Atrial Septal Defect

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KEYWORDS

• Atrial septal defect • Congenital heart disease • Pulmonary arterial hypertension
• Ostium secundum defect • Ostium primum defect • Sinus venosus defect

KEY POINTS

- Atrial septal defects are among the most common types of congenital heart disease that may go undiagnosed in childhood and may initially be found in adulthood.
- Adults with an atrial septal defect are often asymptomatic, but may present with nonspecific symptoms such as dyspnea on exertion or exercise intolerance.
- Pulmonary arterial hypertension and atrial arrhythmias may develop as a consequence of a long-standing unrepaired atrial septal defect.
- Management of the adult with an atrial septal defect must include consideration of whether or not pulmonary arterial hypertension is present, degree of shunting, and anatomy.
- Therapeutic considerations for an unrepaired atrial septal defect in the adult include pulmonary arterial vasodilator therapy, interatrial septal rim assessment, and candidacy for percutaneous versus surgical repair.

Video content accompanies this article at http://www.cardiology.theclinics.com.

INTRODUCTION

Atrial septal defects (ASD) are considered one of the most common congenital heart defects (CHD) found in the adult. The estimated prevalence of ASDs in adults is 0.88 per 1000 patients.[1] Frequently, the reason that this lesion is not detected sooner is that many patients are asymptomatic until the second to fourth decades of life, a time after which increased pulmonary blood flow may lead to pulmonary vascular remodeling and ultimately affect shunt direction and end-organ perfusion. Although this lesion is classified as a simple form of CHD, complex physiologic changes related to pulmonary vascular remodeling and shunt direction often complicate the presentation. Therefore, the assessment and treatment options vary widely between patients and require evaluation by specialized and experienced providers in the field of adult CHD.[2]

The purpose of this review is to describe ASD anatomy and various physiologic presentations in the adult. The goal is to review common clinical presentations and findings on imaging and special testing, and to discuss both practical and advanced management strategies inclusive of medical therapeutic considerations, surgical repair options, and percutaneous closure.

ANATOMY AND PHYSIOLOGY

Anatomy

There are 4 main types of defects that occur in the atrial septum and lead to the formation of an ASD (**Fig. 1**).[2] The most common type of ASD is the ostium secundum defect, which accounts for

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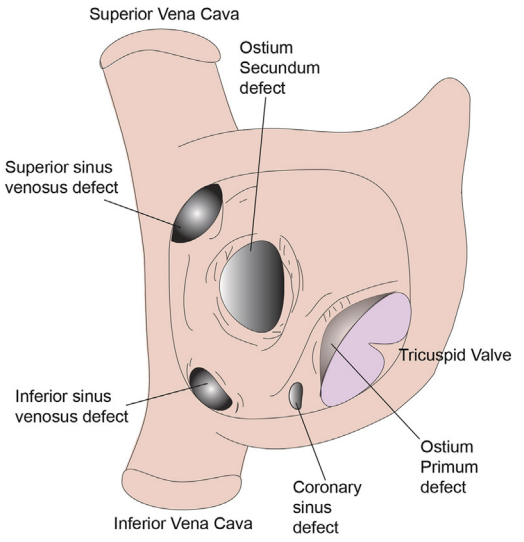

Fig. 1. Anatomy of the interatrial septum and septal defects. Anatomy of the interatrial septum demonstrating the location(s) of the 4 main types of ASDs: secundum, primum, sinus venosus, and coronary sinus, as viewed from the RA.

approximately 80% of ASDs. This defect arises owing to a deficiency of tissue at the level of the fossa ovalis. Ostium primum ASDs account for about 10% of septal defects and develop owing to a deficiency in tissue near the atrioventricular valves. Ostium primum ASDs are associated with a cleft in the left-sided atrioventricular valve and are often more aptly referred to by the synonymous term, partial atrioventricular septal defect. Sinus venosus defects occur more commonly in the superior (vs inferior) portion of the embryologic sinus venosus and commonly occur with partial anomalous pulmonary venous return, particularly of the right upper pulmonary vein. Coronary sinus defects, frequently referred to as unroofed coronary sinus, are the least common type of ASD and often are missed on traditional imaging modalities. However, an unroofed coronary sinus may be detected when agitated saline contrast bubbles from the left upper extremity enter the left atrium (LA) first, before the right atrium (RA).

