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Atrial Septal Defects in the Adult Recent Progress and Overview

Gary Webb, MD; Michael A. Gatzoulis, MD, PhD

Patients with isolated atrial septal defects (ASDs) have benefited from important recent advances in the diagnosis, evaluation, and management of their conditions. This review will focus on adolescent and adult patients with sizeable ASDs who do not have other major associated cardiac defects.

Nomenclature and Classification

There are 3 major types of ASDs or interatrial communications: ostium secundum, ostium primum, and sinus venosus (Figure 1A) defects. The ostium secundum is a true defect of the atrial septum and involves the region of the fossa ovalis. The ostium primum defect is within the spectrum of the atrioventricular (AV) septal defects (Figure 1B; also known as AV canal defects or endocardial cushion defects), the complete form of which also includes a large ventricular septal defect and a common AV valve. The sinus venosus defect is usually located at the junction of the right atrium and superior vena cava and is almost always associated with partial anomalous pulmonary venous return. Two very uncommon types of ASDs may be mentioned briefly: the inferior vena cava form of the sinus venosus defect and the coronary sinus septal defect (in which a defect between the coronary sinus and the left atrium allows a left-to-right shunt to occur through an “unroofed” coronary sinus).

Prevalence

ASDs are common and can present at any age. Females constitute 65% to 75% of patients with secundum ASDs, but the gender distribution is equal for sinus venosus and ostium primum ASDs.

Genetic Factors

Down syndrome is associated primarily with AV septal defects, but secundum defects also occur with increased frequency. Approximately 40% of subjects with Down syndrome have congenital heart disease. Of these, 40% have an AV septal defect, usually the complete form. Ostium primum ASDs may also be associated with DiGeorge syndrome and Ellis-Van Creveld syndrome. Adults with AV septal defects

have an approximate 10% risk of recurrence of heart disease in their offspring.^{1,2} ASDs are the most common cardiac manifestation of Holt-Oram syndrome, which has been shown to be caused by mutations of *TBX5*.³ The familial forms of secundum ASDs have also been associated with *GATA4* and *NKX2.5* mutations.^{4–6} Conduction abnormalities are very common among them.

Sinus Venosus Atrial Septal Defects

The superior form of the sinus venosus ASD constitutes 5% to 10% of all ASDs. Its posterior aspect is the right atrial free wall, and its superior border is often absent because of an overriding superior vena cava (SVC; Figure 2A). Anomalous connection of some or all of the right pulmonary veins to the SVC or the right atrium is very common. Diagnosis is often more difficult than for other forms of ASD and may require special imaging, such as transesophageal echocardiography, magnetic resonance imaging (MRI), and computed tomographic scanning, and the possibility of a sinus venosus ASD should be considered for any patient with unexplained right atrial and right ventricular dilation. Catheter closure is not possible, and the treatment is surgical.

Atrioventricular Septal Defects

This group of anomalies share a common AV junction with abnormalities of the AV valves (separate valves in partial AV septal defect, common AV valve in the complete form; see Figure 1B). The left AV valve is trileaflet (Figures 1B and 2B), composed of the mural leaflet and the inferior and superior leaflets, which are fused and point toward the left ventricular outflow (“11th hour”). The distance from the left AV valve annulus to the left ventricular apex is appreciably less than that from the apex to the aortic annulus, whereas normally the 2 distances are equal. This inlet to outlet disproportion creates the characteristic “gooseneck deformity” that used to be a major diagnostic feature on left ventriculography. Furthermore, this elongation of the left ventricular outflow tract, combined with the fact that there are chordal attachments of the left AV valve to the ventricular septum in these patients, forms the basis for the development

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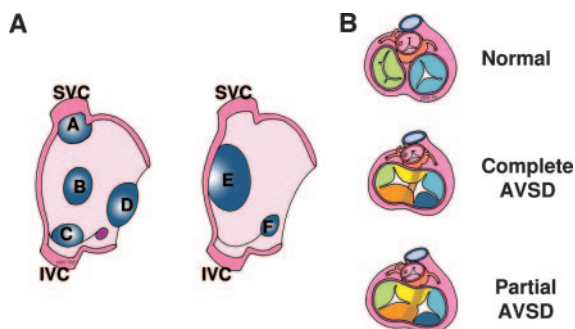


Figure 1. A, A indicates superior sinus venous ASD; B, secundum ASD; C, inferior sinus venous ASD; D, ostium primum ASD or partial AV septal defect; E, secundum ASD without posterior septal rim; F, coronary sinus ASD; and IVC, inferior vena cava. B, AV junction viewed from the atrial aspect. Normal indicates normal heart; complete AVSD, complete AV septal defect with a common AV junction and a common, single AV valve, guarded by 5 leaflets (counterclockwise: superior bridging, left mural, inferior bridging, right inferior, and right anterosuperior); partial AVSD, partial AVSD or primum ASD with a common AV junction but 2 separate AV valves produced by fusion of the superior and inferior bridging leaflets (note the trileaflet nature of the left AV valve). Figures courtesy of Dr Yen Ho, MD, PhD, Royal Brompton Hospital and the National Heart & Lung Institute, Imperial College, London, UK.

of discrete subaortic obstruction, which may occur even late after successful repair of the defect.⁷ The abnormal AV junction results in an “unwedged” aorta and leads to a displacement of the AV conduction tissue, which in turn

produces the characteristic left-axis deviation and predisposes these patients to heart block.

