Canadian Cardiovascular Society 2009 Consensus Conference on the management of adults with congenital heart disease: Shunt lesions

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With advances in pediatric cardiology and cardiac surgery, the population of adults with congenital heart disease (CHD) has increased. In the current era, there are more adults with CHD than children. This population has many unique issues and needs. Since the 2001 Canadian Cardiovascular Society Consensus Conference report on the management of adults with congenital heart disease, there have been significant advances in the field of adult CHD. Therefore, new clinical guidelines have been written by Canadian adult CHD physicians in collaboration with an international panel of experts in the field. Part I of the guidelines includes recommendations for the care of patients with atrial septal defects, ventricular septal defects, atrioventricular septal defects and patent ductus arteriosus. Topics addressed include genetics, clinical outcomes, recommended diagnostic workup, surgical and interventional options, treatment of arrhythmias, assessment of pregnancy risk, and follow-up requirements. The complete document consists of four manuscripts, which are published online in the present issue of *The Canadian Journal of Cardiology*. The complete document and references can also be found at www.ccs.ca or www.cachnet.org.

Key Words: *Adult congenital heart disease; Atrial septal defect; Congenital heart disease; Guidelines; Patent ductus arteriosus; Ventricular septal defect*

La conférence consensuelle 2009 de la Société canadienne de cardiologie sur la prise en charge des adultes ayant une cardiopathie congénitale : Les lésions des shunts

Étant donné les progrès de la cardiologie pédiatrique et de la chirurgie cardiaque, la population d'adultes ayant une cardiopathie congénitale (CPC) a augmenté. Il y a maintenant plus d'adultes que d'enfants ayant une CPC. Cette population a de nombreux problèmes et besoins uniques. Depuis le rapport de la conférence consensuelle 2001 de la Société canadienne de cardiologie sur la prise en charge des adultes ayant une CPC, on constate d'importantes avancées dans le domaine des CPC chez les adultes. Par conséquent, de nouvelles lignes directrices cliniques ont été rédigées par des médecins canadiens s'occupant des CPC chez les adultes, en collaboration avec un groupe d'experts internationaux dans le domaine. La partie I des lignes directrices contient des recommandations sur les soins des patients ayant une communication interauriculaire, interventriculaire ou auriculoventriculaire ou une persistance du canal artériel. Les sujets abordés incluent la génétique, les issues cliniques, les bilans diagnostiques recommandés, les possibilités chirurgicales et d'intervention, le traitement des arythmies, l'évaluation des risques de la grossesse et de la contraception et les recommandations de suivi. Le document complet se compose de quatre manuscrits publiés par voie électronique dans le présent numéro du *Journal canadien de cardiologie*. Le document complet et les références figurent également aux adresses www.ccs.ca et www.cachnet.org.

ATRIAL SEPTAL DEFECT

Part I. Background information

Atrial septal defect (ASD) includes the following types: ostium secundum, sinus venosus and coronary sinus septal defect. Ostium primum (partial atrioventricular septal defect [AVSD]) is discussed in Part III of the present guidelines series.

A 'clinically significant' ASD:

- Causes right heart volume and, sometimes, pressure overload.
- May cause exercise limitation.
- May be associated with atrial tachyarrhythmias (atrial fibrillation and atrial flutter).
- May cause late right heart failure.
- May permit paradoxical embolism resulting in transient ischemic attack or stroke.
- May lead to late pulmonary hypertension, although pulmonary hypertension may also develop from other causes. Severe pulmonary vascular disease from ASD is rare in older adults.

Part II. Prevalence and genetics

Although usually sporadic, some ASDs are inherited as autosomal dominant syndromes and/or are associated with other congenital lesions such as Holt-Oram syndrome, an autosomal dominant syndrome associated with pre-axial limb defects caused by mutations in the *TBX5* gene on chromosome 12q24.1. Familial ASD with progressive atrioventricular (AV) block should prompt the search for mutations or haploinsufficiency of the *Nkx2.5* gene on chromosome 5, while familial ASD without AV block may be associated with *GATA4* mutations (1,2). Exposure to teratogens are another cause of ASD and may occur in the context of fetal alcohol syndrome.

Part III. History and management of unoperated patients

Many patients with 'clinically significant' ASDs (see above) will eventually develop symptoms, although the timing of symptom development is unpredictable, sometimes beyond the fifth decade of life. The most common symptoms are exercise intolerance (dyspnea and

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fatigue) and symptomatic supraventricular arrhythmias (atrial fibrillation, atrial flutter, atrial tachycardia or sick sinus syndrome). Other complications include paradoxical emboli, heart failure or right ventricular (RV) failure, and pulmonary vascular disease (the latter occurs in 5% to 9% of patients).

Any condition causing reduced left ventricular (LV) compliance (eg, aging, LV hypertrophy due to hypertension, cardiomyopathy or myocardial infarction) will tend to increase the left-to-right shunt through an ASD, and worsen symptoms. This may justify closure of defects considered to be anatomically borderline.