Normal Physiology

When resting cardiopulmonary hemodynamics are normal in the presence of an ASD, blood shunts from the oxygenated LA through the ASD to the deoxygenated blood pool in the RA, creating a step-up in oxygen saturation at the level of the RA. Hemodynamics in the setting of an ASD are governed by Ohm's law as it relates to fluid flow in the pulmonary vascular bed (ΔPressure = Flow $\times$ Resistance, $\Delta P = QR$). So long as flow and resistance are low, the degree of shunting that occurs is based on end-diastolic filling pressures, compliance, and the anatomy and size of the defect. This lesion is generally well-tolerated in children, adolescents, and the young adult, in part owing to low filling pressures in the heart and high compliance in a system with normal pulmonary vascular resistance (PVR). However, in the case of a sizable ASD, over time the increased left-to-right flow across the defect leads to enlargement of the RA and right ventricle. This finding may be the first clue to the presence of an ASD.

Abnormal Physiology

In a minority of patients, the pulmonary overcirculation that results from a septal defect may contribute to abnormal pulmonary vascular remodeling and elevation in PVR, culminating in the development of pulmonary arterial hypertension (PAH). Up to 16% of adults who present with an ASD have concomitant PAH.[3] In most cases, although pulmonary artery pressures are elevated, they remain lower than the systemic blood pressure. However, in a minority of cases, the pulmonary vascular pressures increase to systemic or suprasystemic levels, resulting in reversal of the shunt (right-to-left flow) and peripheral desaturation with cyanosis, a condition called Eisenmenger syndrome. In general, therapeutic options for the patient that has developed frank Eisenmenger syndrome are limited in comparison with the adult with an unrepaired ASD and mild to moderate PAH. Recent studies have shown that those patients with ASD and mild to moderate PAH may respond favorably to PAH-specific medical therapy, and potentially regress PVR to a level at which septal defect repair may be possible, and perhaps impact long-term morbidity and mortality (**Table 1**).

CLINICAL PRESENTATION

Most adults who present with a newly diagnosed unrepaired ASD are asymptomatic, and the finding is incidental. However, in a minority of patients, a careful medical history and clinical examination may suggest the presence of an unrepaired ASD. In these patients, the history often reveals a gradual change in exercise capacity, commonly reported as subtle, and occasionally overt, dyspnea on exertion. Typically, a patient may describe this change occurring over the preceding months to years; however, if PAH is present, this change can occur more abruptly, on the order of weeks to months. Less frequently, palpitations may

Table 1
Studies evaluating delayed ASD closure in moderate to severe PAH

Author, Year	Timeframe	Location	N	Therapy	Outcomes
Cho et al,[17] 2011	2004–2009	Korea	16	PDE5i, ERA, Inh Prost	All closed with fenestration (PVR od 9.8)
Fujino et al,[12] 2015	2013	Japan	5	ERA, Inh Prost	1 patient had preclosure treatment
Bradley et al,[13] 2013	1998–2012	U.S.	15	PDE5i, ERA, Prost	5 (33%) underwent closure PVR of 8.8 (7.2 ➔ 4.6 vs 9.9 ➔ 8.2)
Kijima et al,[14] 2016	2006–2014	Japan	8 (22)	PDE5i, ERA, Inh Prost	All received closure (PVR 9.6 ➔ 4.0)
Song et al,[15] 2016	2001–2012	Korea	7 (17)	PDE5i, ERA, Inh Prost	All closed with fenestration (PVR 9.2 ➔ 6.3)
Bradley et al,[16] 2018	1996–2017	US	69	PDE5i, ERA, PC	19 (28%) underwent closure, closure group: ↑ RV function, ↑ 6MWTD, trend ↑ survival.

Abbreviations: 6MWTD, 6-minute walk test distance; ERA, endothelin receptor antagonist; Inh, inhaled; PC, prostacyclin; PDE5i, phosphodiesterase type 5 inhibitor; RV, right ventricle.

occur, especially in those that have developed an occult atrial arrhythmia, which is more common in the patient who presents at an older age. On physical examination, there may be a soft systolic crescendo–decrescendo outflow tract murmur owing to increased flow across the pulmonary valve, accompanied by a fixed split in the S2 heart sound owing to delayed closure of the pulmonic valve.

INVESTIGATION AND ASSESSMENT

Often the first test that a new patient with dyspnea receives is an electrocardiogram. This test can be helpful if an ASD is suspected, because these patients commonly demonstrate an incomplete right bundle branch block. More specifically, in the presence of a secundum ASD right axis deviation and crochetage (crochet-like hook) of the inferior lead R waves may be seen. In primum ASD, incomplete right bundle branch block is more likely to occur in the presence of left axis deviation. If a chest radiograph is sought, it is often normal. However, if the patient has developed PAH, there may be cardiomegaly and increased pulmonary vascularity.