The most common associated anomalies are a secundum ASD and a persistent left SVC draining into the coronary sinus. Most primum ASDs are relatively large and lead to right heart dilation. Because of the trileaflet nature of the left AV valve (the so-called cleft mitral valve), variable degrees of valvular regurgitation are exceedingly common, whereas valvular stenosis is rare. A parachute type or double-orifice “mitral” valve may be present and may have prognostic implications. Depending on the severity of dysfunction of the left AV valve, patients with ostium primum ASDs may become symptomatic at a much younger age than patients with other types of ASDs. Surgical repair includes closure of the interatrial communication and restoration or preservation of left AV valve competence. In a series of 199 patients⁸ with a mean follow-up of 15.2 years, there were 7 late deaths, none of which were cardiac. Fifteen patients underwent reoperation for residual or recurrent left AV valve regurgitation, and 3 patients underwent reoperation for subaortic stenosis. Freedom from reoperation was 86%, and survival was 96% to 20 years. The occurrence of surgical complete heart block in these patients has practically disappeared in the modern era.⁹

Pathophysiology

The magnitude of and direction of flow through any ASD depend on the size of the defect and the relative diastolic filling properties of the left and right ventricles. Conditions

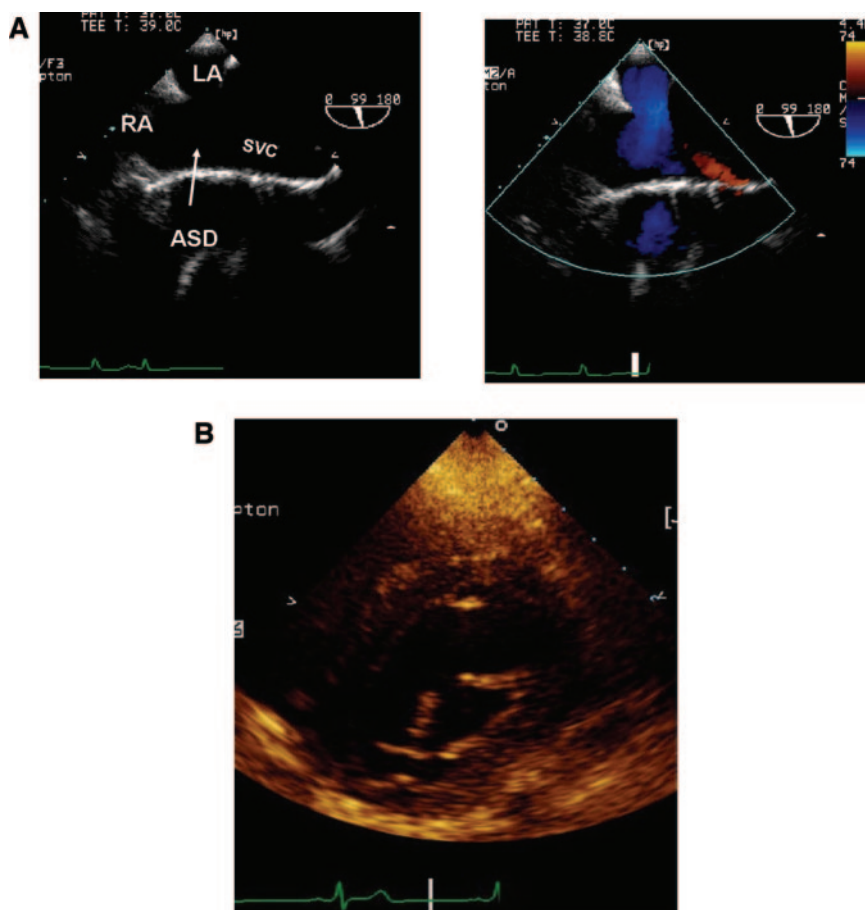


Figure 2. A, Sinus venous ASD (superior); vertical section from a transesophageal echocardiogram. Note the SVC overriding the ASD (left-to-right atrial shunt, blue on color Doppler). RA indicates right atrium; LA, left atrium. B, Trileaflet left AV valve in a patient with a primum ASD or partial AV septal defect (short axis); note that the “cleft” points to the 11th hour and not to the 13th hour that true cleft mitral valves usually point to. Figures courtesy of Dr Wei Li, MD, PhD, Royal Brompton Hospital and the National Heart & Lung Institute, Imperial College, London, UK.

that cause reduced left ventricular compliance (eg, left ventricular hypertrophy or scarring) and mitral stenosis will increase left-to-right shunting. Conditions that cause reduced right ventricular compliance (eg, pulmonary hypertension or pulmonary stenosis) and tricuspid stenosis will have the opposite effect of reducing a left-to-right shunt and/or causing a right-to-left shunt. As a rule, an ASD must be at least 10 mm in diameter to carry a significant left-to-right shunt, although most ASDs are not circular, and maximum diameter may be difficult to measure accurately. A left-to-right atrial shunt is considered significant when the Qp/Qs ratio is greater than 1.5/1.0, or if it causes dilation of the right heart chambers.¹⁰ Although there are limitations in estimating Qp/Qs with any method, this level of shunting is usually associated with right heart dilation and has been associated with adverse long-term outcomes.

