improved pulmonary blood flow, improved functional capacity, and may improve survival in patients with Eisenmenger syndrome.⁴⁵⁻⁴⁸ Although isolated cases and small series of successful defect closure in Eisenmenger syndrome have been published, the majority of cases are deemed too high risk and closure is contraindicated.^{2,49} Larger defects may be repaired in the absence of severe PH and severely elevated pulmonary vascular resistance, which incurs a high perioperative risk (Table 1).^{2,50,51} Postoperative life expectancy is not normal but has improved over the past 50 years with improved surgical techniques and experience. Postoperative conduction defects

are common but complete heart block is rare in the current era. Transcatheter device occlusion of muscular and perimembranous VSD is feasible and trials demonstrate a good safety and efficacy profile (Figure 4).⁵²⁻⁵⁵ Complete heart block has been noted to occur in up to 6% of children and 1% of adults.^{52,55} Hybrid techniques, those involving surgical and transcatheter components, are being increasingly applied and may obviate the need for cardiopulmonary bypass. They are especially attractive for defects that may prove challenging to close via transvascular or surgical approaches alone or in infants with concerns over vascular access.^{56,57} Patients with small restrictive defects ($Q_p:Q_s \leq 1.5:1$ and low pulmonary artery pressure) are generally asymptomatic and do not require intervention unless they have aortic regurgitation or infective endocarditis.²

PATENT DUCTUS ARTERIOSUS

The ductus arteriosus is an essential communication during fetal life that (along with the foramen ovale) allows oxygenated maternal blood to be directed to the systemic circulation, thus avoiding the high resistance, kinked and collapsed, fetal pulmonary arterial circulation. Within 48 hours of birth, and under the influence of higher oxygen levels in the newborn as compared to the fetus in utero, the ductus arteriosus begins to close. In a small subset of human beings, occurring either spontaneously or more rarely as part of a family cluster, the ductus arteriosus remains open and is appropriately named a PDA. Patent ductus arteriosus is associated with other congenital malformations such as VSD or coarctation of the aorta. Those born at high altitude, presumably due to the lower oxygen tension, have a higher prevalence of PDA. The consequences of a PDA are largely dependent on the size of the duct and the magnitude of the shunt; very small PDA with negligible shunts are rarely problematic and do not result in PH or heart failure, but are rarely associated with endarteritis. Large defects with a $Q_p:Q_s$ of $\geq 1.5:1$ often result in left sided volume overload and progressive increases in pulmonary arterial pressure and resistance. If unrepaired



Figure 7: Differential cyanosis in a patient with patent ductus arteriosus, severe PH, and right to left shunt (Eisenmenger syndrome). Note the severe clubbing and cyanosis of the toes as compared to the lesser degree of clubbing and cyanosis of the fingers.

surgically or via transcatheter techniques, these defects often result in Eisenmenger syndrome with suprasystemic pulmonary arterial resistance and shunt reversal. Given that the location of the PDA is usually beyond the takeoff of the left subclavian artery, the deoxygenated pulmonary arterial blood shunts to the lower body resulting in differential cyanosis (Figure 7). Indications for surgical or transcatheter closure are similar to those for ASD and VSD (Table 1). Patients with severe PH without reactivity to pulmonary vasodilators or improvement with transient balloon occlusion are generally not considered candidates for PDA closure; however, there is a growing body of evidence that responsiveness to treatment with pulmonary vasodilators may facilitate subsequent defect closure using a variety of commercially available Nitinol devices.⁵⁸⁻⁶⁰

CONCLUSION

Pulmonary hypertension is often present in patients with native or operated congenital heart disease. The care of these patients is often challenging given the de-

gree of heterogeneity of native defects, including variations in defect location, size, shunt magnitude, shunt direction, coexistent conditions, the presence of multiple defects, and a wide spectrum of potential anatomic variations. The clinician seeking to provide care to this population should be familiar with the various surgical and transcatheter interventions that are currently utilized, their outcomes, potential complications, and expected sequelae. The indications and contraindications to surgical or transcatheter interventions in patients with PH and congenital heart disease are outlined. The outcomes of surgical and transcatheter procedures in appropriately selected patients are usually excellent.

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