Part IV. Diagnostic workup

The initial workup should include the following (at a minimum):

- A thorough clinical assessment.
- Electrocardiogram (ECG).
- Chest x-ray.
- Transthoracic echocardiographic (TTE)-Doppler evaluation by an appropriately trained individual. In some cases, contrast echocardiography (echo) with a saline contrast injection may be needed to determine whether there is an intracardiac shunt.
- Transesophageal echo (TEE)-Doppler examination to prove the existence of one or more ASDs, better define its/their location(s), size(s) and shape(s), assess pulmonary venous connections and evaluate the cardiac valves, if this information is not provided by TTE. TEE is mandatory to determine whether the ASD is suitable for device closure.
- Resting oxygen saturation.

An adequate diagnostic workup includes cardiac imaging to assess the following:

- The presence and type of ASD(s).
- The size (diameter) of the defect(s).
- The functional importance of the defect as manifested by:
  - shunt size (pulmonary-to-systemic flow ratio [Qp:Qs]);
  - RV size, function and volume overload, and right atrial size; and
  - pulmonary artery pressures (PAPs) and, if elevated, pulmonary vascular resistance.
- Other associated conditions that may influence management (eg, anomalous pulmonary venous connection, significant valve disease or coronary artery disease).

The diagnostic workup may require the following:

- Heart catheterization (if determination of PAPs and resistances is needed to assess pulmonary vascular reactivity or to delineate anomalous pulmonary venous connections).
- Coronary angiography in patients at high risk of coronary artery disease or in patients older than 40 years of age if surgical or device repair is planned.
- Magnetic resonance imaging (MRI) to prove the existence of an ASD (although TEE is the superior imaging method), to estimate Qp:Qs, to determine the size and function of the right ventricle, and to assess pulmonary venous connections if doubts remain after other imaging modalities.
- Contrast-enhanced cine computed tomography (CT) can also be used to determine RV size and function, and pulmonary vein anatomy; however, because of the associated radiation exposure, CT imaging should only be used when other imaging modalities are unable to provide sufficient information.
- Oxygen saturation with exercise if there is any suggestion of pulmonary hypertension. If there is severe pulmonary hypertension or a resting oxygen saturation of less than 85%, exercise should be avoided.
- Genetic assay for a *TBX5* mutation can confirm the diagnosis of the Holt-Oram syndrome in suspected cases. However, the absence of a *TBX5* mutation does not preclude the diagnosis.

Genetic testing is helpful in establishing the diagnosis in family members of a patient with a known *TBX5* mutation (3,4).

Part V. Indications for intervention/reintervention/medical therapy

Surgical or percutaneous closure of an ASD is indicated in the presence of a hemodynamically significant ASD with or without resulting symptoms. A hemodynamically significant ASD is defined as an ASD with resultant RV volume overload as measured by echo or MRI.
Class I, level B (5-15)

Closure of an ASD may be indicated in patients with orthodeoxia-platypnea.
Closure of an ASD may be indicated in patients with paradoxical emboli.
Surgical closure of an ASD should be considered if patients are undergoing tricuspid valve repair or replacement.
Class IIa, level C (10,16)

In a patient with an unrepaired ASD, venous thromboemboli from any source are a particular hazard because of the risk of paradoxical emboli.

Closure can be considered if pulmonary arterial hypertension (PAH) is present and there is a net left-to-right shunt of greater than 1.5:1; or evidence of pulmonary artery reactivity when challenged with a pulmonary vasodilator (eg, oxygen, nitric oxide and/or prostaglandins). Such patients should receive care from a specialist with expertise in PAH.
Class IIa, level C (17-19)

If PAH is present (PAP of greater than two-thirds the systemic arterial blood pressure [SABP] or pulmonary arteriolar resistance of greater than two-thirds the systemic arteriolar resistance) and there is irreversible PAH, the ASD should not be closed. Such patients should receive care from a specialist with expertise in PAH.
Class III, level C (20,21)

Arrhythmia interventions (catheter ablation or surgical maze procedure) should be considered in patients with atrial tachyarrhythmias. Catheter ablation should be considered before device closure, while surgical maze would be performed concomitant with ASD closure.
Transvenous pacing should be avoided in patients with unrepaired ASDs because paradoxical emboli may occur.
Class IIa, level B (22,23)

If closure of ASDs is being planned, it is recommended that closure be performed without undue delay before 24 years of age to ensure mortality benefit from surgery, and probably before 40 years of age for arrhythmia benefit for either surgery or device closure). As a rule, younger patients have a better prognosis after repair (6,22,24-26).

Part VI. Surgical/interventional technical options

In patients with secundum ASD, percutaneous ASD closure is the most frequently used closure method, and offers results comparable with surgical closure (9,27-29). The procedure is guided by either TEE or intracardiac echo. After percutaneous ASD closure, a TTE should be performed at 24 h after implantation to ensure that there is no significant pericardial effusion. Antiplatelet therapy with acetylsalicylic acid is usually given for six months following device closure.

Patients who undergo device closure must be 'ready' to undergo a surgical procedure in the event of complications.

Percutaneous ASD closure should be performed by individuals with expertise in the technique and its clinical evaluation.
Class I, level C

Surgical closure may also be offered, and may be especially attractive should the patient prefer the time-honoured surgical approach, or

especially if atrial arrhythmia surgery (atrial maze procedure for atrial fibrillation, and radiofrequency or cryoablation for atrial flutter) is offered concurrently. Catheter-based ablation techniques may be an alternative and should be attempted before device closure. Surgical approaches, such as the inframammary, right mini thoracotomy or mini sternotomy approach to a typical secundum ASD should be made known to interested patients considering surgery.