Clinical Features

Many patients with ASDs are free of overt symptoms, although most will become symptomatic at some point in their lives. The age at which symptoms appear is highly variable and is not exclusively related to the size of the shunt. Exercise intolerance in the form of exertional dyspnea or fatigue is the most common initial presenting symptom. Atrial fibrillation or flutter is an age-related reflection of atrial dilation and stretch that seldom occurs at <40 years of age¹¹; its arrival usually causes substantial symptoms because of both the tachycardia and the underlying hemodynamics (governed by impaired left ventricular filling and reduced systemic cardiac output). Less commonly, decompensated right heart failure may occur, almost always in the older patient, often in the context of substantial tricuspid regurgitation (secondary to severe right heart and tricuspid annular dilation) and often with coexistent pulmonary arterial hypertension of variable severity (developing slowly in response to excessive pulmonary blood flow over a long period of time). Occasionally, a paradoxical embolus or transient ischemic attack may be the first clue to the presence of an ASD. Even less commonly, the discovery of cyanosis may lead to the diagnosis of an intraatrial communication, cyanosis being more common in inferior sinus venosus defects.

Diagnostic Evaluation

Physical Examination

The absence of clinical signs does not necessarily exclude a hemodynamically important ASD. Nevertheless, physical examination is in most instances informative and assists in diagnosis and management:

- Patients are usually pink at rest and during exercise, unless advanced pulmonary hypertension is present.
- A right ventricular lift may be felt, especially on held expiration or in the subxiphoid area on deep inspiration.
- A dilated pulmonary artery may be palpable in the second left interspace.
- A wide and fixed split of S₂ is the auscultatory hallmark of an ASD but is not always present.
- A loud P₂ will reflect pulmonary hypertension.

- A systolic ejection murmur, typically of soft intensity and scratchy quality, is best heard at the upper left sternal border.
- A diastolic rumble heard at the lower left sternal border reflects a large shunt (relative tricuspid stenosis).
- A murmur of tricuspid regurgitation may be heard in older patients or those with pulmonary hypertension.
- A pansystolic murmur of “mitral” regurgitation is characteristic of the patient with a primum ASD.
- In patients with a significant ASD, left and right atrial pressures are equal, so the jugular venous pressure is a direct reflection of left atrial pressure.
- The presence of cyanosis usually suggests advanced pulmonary hypertension, but it may result from associated anomalies such as pulmonary stenosis or even from a prominent eustachian valve directing inferior vena cava flow to the left atrium through an ASD (particularly of the inferior sinus venosus type).

Electrocardiogram

The ECG may be an important clue to diagnosis (Figure 3).^{12–15} The rhythm may be sinus, atrial fibrillation, or atrial flutter. Inverted P waves in the inferior leads suggest an absent or deficient sinus node, as may be seen in a sinus venosus defect.^{16,17} Right atrial overload is often present. First-degree heart block suggests a primum ASD¹⁸ but may be seen in older patients with a secundum ASD. The QRS axis is typically rightward in secundum ASD, markedly so if pulmonary hypertension is present. The QRS axis is leftward or extremely to the right in ostium primum ASDs. Voltage evidence of right ventricular hypertrophy may be seen in all ASDs, often in the form of “incomplete” right bundle-branch block, with the more extreme forms usually found in patients with pulmonary hypertension. Patients with mitral valve insufficiency may have left ventricular hypertrophy or left atrial overload.

Chest Radiograph

The chest x-ray film is often, but not always, abnormal in patients with significant ASDs.^{19,20} Cardiomegaly may be present from right heart dilation and occasionally from left heart dilation if significant mitral regurgitation is present in the patient with an ostium primum ASD. Right heart dilation is better appreciated in lateral films. The central pulmonary arteries are characteristically enlarged, with pulmonary plethora indicating increased pulmonary flow. A small aortic knuckle is characteristic, which reflects a chronically low systemic cardiac output state, because increased pulmonary flow in these patients occurs at the expense of reduced systemic flow.