Ultimately, imaging is required to confirm the diagnosis of an ASD. Frequently, a transthoracic echocardiogram is the preferred initial imaging test. The limitation of the transthoracic echocardiogram is that it may be impacted by poor acoustic windows related to the adult body habitus. However, image quality is often sufficient to evaluate the size of the RA and right ventricle, which are typically enlarged. This study can also provide information about pulmonary artery pressure, and may be the first clue as to the presence of PAH. In the patient with good transthoracic echocardiogram image quality, the interatrial septum can be visualized and color Doppler interrogation may be used to determine if a defect is present. Agitated saline contrast is often administered to determine if there is a septal defect present and, in the case of an ASD, demonstrates extravasation of saline contrast microbubbles from the RA to the LA at the level of the interatrial septum.

In most cases, a transesophageal echocardiogram (TEE) is required to more closely examine the interatrial septum to determine both the type and size of the ASD. These factors become important when considering therapeutic options with respect to closure and repair of the defect. Typically, the interatrial septum and defect are imaged in at least 3 different TEE planes: 0° and 90° at the mid esophagus, and 30° at the high esophageal level (**Fig. 2**, Videos 1–3). Although these views provide an adequate evaluation of the interatrial septum and rims, the inferior vena caval rim is often not well-visualized on TEE and, if it is suspected to be deficient, may require intravascular echocardiography at the time of hemodynamic evaluation.

Although advanced cardiac imaging such as computed tomography and cardiac MRI are not required to make the diagnosis of an ASD, these