In patients with large secundum ASDs (larger than 38 mm) not amenable to device closure, surgical closure should be undertaken. Patients with a sinus venosus defect or ostium primum ASD cannot be closed by percutaneous devices and should be surgically repaired by congenital heart surgeons.
Class I, level B (30,31)

Part VII. Surgical/interventional outcomes

Immediately after ASD closure, patients are at risk for atrial arrhythmias. Following this initial at-risk period, with surgical or percutaneous repair, preoperative symptoms, if any, should decrease or abate. Functional capacity improves and supraventricular arrhythmias occur less commonly in the intermediate term. In general, pulmonary pressures decrease. Pre-existing atrial arrhythmias may persist unless an arrhythmia intervention, as outlined above, has been performed. Atrial arrhythmias may also arise de novo after repair, especially if ASD closure was performed after the age of 40 years.

Device closure: For secundum ASD without pulmonary hypertension, early and intermediate follow-up is excellent. The intermediate results are comparable with surgery, with a high rate of shunt closure, early improvement in cardiopulmonary function and few major complications.

Potential complications after percutaneous ASD closure are rare and include residual shunting, PAH, new-onset or recurrent arrhythmias, device embolization, device erosion, device impingment on valves, veins or other vessels such as the aorta, cardiac tamponade, thrombosis arising on the device, clinical right heart failure (typically in patients with elevated PAPs) and endocarditis. Small residual shunts in patients with normalized RV volumes require no specific additional treatment.

After percutaneous device insertion, chest pain or syncope may represent device erosion and should be evaluated immediately, preferably at a centre that performs cardiac surgery.
After percutaneous device insertion, early (three months) and intermediate (one year) follow-up is recommended with echo surveillance. Periodic follow-up is required thereafter.
Class I, level C

Surgical closure: For secundum ASD without pulmonary hypertension, surgical closure should result in a very low (less than 1%) operative mortality. Early and long-term follow-up is excellent.

Potential postoperative complications include death, residual shunting, PAH, arrhythmias, postpericardiotomy syndrome, cardiac tamponade and right heart failure. LV failure may occur in patients with associated cardiovascular disease (eg, coronary artery disease, hypertension, mitral valve incompetence).

Postoperative ASD patients may be prone to cardiac tamponade for the first several weeks after surgery.
Class I, level C

Part VIII. Arrhythmias

Patients with previously undiagnosed ASDs may initially present with palpitations. Typical atrial flutter and atrial fibrillation are the most common arrhythmias. In patients following ASD closure, common substrates include macro-reentry, along the lateral right atrial wall, around atriotomy incisions and double-loop circuits. The prevalence of late atrial tachyarrhythmias, including persistent atrial fibrillation, increases with age and may occur following closure, especially at the time of closure in adults older than 40 years of age and/or if atrial arrhythmias were present preoperatively. In complex cases, assessment by an electophysiologist is advisable.

If atrial fibrillation/flutter occurs, anticoagulation is usually indicated in accordance with existing guidelines. **(Level A)**
Atrial arrhythmias can be managed with either rate or rhythm control strategies. The approach should be tailored to the individual patient. **(Level B)**
Class I, level A or B (32)

The presence of preoperative atrial flutter/fibrillation may warrant surgical closure of the defect with concomitant cryosurgical/ablative therapy or an atrial maze procedure. Whereas atrial macro-reentrant tachyarrhythmias may usually be addressed by a right-sided atrial maze, atrial fibrillation requires a left-sided maze as well (33,34).

In patients with sustained atrial arrhythmias under consideration for transcatheter ASD closure, referral to an electrophysiologist is recommended. Catheter ablation should be considered before ASD closure because the presence of a septal closure device will impede access to the left atrium.
Class IIb, level C

Part IX. Pregnancy and contraception

Pregnancy is well tolerated in patients after ASD closure. In general, pregnancy is well tolerated in women with unrepaired ASDs, but the risk of paradoxical embolism is increased during pregnancy and the postpartum period. Global (ventricular systolic dysfunction, degree of cyanosis, history of cardiac complications) (35) and lesion-specific risks need to be taken into account when determining the risk of pregnancy.

Pregnancy in women with Eisenmenger's syndrome is not advised because of the high maternal and fetal mortality.
Class III, level B (36-39)

The rate of transmission of congenital heart disease (CHD) to offspring of women with sporadic secundum ASD is approximately 5% to 10%.

Part X. Follow-up

It is advisable that adults with repaired ASDs who have the following features undergo periodic follow-up by an adult CHD (ACHD) cardiologist:
- Repair completed as an adult.
- Elevated PAP at the time of repair.
- Atrial arrhythmias pre- or postoperatively.
- Ventricular dysfunction preoperatively.
- Coexisting heart disease (eg, coronary artery disease, valvular heart disease, hypertension).
- Familial ASD with *Nkx2.5* gene mutations because of the risk of progressive AV block.

Class I, level C

Endocarditis prophylaxis is recommended for six months following ASD closure (surgical or device).
Acetylsalicylic acid is recommended for six months following percutaneous device closure of an ASD.
Class I, level C (40)

For patients with unrepaired ASD, clinical examinations and TTEs should be performed periodically. TTE should re-examine RV size and function, and assess pulmonary artery systolic pressure.