Echocardiography

Transthoracic echocardiography documents the type(s) and size of the ASD(s), the direction(s) of the shunt, and, in experienced hands, the presence of anomalous pulmonary venous return. The functional importance of the defect can be estimated by the size of the right atrium and ventricle, the presence/absence of paradoxical septal motion (right ventricular volume overload), ventricular septal orientation in dias-

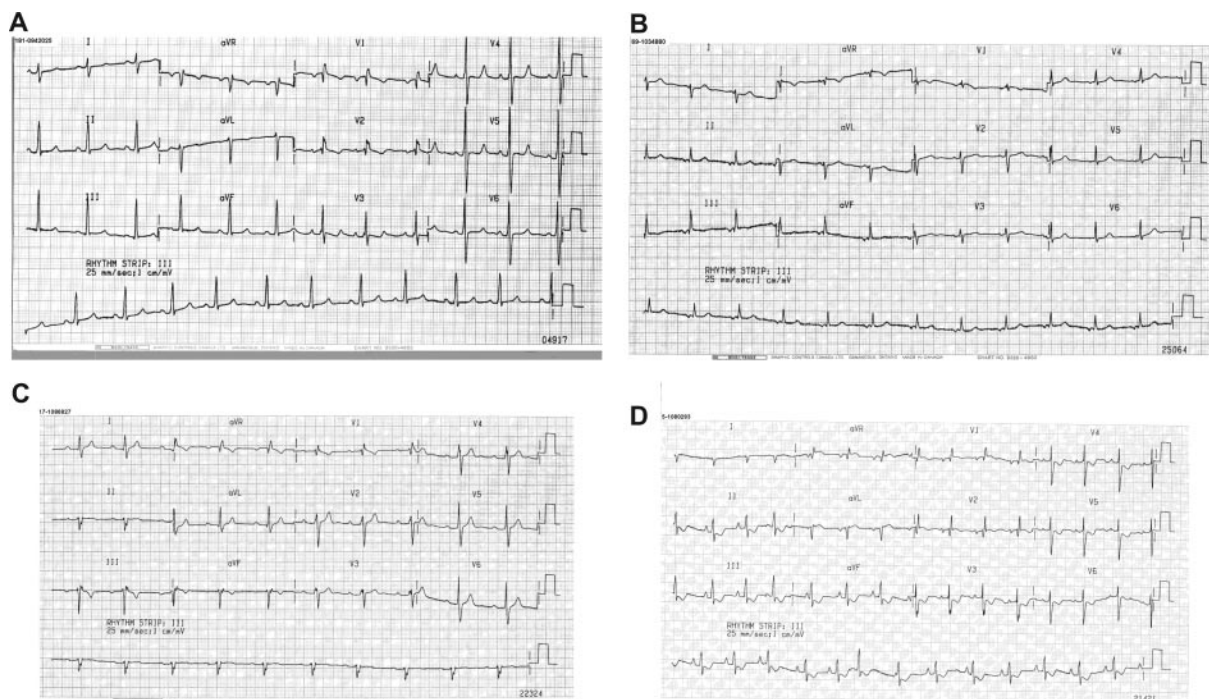


Figure 3. A, Ostium secundum ASD. Mild right-axis deviation, voltage evidence of right ventricular hypertrophy. B, Sinus venosus ASD. Inverted inferior P waves, right-axis deviation. C, Ostium primum ASD. First-degree AV block, left-axis deviation, voltage evidence of right ventricular hypertrophy. D, Eisenmenger ASD. Marked right-axis deviation, right atrial overload, right ventricular hypertrophy with extensive repolarization abnormalities (“strain pattern”).

tole (volume overload) and systole (pressure overload), and an estimation of the shunt ratio (based on pulmonary and aortic flows). Pulmonary artery systolic pressures may be estimated from the Doppler velocity of tricuspid regurgitation. In a patient with a primum ASD, the left AV valve is trileaflet (Figure 2B) and almost always demonstrates some regurgitation.

Transesophageal echocardiography may be useful to confirm the type of ASD and to delineate the pulmonary venous return. It is also commonly used in support of device closure of ASDs.

Cardiac Magnetic Resonance Imaging and Computed Tomographic Scanning

Cardiac MRI may be useful and may give the same type of information that echocardiography can provide. It is seen as providing the “gold standard” for the assessment of right ventricular size and function, and it may help define whether the right heart chambers are in fact enlarged (Figure 4). MRI

is also excellent at assessing pulmonary venous return.²¹ In patients who cannot have an MRI, computed tomographic scanning and angiography can offer similar information.

Cardiac Catheterization

Cardiac catheterization is no longer a diagnostic necessity for many patients but has become increasingly important in delivering therapy to patients with secundum ASDs. A diagnostic catheter study may be required to evaluate pulmonary artery pressures, evaluate left heart function and hemodynamics, evaluate comorbid conditions, or assess the coronary arteries for the older patient.

Management

As a general rule, patients with a significant ASD as defined above (with signs of right heart dilation) should be offered elective closure soon after the diagnosis is established, irrespective of age (Table).²² There can be, however, several reasons for not closing an ASD:

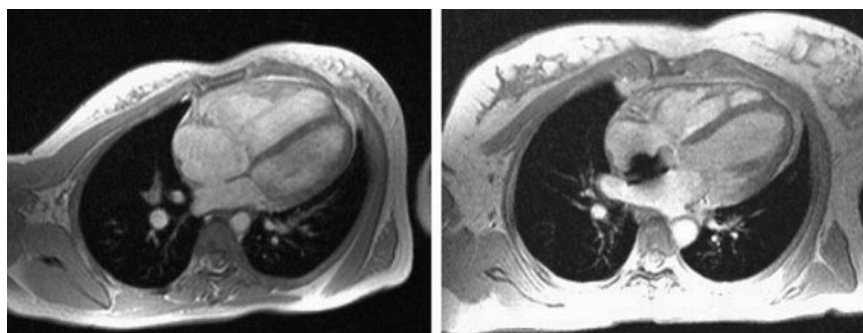


Figure 4. Cardiac MRI showing right heart remodeling after closure of a secundum ASD with an Amplatzer device. Interval between the baseline MRI (left) and the post-ASD closure MRI (right) was 6 months. The magnitude of reduction in right heart dilation is inversely related to age and leads to improved left ventricular filling, increased cardiac output, and better exercise capacity. Reprinted with permission from Gatzoulis et al, eds. *Adult Congenital Heart Disease: A Practical Guide*. Copyright 2005, BMJ/Blackwell Publishing.

- The defect may be too small to be “hemodynamically important”; such patients should be kept under periodic review, because some of them may go on to develop right heart dilation later in life due to a relative increase of left ventricular diastolic pressures and consequent increase of left-to-right shunting (this does not apply to persistent foramen ovale).
- Pulmonary arterial hypertension may be too advanced, contraindicating ASD closure; the ASD may be physiologically needed by the patient (eg, as a “pop-off” valve in a patient with severe pulmonary hypertension). Such patients are often cyanotic at rest and become more cyanosed during exercise.
- In most instances, in pregnant women diagnosed with an ASD during pregnancy, closure can be deferred for ≈ 6 months after delivery.
- When severe left ventricular dysfunction is present and the ASD is functioning as a pop-off valve for the systemic ventricle, closure should not be performed.

Surgical closure is required for patients with ostium primum and sinus venosus ASDs, as well as for patients with secundum ASDs whose anatomy is unsuitable for device closure. In some settings, surgical closure of secundum defects is still preferred or required.²³ A secundum ASD may be closed with direct sutures (“primary closure”) or with a patch using pericardium or synthetic material. Ostium primum defects require patch closure and repair of the “cleft” AV valve. The repair of sinus venosus defects with anomalous pulmonary venous return can be technically challenging, and several approaches are used to achieve this.^{24–27} Care must be taken to see that the lower end of the SVC is large enough to accommodate both the SVC and the pulmonary venous return being baffled to the left atrium. Alternatively, 2 separate channels may be created to ensure these 2 sources of venous return are unobstructed.

In most centers in the developed world, device closure has become the treatment of choice for secundum ASDs. The procedure is supported by transesophageal or intracardiac echocardiography.²⁸ Catheter closure minimizes hospital stay and recovery, avoids surgical wounds and their potential complications, and conveys the same hemodynamic benefits as does surgery. Indications for catheter closure are the same as for surgical closure, but patient selection criteria are more narrowly defined. Patients with a stretched secundum ASD >36 mm, those with inadequate atrial septal rims to permit stable device deployment, or those with proximity of the defect to the AV valves, the coronary sinus, or the vena cavae are usually referred for surgical repair. Device closure is a safe and effective procedure in experienced hands, with major complications such as cardiac perforation or device embolization occurring in fewer than 1% of patients.^{29–33} Successful closure is achieved in up to 95% of patients,³⁴ although small residual shunts are often seen on echocardiography at the end of the procedure; these are not hemodynamically important, and most will close spontaneously within 1 year. Device closure of secundum ASDs can produce rapid and favorable cardiac remodeling, as described below.

Management of Atrial Septal Defects in Adults

Indications for ASD closure

Right atrial and right ventricular dilation by echocardiography, MRI, or CT (in the presence of an ASD and in the absence of advanced pulmonary arterial hypertension) manifested with 1 or more of the following:

ASD minimum diameter >10 mm on echocardiography

Qp:Qs $>1.5:1$ by echocardiographic or cardiac MRI flow assessment, or from oxygen saturation runs, when cardiac catheterization is performed (for other reasons)

Anticipated benefits from ASD closure

Improved functional class, dyspnea index, and exercise capacity (irrespective of age⁴⁰). Improvement occurs earlier after device closure than with surgical closure. Physical reconditioning is recommended.

In addition, the following long-term prognostic benefits can be anticipated:

Improved survival after youthful repair²²

Improved quality of life

Prevention of right heart failure

Prevention of pulmonary arterial hypertension

Potential midterm/long-term complications after ASD closure in adulthood

Tachyarrhythmia (atrial flutter or atrial fibrillation) may persist or develop in the older patient¹¹; tachyarrhythmia should be better tolerated and easier to manage after ASD closure. Consider arrhythmia-targeting intervention (surgical or catheter) either before or at the time of ASD closure for high-risk patients and those with preexisting sustained tachyarrhythmia.⁴¹

Bradyarrhythmia, potentially leading to permanent pacing:

caused by sinus node dysfunction, secondary to longstanding right atrial dilation and stretch (among patients who underwent late ASD closure⁴⁰)

caused by complete heart block, to which patients with AV septal defects (any AV septal defect including primum ASD) are predisposed.

Stroke risk higher in older patients. Consider empiric thromboprophylaxis for patients >40 years of age and those who required complex repair.