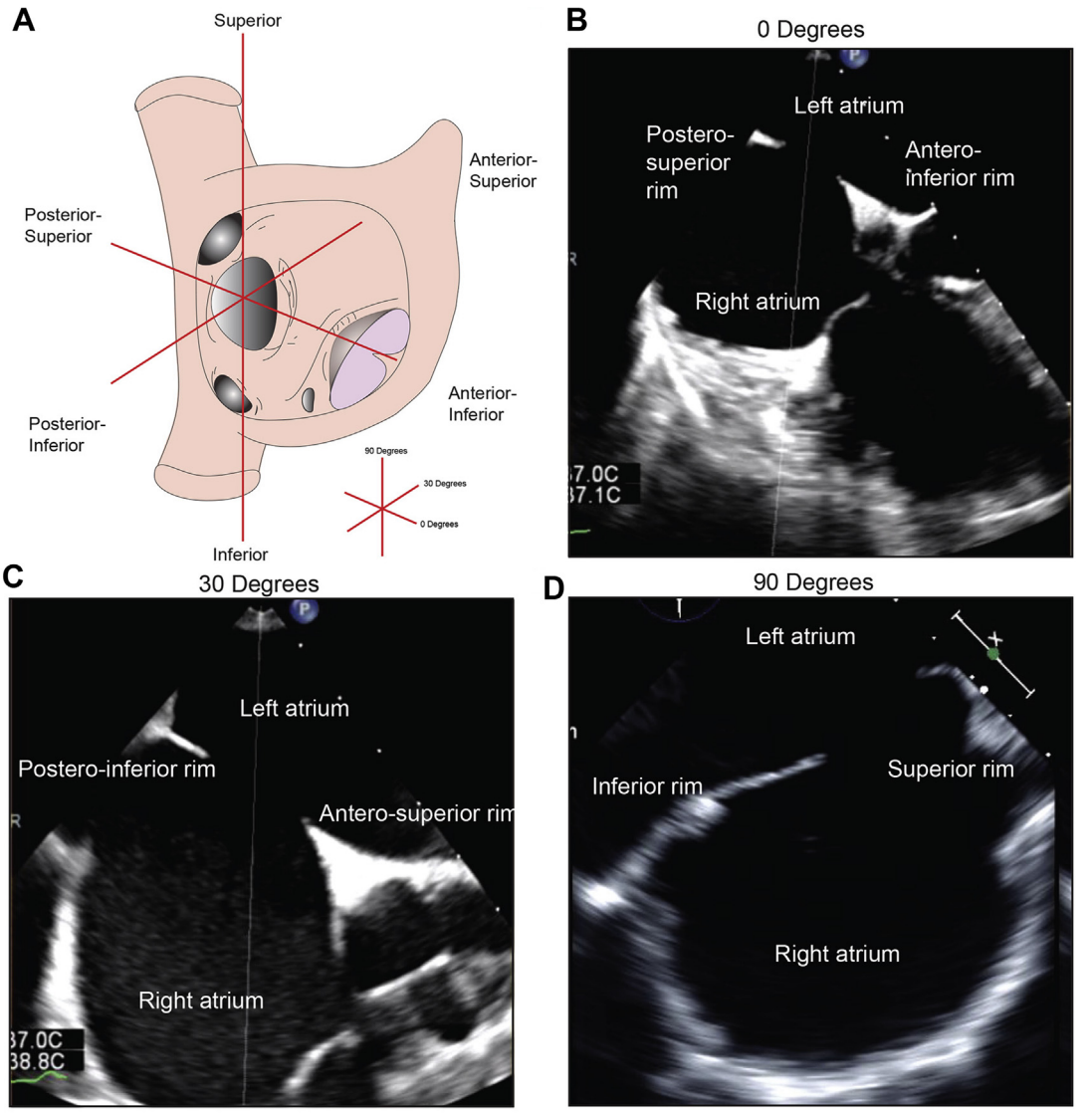

Fig. 2. Transesophageal imaging planes of the interatrial septum. Imaging planes of the interatrial septum (*A*) when evaluated by TEE include mid esophageal views at 0° (*B*) demonstrating the posterosuperior and anteroinferior rims and at 90° show the superior and inferior rims (*D*). High esophageal views at 30° (*C*) are required to demonstrate the posteroinferior and anteroinferior rims.

tests may be completed during the clinical workup. Advanced imaging provides high quality data on chamber size and function and can be helpful in determining whether or not anomalous pulmonary venous return is present, particularly when the pulmonary veins are not fully evaluated on TEE (Fig. 3). Additionally, flow quantification on cardiac MRI may be used to evaluate Qp:Qs in the presence of a septal defect.

Invasive hemodynamic right heart catheterization (RHC) is usually one of the last tests to be completed in the presence of an ASD, particularly when defect repair is being considered. RHC allows for the evaluation of shunt flow and in particular is helpful in quantifying the degree and direction of shunting. Intravascular echocardiography is frequently undertaken during RHC if TEE images are inadequate in evaluation of the defect, and if or when percutaneous closure is being considered. Intravascular echo is often used to provide direct visualization of the interatrial septum and allows for real-time 2-dimensional imaging guidance at the time of percutaneous closure.

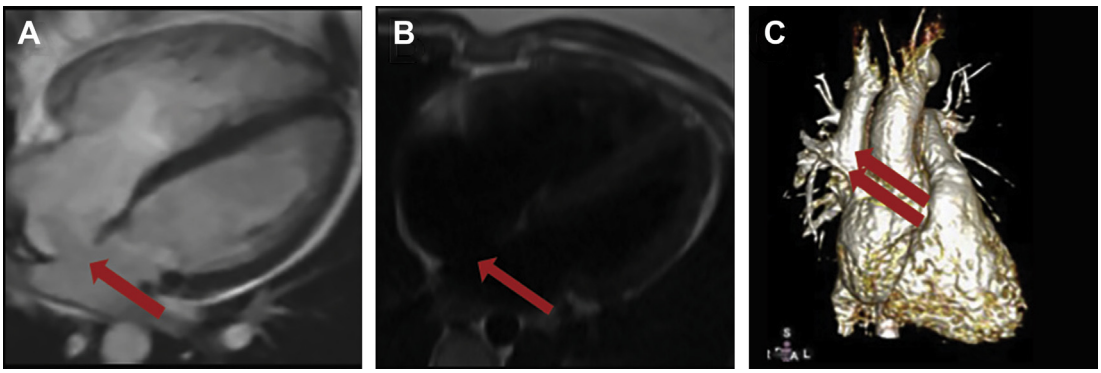

Fig. 3. Cardiac MRI evaluation for ASDs. Routine cardiac MRI sequences used to define the atrial septum on bright blood images (gradient echo sequences) (*A*) and dark blood images (fast spin echo sequences) (*B*). These images allow definition of atrial septal anatomy (*red arrow,* secundum ASD), atrial and ventricular morphology and are used to assess volumetric data and to quantify ventricular function. High spatial resolution MR angiography with 3-dimentional volume rendered imaging is used to define cardiac anatomy and morphology of the great vessels and systemic and/or pulmonary veins (*C*). The *double red arrows* demonstrate anomalous return of right-sided pulmonary veins to the superior vena cava.