Endocarditis prophylaxis is not recommended in patients with an isolated ASD or a repaired (surgical/device) ASD without residual shunt.
Class III, level B (40)

VENTRICULAR SEPTAL DEFECT

Part I. Background information

Only isolated ventricular septal defects (VSD) will be considered. Eisenmenger's VSD is further discussed in a separate section of the present guidelines series.

Hemodynamic severity grading of isolated VSD in adults (40):
Small: Pressure low (pulmonary/aortic systolic pressure ratio of less than 0.3 or main pulmonary artery mean pressure of lower than 20 mmHg or main pulmonary systolic artery pressure of lower than 35 mmHg) and Qp:Qs of less than 1.5:1.
Moderate: Pressure high (systolic pressure ratio of 0.3 or greater, or main pulmonary artery mean pressure of 20 mmHg or greater, or main pulmonary systolic artery pressure of 35 mmHg or greater), and pulmonary/systemic vascular resistance ratio of less than 0.2, and Qp:Qs of greater than 1.2:1.
Large: Pressure high and vascular resistance ratio between 0.2 and 0.7.
Eisenmenger's: Pressure high and vascular resistance ratio of greater than 0.7 and Qp:Qs of less than 1.2:1.
Physiological classification of isolated VSD in adults:
Restrictive: RV pressure lower than the LV pressure in the absence of RV outflow tract obstruction.
Nonrestrictive: Equal right and LV pressures in the absence of RV outflow tract obstruction.
Clinical severity grading of isolated VSD in adults:
Small: Causes negligible hemodynamic changes. LV size is usually normal without any pulmonary hypertension.
Moderate: Causes enlargement of the left ventricle and left atrium, and usually some pulmonary hypertension (reversible).
Large: Results in pulmonary vascular obstructive disease and Eisenmenger's physiology, unless there is coexistent RV outflow tract obstruction.
Surgical classification (41):
Type 1: Subarterial (synonyms: conal, subpulmonary, infundibular, supracristal, doubly committed). A VSD that lies beneath the semilunar valve(s) in the conal or outlet septum.
Type 2: Perimembranous (synonyms: paramembranous or conoventricular). A VSD that involves the membranous septum and is bordered by an AV valve, not including the type 3 VSD.
Type 3: Inlet (synonym: AV canal type). A VSD that involves the inlet of the RV septum inferior to the AV valve apparatus.
Type 4: Muscular. A VSD completely surrounded by muscle.
Gerbode type: A rare form of VSD in which the communication is between the LV and right atrium.

VSDs may coexist with other cardiac lesions such as valvar or subvalvar pulmonary stenosis, transposition of the great arteries, subaortic stenosis and coarctation of the aorta, and may result in aortic regurgitation from aortic cusp prolapse.

Part II. Prevalence and genetics

Subarterial VSDs are more common in Asian patients. Inlet VSDs typically occur in patients with Down's syndrome. VSDs can occur in the context of several deletion syndromes, chromosomal disorders, single gene defects and following exposure to certain teratogens such as alcohol. VSDs that occur in the context of other associated anomalies or in the context of a positive family history of birth defects, require further genetic evaluation.

Part III. History and management of unoperated patients

Small VSDs are associated with a normal life expectancy. They present as systolic murmurs. Atrial arrhythmias may occur. Spontaneous closure of small VSDs can still occur occasionally in adult life (41-43).

Moderate VSDs are unusual in the adult, but may occur when a prolapsing aortic valve cusp partially obstructs the defect. They are associated with the development of left heart dilation and shunt-related pulmonary hypertension (which often reverses with correction of the defect), and resultant congestive heart failure and atrial fibrillation.

Large VSDs without pulmonary hypertension exist in adults only when associated with obstruction to RV outflow, and are rare. These patients are at risk for endocarditis, especially if they are cyanotic because of severe RV outflow tract obstruction at the infundibular or valvular level, with secondary right-to-left shunt through the VSD.

VSD patients with Eisenmenger's syndrome (see section on Eisenmenger's syndrome) are at continuous risk for mortality and morbidity. Poor prognostic features are atrial flutter/fibrillation, syncope, heart failure, hemoptysis and aneurysmal dilation of proximal hypertensive pulmonary arteries, which may rupture, even with laminated thrombus in such dilated arteries.

Five per cent of VSDs develop aortic valve regurgitation (41,42). Patients with subarterial VSD are more likely to develop aortic regurgitation from progressive prolapse of the aortic valve cusps than those with a perimembranous VSD (41).

Part IV. Diagnostic workup

An adequate diagnostic workup should include the following:

- Documentation of the number and type(s) of VSDs.
- Determination of the size (restrictive/nonrestrictive) and functional importance (left-to-right shunt estimate; left and RV size/function; ventricular volume and pressure overload; PAP and resistance) of the defect.
- Identification of other associated conditions that may influence management (aortic regurgitation; subaortic stenosis; RV outflow obstruction; significant valve disease; coronary artery disease; coarctation of the aorta).

The initial workup should include the following (at a minimum):

- A thorough clinical assessment.
- ECG.
- Chest x-ray.
- TTE-Doppler evaluation by an appropriately trained individual.