Residual ASDs

Small: relatively common after catheter device closure (most are hemodynamically insignificant and usually close spontaneously over a period of 12 months from intervention)

Large: may be caused by a dehiscence ASD patch (good practice to review all patients at least once, in the year after ASD closure, to confirm the absence of residual atrial communications; ASD dehiscence leading to hemodynamically important atrial communication is unlikely to occur thereafter)

Right heart failure or progressive pulmonary arterial hypertension; overall risk is small and inversely related to age of patient at time of ASD closure

Left AV valve regurgitation and subaortic stenosis (seen primarily in patients with primum ASDs)

Device migration or erosion (the latter when very large devices are used); both rare

Left atrial hypertension and pulmonary venous congestion; a very uncommon complication that can be seen soon after ASD closure in the occasional older patient with poor left ventricular compliance (which in itself can be difficult to delineate before ASD closure)

CT indicates computed tomography.

There is no consensus as to what constitutes appropriate follow-up of patients after ASD device closure. Although late complications appear rare, there is the potential for mitral valve dysfunction, obstruction to systemic and pulmonary venous pathways, and erosion or perforation of the atrial wall or aorta. Most physicians would follow up adult patients for at least 1 year, or longer if a particularly

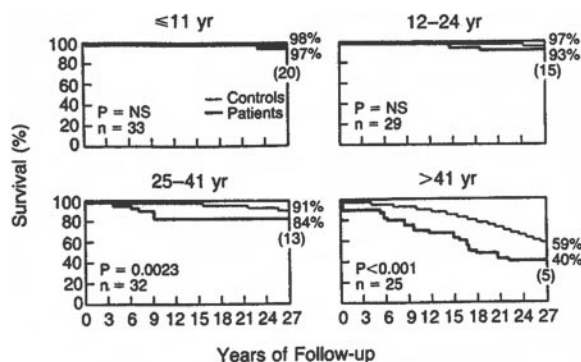


Figure 5. Survival curves for patients who underwent surgical closure of ASD at the Mayo Clinic (and survived to hospital discharge); note that patients who underwent repair before the age of 25 years had normal survival compared with healthy controls. Reprinted with permission from Murphy et al.²²

large device was deployed. After closure, a combination of low-dose aspirin and clopidogrel is usually prescribed for a minimum of 3 months.

Pregnancy

Pregnancy is well tolerated by most women with an unoperated ASD, and pregnancy can usually be allowed to continue.² Cardiological review is recommended because of the small risk of paradoxical embolus and stroke, arrhythmia, and heart failure. If circumstances allow, ASDs should be closed before pregnancy. For a secundum defect, catheter device closure can be performed during pregnancy if necessary (with transesophageal or intracardiac echocardiographic guidance). The only contraindication to pregnancy in women with ASDs, operated or not, is the presence of severe pulmonary arterial hypertension.

Natural History and Long-Term Sequelae

Survival

Significant ASDs are associated with increased morbidity and mortality.³⁵ An important study that examined the long-term outcomes of surgical repair of secundum ASDs showed normal long-term survival among hospital survivors of ASD closure when patients were operated on before 25 years of age (Figure 5). In contrast, patients having surgical repair after age 25 years experienced increased mortality compared with healthy controls. Kaplan-Meier estimates of survival of the 119 patients included in the survival analysis from this study were 97% at 5 years, 90% at 10 years, 83% at 20 years, and 74% to 30 years compared with 99%, 98%, 94%, and 85%, respectively, in an age- and sex-matched control population. There were 27 late deaths in this series, of which 18 were cardiovascular in nature (13 cardiac and 5 stroke deaths). All patients who died of stroke had been in atrial fibrillation during follow-up. Of 104 patients in sinus rhythm preoperatively, 80 (77%) remained in sinus rhythm during long-term follow-up.

Two large studies have examined mortality and morbidity in surgically versus medically managed patients with ASDs over age 40 years, and neither showed a clear-cut survival benefit with the surgical strategy. The first retrospective study³⁶ showed a survival benefit that favored the surgical patients, but this was

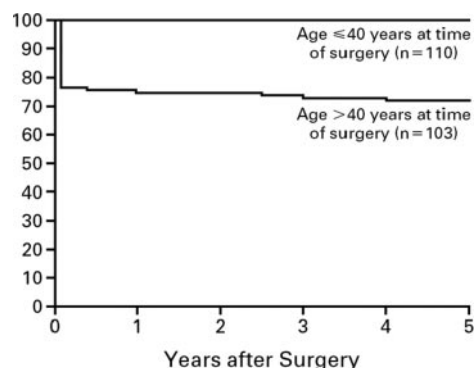


Figure 6. Kaplan-Meier estimates of freedom from late postoperative atrial flutter or fibrillation after surgical closure of ASD. The initial downward slope of the curve for the patients older than 40 years at the time of surgery reflects patients who had atrial flutter or fibrillation 1 month after surgery (all these 24 patients had documented atrial flutter or fibrillation before surgery). Mean follow-up time of the study was 3.8 ± 2.5 years (for all 213 patients). Reprinted with permission from Gatzoulis et al.¹¹

after the exclusion of patients with coronary artery and mitral valve disease. The second study, a prospective, randomized trial conducted at the National Institute of Cardiology in Mexico City, Mexico,³⁷ showed, perhaps surprisingly, no clear survival benefit to surgical closure. However, over the study period (of 15 years), surgery was superior to medical therapy for a composite clinical end point that included recurrent pneumonias, the latter being a major contributor toward the differences observed between the 2 subgroups. These 2 studies also highlight the challenge of conducting clinical trials in congenital heart disease, in which patient heterogeneity, even within the same diagnostic groups, and low mortality rates are often present. Furthermore, the low rates of clinical end points, such as death, reinforce the need for developing robust surrogate markers for monitoring congenital heart disease and its response to therapies.