Finally, exercise testing may be done before or after RHC in select cases. This testing can be accomplished in the form of a 6-minute walk test or more formal cardiopulmonary exercise testing. The purpose of exercise testing is not only to evaluate objective exercise tolerance, but also to assess oxygenation at rest and with peak exercise. In patients with normal resting hemodynamics (and in the absence of significant lung disease), oxygen saturation is typically normal. However, with exercise, a minority of patients demonstrate significant increases in the PVR. This hemodynamic change can cause a previous left-to-right or minimally bidirectional shunt to become right-to-left with activity, and results in exercise-induced desaturation. In this situation, closure of the defect may be unsafe and often PAH-specific medical therapy may be considered, even when resting pulmonary artery pressures may be normal (see **Table 1**).

MEDICAL DECISION MAKING AND THERAPEUTIC CONSIDERATIONS

Indications for Repair

Small ASDs may spontaneously close in childhood; however, larger defects may contribute to hemodynamic abnormalities and clinical symptoms if left unrepaired. The decision to repair an ASD is based on clinical and anatomic information, including the size and location of the defect, magnitude of hemodynamic impact of the shunt, and the presence and degree of PAH, if present. Patients with decreased functional capacity caused by hemodynamically significant ASD's (moderate or large left-to-right shunts, a Qp:Qs of >1.5 and evidence of right heart volume overload in the absence of significant PAH) typically benefit from surgical or transcatheter closure of the ASD.[4] Asymptomatic patients with a significant left-to-right shunt (Qp:Qs of >1.5) and evidence of right heart enlargement also benefit from closure, because continued overcirculation in an already dilated right heart increases the likelihood of late clinical complications, including decreased functional capacity, atrial arrhythmia, and the development of PAH.[5,6]

Contraindications for Repair

Closure of an ASD is not recommended in patients with a clinically significant right-to-left shunt and those with severe PAH (PVR of >8 Wood units or irreversible pulmonary vascular occlusive disease, desaturated at rest). There are emerging data that support that patients with a pulmonary artery pressure of less than two-thirds of the systemic arterial pressure, a PVR of less than two-thirds of the systemic resistance, or a positive response to pulmonary vasodilator testing may be considered for ASD closure.[6] A fenestrated device is often considered in these cases to ensure that an adequate "pop-off" is present so that if RA pressure rises above the LA pressure, cardiac output is conserved. Relative contraindications to closure typically are regarded for percutaneous cases and include: defects larger than 36 mm, inadequate margins and rims to safely anchor the device, and/or interference of the device with the atrioventricular valves or venous drainage.[7]

Surgical Repair Options and Outcomes

Cardiothoracic surgery is the gold standard approach for ASD repair and implies direct visualization of the defect using an open sternotomy approach with cardiopulmonary bypass. Surgical repair is typically achieved by the use of autologous pericardial or synthetic patches made of polyester polymer (Dacron) or polytetrafluoroethylene. In an ostium primum defect, surgical repair may be more complicated because the patch has to be attached at the crux of the ventricular septum and atrioventricular valves. Mitral valve repair, including closure of the cleft mitral leaflet with possible annuloplasty, may be necessary. In rare cases, mitral valve replacement may be required. In the case of a sinus venosus defect, partial anomalous pulmonary venous return is typical, with 1 or more of the pulmonary veins draining into the RA. The ASD must be patch closed, allowing for anomalous pulmonary venous drainage to be diverted into the LA. Surgical repair before 25 years of age results in a 30-year survival rate comparable to that of age- and sex-matched control subjects; however, with repair between the ages of 25 and 40 years, surgical survival is attenuated, although not significantly if pulmonary artery pressures are normal.[8] Although surgical repair of an ASD in adulthood is associated with a significant reduction in mortality, there is no beneficial impact on the risk of current or future atrial arrhythmias. Overall mortality with ASD repair is low; however, morbidities such as atrial arrhythmia, bleeding, pneumothorax, and pericardial or pleural effusions may occur.[7]