The diagnostic workup may require the following:

- Oximetry.
- Heart catheterization (to determine PAPs and resistances [with or without reversibility using oxygen, nitric oxide and/or prostaglandins]; to assess intracardiac shunting; to evaluate associated lesions, particularly if aortic regurgitation is present; and to exclude multiple VSDs).
- Coronary angiography in patients at risk for coronary artery disease or in patients older than 40 years of age.
- MRI, occasionally, to confirm the presence or absence of other associated lesions, or to help define the anatomy of the VSD and the aortic cusps to clarify aortic valve prolapse. MRI can also be used to estimate Qp:Qs.

Part V. Indications for intervention/reintervention/medical therapy

The following situations warrant closure:

- The presence of a 'significant' VSD (symptomatic; LV volume overload; deteriorating ventricular function due to volume [LV] or pressure [RV] overload, Qp:Qs of 2:1 or greater; pulmonary artery systolic pressure of greater than 50 mmHg).
- Significant RV outflow tract obstruction (catheter gradient or mean echo gradient of greater than 50 mmHg).
- A perimembranous or subarterial VSD with more than mild aortic incompetence.
- In the presence of severe pulmonary hypertension (PAP greater than two-thirds the SABP or pulmonary arteriolar resistance greater than two-thirds the systemic arteriolar resistance), there must be a net left-to-right shunt of at least 1.5:1, or evidence of pulmonary artery reactivity when challenged with a pulmonary vasodilator (eg, oxygen, nitric oxide and/or prostaglandins).

Class I, level B (42-47)

The following situations may warrant closure:

- A history of endocarditis (especially recurrent).
- If transvenous pacing is required, closure may be reasonable to prevent paradoxical emboli.

Class IIa, level B (23,48)

If PAH is present (PAP greater than two-thirds the SABP or pulmonary arteriolar resistance greater than two-thirds the systemic arteriolar resistance) and irreversible, the VSD should not be closed. Such patients should receive care from a specialist with expertise in PAH.
Class III, level C

Part VI. Surgical/interventional technical options

Patients with an isolated VSD with or without associated lesions (RV outflow tract obstruction, aortic valve prolapse, subaortic stenosis or infective endocarditis) should be repaired by congenital heart surgeons.
Class I, level C (30,31)

Device closure may be performed in the setting of:
- Isolated trabecular muscular VSDs, especially if the VSD is remote from the tricuspid valve and the aorta.
- Perimembranous VSD if the defect is far enough from the aortic valve, although the risk of complete heart block is greater with device closure than with surgical closure.

Class IIb, level B (49-52)

Part VII. Surgical/interventional outcomes

Successful surgical closure is associated with excellent survival if ventricular function is normal (53).

Success rates of device closure are between 90% and 95% (50-52). Complications of interventional closure have been reported in 10% of patients and include hypotension, device embolization, rhythm and conduction abnormalities, and new aortic or tricuspid regurgitation. The major concern of device closure of perimembranous VSD is the 1% to 6% incidence of complete AV block that can occur early or late after closure (51).

Elevated PAPs preoperatively may progress, regress or remain unchanged postoperatively.

Part VIII. Arrhythmias

Atrial fibrillation may occur, especially if there has been longstanding volume overload of the left heart, or if other reasons for left atrial dilation are present.

Patients with unoperated VSDs experience an increased prevalence of isolated premature ventricular contractions, couplets, multiform premature ventricular contractions and nonsustained ventricular tachycardia, particularly in association with higher PAPs. Late ventricular arrhythmias and sudden death are potential risks, especially in patients repaired late in life (44,53,54).

Complete heart block may also occur early or late after surgical repair (1% to 4%) (54).

Part IX. Pregnancy and contraception

Pregnancy is well tolerated in women with small or moderate VSD, and in women with repaired VSDs. Global (ventricular systolic dysfunction, degree of cyanosis, history of cardiac complications) (35) and lesion-specific risks need to be taken into account when determining the risk of pregnancy.

Pregnancy in women with Eisenmenger's syndrome is not advised because of the high maternal and fetal mortality.
Class III, level B (36-39)

Part X. Follow-up

Patients with the following problems benefit from periodic evaluation by an ACHD cardiologist **(Level C)**:
- Patch leaks or residual VSDs (which seldom require reoperation).
- Elevated pulmonary vascular resistance at the time of surgery.
- Aortic valve surgery.
- Late repair of moderate or large defects.
- Residual right or LV dysfunction.
- Significant atrial or ventricular arrhythmias.
- Associated cardiac lesions (eg, RV outflow tract obstruction or aortic regurgitation).

Endocarditis prophylaxis is recommended for six months following VSD closure (surgical or device) or for life if any residual defect persists after surgical or device closure. **(Level B)**
Class I, level B or C as indicated

Endocarditis prophylaxis is not recommended in patients with isolated VSDs or patients with repaired (surgical/device) VSD without residual shunts.
Class III, level B (40)

AVSD

Part I. Background information

Definition: The terms AVSDs, AV canal defects and endocardial cushion defects can be used interchangeably to describe this group of defects. AVSDs cover a spectrum of anomalies caused by abnormal development of the endocardial cushions. The defect may be only at the atrial level (ostium primum ASD) or may include an inlet-type VSD. The AV valves are fundamentally abnormal, being derived from five leaflets (a right anterosuperior leaflet, a right inferior leaflet, a superior bridging leaflet, an inferior bridging leaflet and a left mural leaflet). This may result in separate right and left AV valves (with the left AV valve having a 'cleft' at the junction of the superior and inferior bridging leaflets) or a common valve (see classification below). Eisenmenger's AVSD is further discussed in a separate section of the present guidelines series.