Arrhythmia

Although atrial flutter and fibrillation are common and indeed anticipated in older patients with sizeable ASDs, sudden cardiac death is rare. Atrial tachyarrhythmia or bradyarrhythmia in these patients is the byproduct of longstanding right atrial dilation and stretch, which may be compounded by tricuspid regurgitation, pulmonary arterial hypertension, heart failure, and death.^{9,38} In the Mayo Clinic series, the prevalence of late atrial flutter or fibrillation rose progressively with mean age at surgery above 11 years,²² whereas in another series of ASD patients aged ≥ 60 years, arrhythmia prevalence was 52%.³⁹ In our surgical series from Toronto, the preoperative and postoperative risks of atrial flutter or fibrillation were closely related to patient age above or below 40 years¹¹ (Figure 6). In contrast, atrial flutter and fibrillation and sick sinus syndrome are very uncommon among patients who underwent ASD closure during childhood or early adulthood, even after long-term follow-up.⁴⁰ Each of these long-term follow-up series highlighted the comorbidity of stroke in such patients. Older patients remain at risk of systemic thromboembolism despite complete closure of the ASD. The pulmonary veins are likely to be involved as a

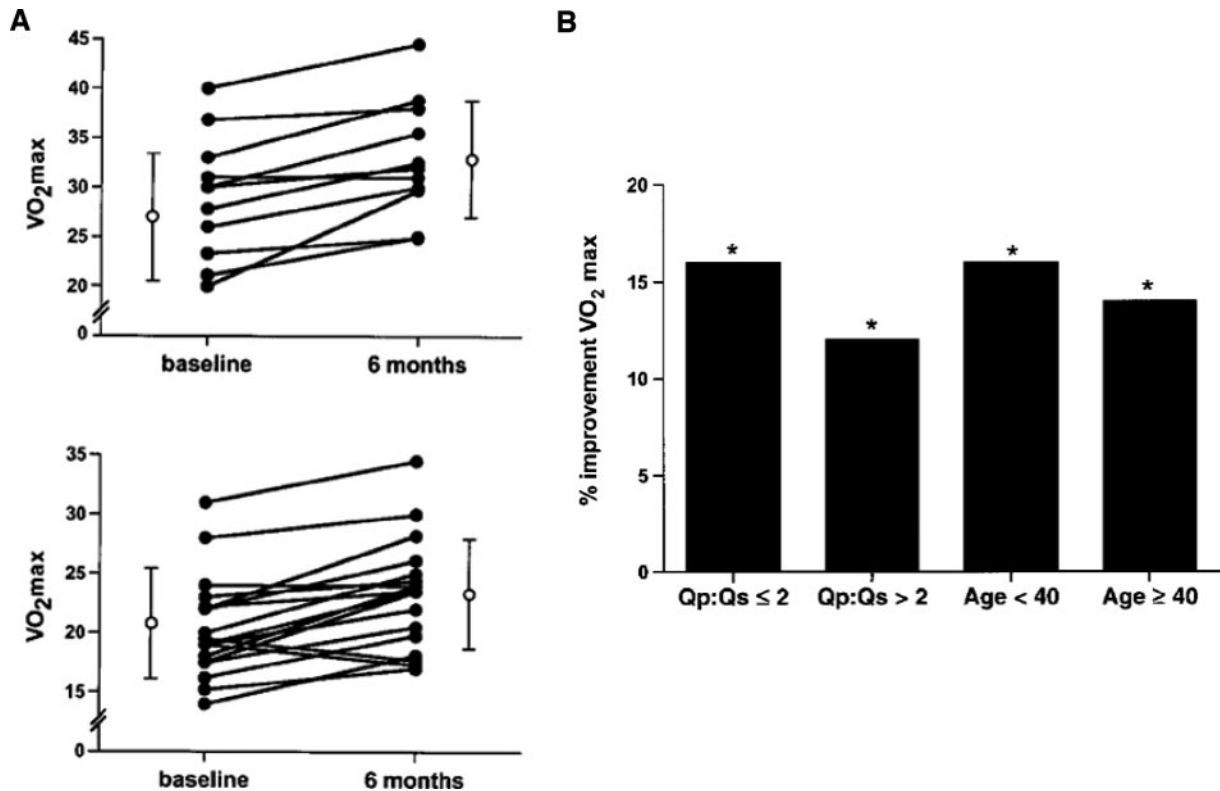


Figure 7. A, $\dot{V}O_2\max$ at baseline and 6 months after procedure. Top, New York Heart Association class I; bottom, New York Heart Association class II. $*P<0.0001$. B, Percentage of improvement of $\dot{V}O_2\max$ according to magnitude of shunt and age. $*P<0.0001$. Reprinted with permission from Brochu et al.⁴⁸