Percutaneous Repair Options and Outcomes

Transcatheter closure has become an accepted alternative for surgical repair in adults with a secundum ASD and adequate tissue rims.[9] Although many devices have been studied, only the following ASD closure devices have become routinely available in the United States: Amplatzer Septal Occluder, the Gore Helex septal occluder, and the Gore Cardioform Septal Occluder (**Table 2**). The Amplatzer Septal Occluder is currently the most widely used device in the United States because it is easy to implant and is manufactured in sizes that permit safe closure of relatively large defects. Percutaneous transcatheter ASD closure has a postprocedural complication risk of 7.2% compared with a postoperative complication risk of 24%.[9] Complications associated with percutaneous closure include arrhythmias, atrioventricular block, device erosion, and thromboembolism. Device embolization and malpositioning typically occur as a result of inadequate sizing or device placement, with an incidence of less than 1%. When ASDs are closed percutaneously, patients require antiplatelet therapy typically for 6 months, although this requirement varies based on operator and center expertise.

Table 2
Percutaneous ASD devices in the United States

Device	Description	Maximum Size of the Defect
Amplatzer Septal Occluder	Self-expanding, recapturable prosthesis made of nitinol wire mesh, 2 round discs with a polyester patch inside, and a connecting short waist.	36 mm
Gore Helex Septal Occluder	Corkscrew-type nitinol wire frame covered by expanded polytetrafluoroethylene to reduce friction with the cardiac adjacent structures; thereby reducing the risk of erosion; size varies from 15 to 30 mm, but is not recommended for defects >18 mm	18 mm
Gore Cardioform Septal Occluder	Flexible, retrievable, double-disc device with a petal design made of a nitinol frame covered by expanded polytetrafluoroethylene to facilitate rapid endothelialization	17 mm
Gore Cardioform ASD Occluder	Implantable occluder and a delivery system to treat a range of defects from 8 to 35 mm with unique conformability to adapt to secundum ASD	35 mm

SPECIAL CASES: SHUNT-RELATED PULMONARY ARTERIAL HYPERTENSION

Improvements in the diagnosis and management of CHD has contributed to an increasing number of adult CHD survivors, including those with PAH and either repaired or unrepaired CHD. This cohort includes patients with unrepaired ASDs with PAH who are evaluated and then classified into 1 of 4 categories of shunt-related PAH.[10] The most well-known of these clinical categories is Eisenmenger's syndrome, which occurs when the PVR increases to systemic levels and the intracardiac shunt reverses, such that there is pulmonary-to-systemic shunting at rest and manifest cyanosis. It is clear that this group of patients would be unsafe to consider defect repair, because cardiac output depends on the shunt in the presence of severely elevated PVR. However, it is less clear that this is the case in the second clinical category, namely, PAH associated with prevalent systemic-to-pulmonary shunt. In this group, the defect is typically moderate to large in size and the PVR is elevated, yet still substantially lower than the systemic vascular resistance, characterized predominantly by systemic-to-pulmonary shunting. Although resting cyanosis is not present in this group, PVR may increase, particularly with exercise, and this may manifest as cyanosis with exercise, implying that physical activity may change hemodynamics such that the Qp:Qs approaches 1.0 (bidirectional shunting). Defect repair in this setting, particularly with significantly elevated PVR and after PAH-specific medical therapy, is controversial. However, several studies have implied that there may be a subset of patients in whom repair may be achieved safely and impact long-term outcome favorably.[11–16] This area requires further study, and to date these decisions are made on an individual basis with careful consideration and coordination of an experienced adult CHD and pulmonary hypertension team. The final 2 categories of CHD with PAH include those patients with PAH and small/coincidental defect and those with PAH after defect correction. In both cases, PAH develops in the absence of a current hemodynamically significant shunt, highlighting that likely more than a single mechanism is responsible for PAH in this CHD patient. As such, ASD repair in these last 2 categories is not typically a therapeutic consideration.

SUMMARY

Although an ASD is considered a type of simple CHD, you can see here that it is not always a simple condition to manage. There is variability in the anatomy of the defect, resultant physiology, and late hemodynamic and arrhythmia-driven comorbidities. These factors ultimately impact therapeutic management and repair strategies. For the straightforward adult patient with a sizable secundum ASD and normal physiology, transcatheter repair is a safe and acceptable option. For an adult with any other type of ASD and abnormal physiology, the management algorithm changes and is impacted commonly by anatomic considerations of the defect(s), arrhythmia, heart failure, and/or PAH. For these reasons, it is important that adult patients with an ASD be referred for specialized and expert care by a team with experience in adult CHD.

DISCLOSURE

The authors have nothing to disclose.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found online at https://doi.org/10.1016/j.ccl.2020.04.001.

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