Classification:

Partial AVSD: The ventricular septum is intact. There is a primum ASD. There is a 'cleft' in the left AV valve. There are two separate AV valve annuli.

Intermediate AVSD: This is the rarest form, and part of a spectrum between complete and partial AVSD. It is characterized by a restrictive VSD, a primum ASD and a cleft mitral valve. The anterior and posterior bridging leaflets are fused, resulting in two distinct AV valve components.

Complete AVSD: There is a nonrestrictive inlet-type VSD. There is usually a primum ASD but, rarely, the atrial septum may be intact. There is a common AV orifice.

Part II. Prevalence and genetics

AVSD may coexist with other lesions, both cardiac and noncardiac. The most common association is with Down's syndrome. Down's syndrome is present in 35% to 60% of patients with AVSD. Approximately 70% of patients with Down's syndrome have AVSDs. While AVSD can also occur in the context of chromosomal abnormalities, including trisomies 13 and 18, as well as in deletion and duplication syndromes, it is more frequently encountered in patients with genetic syndromes such as Smith-Lemli-Opitz, Smith-Magenis and Williams syndromes. Patients with Down's syndrome have a tendency for premature pulmonary vascular disease irrespective of the type of AVSD. Most (more than 90%) partial AVSDs occur in non-Down's syndrome patients. AVSD may occur in association with tetralogy of Fallot and other forms of complex CHD.

Part III. History and management of unoperated patients

Clinical presentation will depend on the presence and size of the ASD and VSD, and competence of the left AV ('mitral') valve.

Clinical presentation may take several forms:
- Symptoms of heart failure or pulmonary vascular disease.
- Atrial arrhythmias, nodal rhythm or complete heart block.
- Subaortic stenosis may or may not be present initially, but may develop or progress.
- No symptoms.

Partial/intermediate AVSD: Presentation of an unrepaired partial (ostium primum ASD) or intermediate AVSD as an adult is uncommon.

Symptoms include decreased exercise tolerance, fatigue, dyspnea, arrhythmias and recurrent pulmonary infections. Symptoms increase with age and most adults are symptomatic by 40 years of age. Patients become symptomatic at a younger age if significant left AV valve regurgitation is present.

Complete AVSD: Most patients with complete defects will have been repaired in infancy, although some may have been palliated with pulmonary artery bands and have variable degrees of pulmonary vascular obstructive disease. The history of unoperated complete AVSD is that of Eisenmenger's syndrome, and is discussed in the Eisenmenger's section. AVSD with Eisenmenger's syndrome has a worse prognosis than ASD, VSD or patent ductus arteriosus (PDA) with Eisenmenger's syndrome. Poor prognostic features are atrial flutter/fibrillation, syncope, heart failure and hemoptysis.

Part IV. Diagnostic workup

An adequate diagnostic workup should include the following:

- Documentation of the presence of each component of the AVSD and whether the ventricular chamber sizes are 'balanced' (although this is usually a pediatric issue).
- Assesses the magnitude and direction of intracardiac shunting.
- Documentation of the PAP.
- Documentation of abnormalities of the AV valves and their connections (straddling of the AV valves/overriding of the AV annulus) and assesses the severity of AV valve regurgitation, if any.
- Documents the presence or absence of subaortic stenosis. This may occasionally require provocative testing with isoproterenol, although it may be impossible to document a gradient in the presence of a nonrestrictive VSD.
- Identifies the presence of associated abnormalities (cardiac and noncardiac), which may have an impact on management (eg, pulmonary hypertension, tetralogy of Fallot, PDA, muscular VSDs, aortic coarctation or Down's syndrome).

The initial workup should include the following (at a minimum):

- A thorough clinical assessment, paying particular attention to AV valve regurgitation.
- ECG.
- Chest x-ray.
- TTE-Doppler evaluation by an appropriately trained individual.

The diagnostic workup may require the following:

- TEE to determine the exact anatomy (if unclear after TTE); the presence of intracardiac shunts; chordal attachments; the presence and severity of left AV ('mitral') valve regurgitation (or stenosis if previous valve repair has been undertaken); the presence and severity of right AV valve regurgitation and subaortic stenosis.
- Heart catheterization to determine the presence and magnitude of intracardiac shunts; PAPs and resistances; the severity of pulmonary vascular disease (with or without reversibility using oxygen, nitric oxide and/or prostaglandins); the presence and severity of left AV ('mitral') valve regurgitation (or stenosis, if previous valve repair has been undertaken); the presence and severity of subaortic stenosis (provocative testing may be necessary).
- Coronary angiography in patients at risk for coronary artery disease or in patients older than 40 years of age if an intervention is planned.
- Holter monitoring to assess AV block or other arrhythmia.
- MRI to help define the anatomy. MRI can also be used to estimate Qp:Qs.