source of both arrhythmogenesis and thrombus formation. Although this is speculative, thromboprophylaxis should be considered for the older patient with an ASD for a period of 6 to 12 months after closure, while right heart and pulmonary venous remodeling takes place. Furthermore, such high-risk arrhythmia patients undergoing late ASD closure should be considered for a concomitant arrhythmia-targeting intervention. Kobayashi and colleagues⁴¹ demonstrated that in this setting, a surgical right atrial Maze procedure alone is usually ineffective in restoring and maintaining sinus rhythm after ASD closure, which supports the concept of left atrial and pulmonary venous involvement in arrhythmogenesis. Indeed, the same investigators showed that when a combined right and left modified Maze approach was used, success rates in restoring and maintaining sinus rhythm after ASD closure were much higher.

It is possible that device closure of ASDs may reduce the risk of atrial flutter and fibrillation if ASDs are closed at a younger age, if smaller defects are treated, and because of the absence of surgical scars, which themselves may act as a reentrant circuit for arrhythmia. Only early data are available on this point,⁴² however, and patients who undergo ASD closure late, whether surgical or catheter, have been subjected to the same chronic hemodynamic burden and thus have a similar arrhythmic potential.

Exercise Capacity

The functional capacity of patients with ASDs is substantially impaired.⁴³ As in most forms of congenital heart disease, the

patient's subjective impression of physical capacity is much more optimistic than can be objectively demonstrated with peak oxygen uptake and other functional measures.⁴⁴ Although patients often reported subjective improvement in their functional class after surgical closure of ASDs,^{36,45} it was only in 1997 that Helber and colleagues⁴⁶ demonstrated a low peak oxygen uptake preoperatively, a slight increase 4 months after repair, and normal levels of performance and oxygen uptake 10 years after surgical ASD repair. Similar data have been reported more recently from device closure series.⁴⁷ The favorable impact of ASD device closure on clinical performance appears both more widespread and faster than that reported in the surgical literature. Brochu and colleagues⁴⁸ reported a 15% improvement in peak oxygen uptake at 6 months after device closure. This improvement was similar regardless of the size of the preprocedural left-to-right shunt (all patients in this series had sizeable ASDs) and regardless of patient age above or below 40 years (Figure 7). Giardini and colleagues^{49–51} showed a similar clinical improvement, and they also documented improved left ventricular filling with concomitant improvement in systemic cardiac output in patients after device closure. The latter appears likely to be the main mechanism by which patients feel better and improve their exercise capacity after ASD closure. It follows that patients who undergo device closure have a much shorter recovery than those who require surgery and thus enjoy the benefits of improved hemodynamics and increased systemic cardiac output much earlier.

Cardiac Remodeling

Cardiac remodeling occurs quite quickly after ASD device closure.^{47,52–55} Reduced right atrial and ventricular volumes are apparent within 24 hours, and probably earlier. The remodeling process appears to continue for at least 1 year (Figure 4) and is more advanced in the right ventricle than the right atrium.⁴² Furthermore, the magnitude of right atrial remodeling is inversely related to patient age at the time of closure, as demonstrated in another study that reported persistent right atrial dilation in up to 64% of patients who underwent late ASD closure, which in turn was associated with elevation of brain natriuretic peptide levels and right ventricular diastolic dysfunction.⁵⁶ All these data clearly argue for early and timely closure of ASDs at the time of diagnosis.

Pulmonary Arterial Hypertension

Pulmonary arterial hypertension occurs to a mild-to-moderate degree in many patients as a reflection of aging and altitude of residence.^{57–60} Pulmonary vascular disease may occur in up to 5% to 10% of patients with untreated ASDs, predominantly in females.⁶¹ The pathogenesis of the pulmonary arterial hypertension in such patients is unknown, but it does not appear to be caused solely by the magnitude of the shunt persisting for decades. As a rule, patients should be considered to have Eisenmenger syndrome when ASDs are large and unrestrictive and when there is resting cyanosis. If a smaller ASD is present in a patient with pulmonary hypertension, other causes should be sought. There are some ASD patients in whom repair is not possible because of high pulmonary arterial pressures and pulmonary vascular resistance, usually when the left-to-right shunt is reversed. There have been case reports of such patients being managed with intravenous epoprostenol or oral bosentan with such success that ASD closure subsequently became possible.^{62,63}

Conclusions

Sizeable ASDs with right heart dilation are associated with important age-related morbidity and mortality. Advanced diagnostic modalities, earlier closure, and the advent of catheter intervention (for secundum ASDs) are all likely to improve long-term prospects for these patients. Current evidence would suggest that all types of ASDs with right heart dilation should be considered for timely closure once the diagnosis is established, irrespective of age.

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Disclosures

None.

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