Part V. Indications for intervention/reintervention/medical therapy

The following situations warrant intervention/reintervention:

- An unoperated AVSD with:
  a. Presumed paradoxic emoblism.
  b. LV dysfunction.
  c. RV volume overload.
  d. Clinical heart failure.
  e. Reversible pulmonary hypertension.
- In the operated AVSD:
  a. Persisting or new hemodynamically significant defects arising after the original repair.
  b. Left AV ('mitral') valve regurgitation (or stenosis from previous repair) causing symptoms.
  c. Deterioration in ventricular function.

Significant subaortic obstruction (catheter gradient or mean echo gradient of greater than 50 mmHg at rest or on provocative testing with isoproterenol)
Class I, level B (55-57)

If PAH is present (PAP greater than two-thirds the SABP or pulmonary arteriolar resistance greater than two-thirds the systemic arteriolar resistance) and irreversible, the AVSD should not be closed. Such patients should receive care from a specialist with expertise in CHD and PAH.
Class III, level C

Transvenous pacing should be avoided if there are residual interatrial or interventricular communications because paradoxical emboli may occur.
Class I, level B (23)

Part VI. Surgical technical options

A primum ASD (partial AVSD) cannot be closed using a percutaneous device and should be surgically repaired by a congenital heart surgeon.
AVSD patients, including those with ostium primum ASD, left AV ('mitral') valve repair, subaortic stenosis or residual defects, should be operated on by congenital heart surgeons.
Class I , level C (30-31)

When left AV valve repair is not possible, valve replacement may be necessary. The operative risk of valve replacement surgery should be similar to routine mitral valve replacement, although the risk of complete AV block may be higher.

Part VII. Surgical outcomes

In the short term, the results of repair of partial AVSD are similar to those following closure of secundum ASD, but sequelae of left AV ('mitral') valve regurgitation, subaortic stenosis and AV block may develop or progress (58-62).

In general, late results after left AV valve repair for these patients have been excellent, with the need for surgical revision in approximately 5% to 10% of patients (59-61). Occasionally, repair of the abnormal left AV valve may result in a stenotic valve, which may necessitate reoperation.

Subaortic stenosis will develop or progress in up to 5% of patients after repair, particularly in patients with primum ASD and some complete defects, especially if the left AV valve has been replaced. The long-term results of repair of complete AVSD are not well known but similar problems, as with partial AVSD, are likely.

Part VIII. Arrhythmias

Characteristic ECG features in the adult with AVSD include first-degree AV block, an incomplete or complete right bundle branch block pattern, and moderate to extreme left-axis deviation. Persistent complete AV block may occur spontaneously, immediately postoperatively or late after repair. Atrial fibrillation or flutter are not uncommon in adults with AVSD. Sinus node dysfunction and increased ventricular ectopy may also occur.

Part IX. Pregnancy and contraception

Pregnancy is well tolerated in patients with complete repair and no significant residual lesions. Women in New York Heart Association

class I and II with unoperated partial AVSD usually tolerate pregnancy very well, but have an increased risk of paradoxical embolization. Global (ventricular systolic dysfunction, degree of cyanosis, history of cardiac complications) (35) and lesion-specific risks need to be taken into account when determining the risk of pregnancy.

Trisomy 21 patients have a 50% risk of transmitting trisomy 21 or other genetic defects to their offspring.

All women with AVSD should be evaluated before conception to assess for possible hemodynamically significant lesions that might complicate management of pregnancy.
Consideration should be given to closure of any significant AVSD before pregnancy to minimize the risk of paradoxical emboli.
Reproductive counselling is warranted for trisomy 21 patients.
Class I, level C

Pregnancy in women with Eisenmenger's syndrome is not recommended because of the high maternal and fetal mortality.
Class III, level B (36-39)

Part X. Follow-up

All patients with AVSD require periodic follow-up by an ACHD cardiologist because of the possibility of progressive AV valve regurgitation (or stenosis); the development of subaortic stenosis; the occurence of significant atrial arrhythmias; or the progression of the commonly present first-degree AV block.
Particular attention should be paid to those with pulmonary vascular disease present preoperatively.
Class I, level B (58-62)

Endocarditis prophylaxis is not recommended in patients with an unrepaired or repaired AVSD unless associated with cyanosis, a residual shunt after closure or a prosthetic valve.
Class III, level B (40)

PDA

Part I. Background information

The ductus arteriosus, in utero, connects the proximal left pulmonary artery to the descending aorta, just distal to the left subclavian artery. Failure of closure at birth represents a congenital malformation. A PDA in an adult is usually an isolated lesion.

Clinical severity grading of PDA in adults:

Silent: Tiny PDA detected only by nonclinical means (usually echo).
Small: Audible continuous murmur. Causes negligible hemodynamic change. Normal LV size without pulmonary hypertension.
Moderate: Audible continuous murmur. Wide pulse pressure (as in aortic regurgitation). Causes enlargement of the left ventricle and some pulmonary hypertension (usually reversible).
Large: Usually does not exist in adults without Eisenmenger's physiology.
Eisenmenger's: Continuous murmur is absent. Causes substantial pulmonary hypertension, differential hypoxemia and, often, differential cyanosis.

Part II. Genetics

Familial PDA is seen with Char syndrome, an autosomal dominant disorder caused by mutations of *TFAP2B* characterized by abnormal facies and aplasia/hypoplasia of the middle phalanges of the fifth fingers (63).

Part III. History and management of unoperated patients

The risk of endarteritis with small silent PDA is unknown, but is likely very low (only sporadic case reports exist).

All other PDAs are associated with a rare risk of endarteritis, which may increase with age.

Adults with a small PDA have a normal life expectancy.

A moderate PDA is unusual in adults. It is associated with the development of left heart dilation and shunt-related pulmonary hypertension (which often reverses with correction of the defect). The majority of patients are symptomatic from dyspnea or palpitations (atrial arrhythmias), although frank heart failure is unusual.

A large PDA is rare in the adult, most having been corrected in infancy and childhood. Pulmonary hypertension is usual and may not reverse entirely with closure of the defect. Most patients are symptomatic from dyspnea or palpitations. Aneurysmal enlargement of the duct is an uncommon but important complication.

Eisenmenger's PDA has a similar prognosis to Eisenmenger's VSD, although symptoms may be less marked and exercise tolerance better. Patients will have differential cyanosis and, therefore, oxygen saturation in the feet must be checked. Eisenmenger's PDA is further discussed in a separate section of the present guidelines series.

Part IV. Diagnostic workup

An initial diagnostic workup should include the following:

- Documentation of the presence of a PDA.
- Determination of the size (systemic-to-pulmonary shunt estimate) and functional importance (PAPs) of the defect. Shunt estimates are often inaccurate because of the difficulty in obtaining a representative pulmonary blood sample for saturation assessment. The anatomical size of the duct is an important indicator of its functional importance. A focused CT scan (to limit radiation exposure) or MRI will provide valuable anatomical data and exclude other potential causes of a continuous flow murmur.
- Identification of whether left heart volume overload is present.
- Identification of whether a ductal aneurysm is present.
- Identification of whether the duct is calcified if surgical repair is planned.

The diagnostic workup should include the following (at a minimum):

- A thorough clinical assessment.
- ECG.
- Chest x-ray.
- TTE-Doppler evaluation by an appropriately trained individual.
- Oximetry (obtained on both fingers and toes).

The diagnostic workup may require the following:

- Heart catheterization (to determine PAPs and resistances with testing of pulmonary vascular reactivity using prostacyclin, inhaled oxygen and nitric oxide if PAPs are greater than two-thirds the systemic pressures).
- Coronary angiography in patients at risk for coronary artery disease or in patients older than 40 years of age if an intervention is planned.
- MRI or CT scan to define the anatomy and detect ductal aneurysm or calcification. MRI can also be used to estimate Qp:Qs.

Part V. Indications for intervention/reintervention/medical therapy

No intervention is indicated if a small silent PDA is detected.
Class I, level C

The following situations warrant intervention:

- The presence of a PDA (except the silent duct at one extreme and the presence of severe, irreversible pulmonary vascular disease at the other extreme).
- Closure of a small but audible PDA is usually recommended, although this indication remains controversial given the low perceived risk of endarteritis.
- The occurrence of an episode of endarteritis on a clinically silent PDA.
- If pulmonary hypertension is present (PAP greater than two-thirds the SABP or pulmonary arteriolar resistance greater than two-thirds the systemic arteriolar resistance), there must be a net left-to-right shunt of at least 1.5:1, or evidence of pulmonary artery reactivity when challenged with a pulmonary vasodilator (eg, oxygen, nitric oxide and/or prostaglandin).

Class IIa, level B (64,65)

If PAH is present (PAP greater than two-thirds the SABP or pulmonary arterial resistance greater than two-thirds the systemic arteriolar resistance) and irreversible, the PDA should not be closed. Such patients should receive care from a specialist with expertise in CHD and PAH.
Class III, level C

Part VI. Surgical/interventional technical options

Device closure is the preferred method for the small ductus and, when possible, should be planned at the same time as the diagnostic catheterization.
The presence of ductal calcification increases surgical risk and favours device closure.
Class I, level B (66,67)

Part VII. Surgical/interventional outcomes

Surgical closure should be reserved for those in whom the PDA is too large for device closure. Examples in which the ductal anatomy may be so distorted that it is not acceptable for device closure might include aneurysm or postendarteritis.
Operative repair should be undertaken by congenital heart surgeons.
Class I, level C (68,69)

Device closure: Successful closure is achieved in the large majority of attempts using a variety of devices (66,70,71). More than 85% of ducts are fully occluded by one year following device placement; these results have continued to improve with newer devices. Recanalization is rare but can occur.
Surgical closure: More than 95% of ducts can be closed by surgery. Recanalization is unusual but recognized. Postoperative complications may include recurrent laryngeal or phrenic nerve damage, and thoracic duct damage.

Part VIII. Arrhythmias
Atrial fibrillation may occur in older adults.

Part IX. Pregnancy and contraception
Pregnancy is well tolerated in women with silent and small PDA or in patients in functional class 1 or 2 before pregnancy. Global (ventricular systolic dysfunction, degree of cyanosis, history of cardiac complications) (35) and lesion-specific risks must be taken into account when determining the risk of pregnancy.

Pregnancy in women with Eisenmenger's syndrome is not advised because of the high maternal and fetal mortality.
Class III, level B (36-39)

Part X. Follow-up

Patients who have been repaired should have periodic evaluation by an ACHD cardiologist because recanalization can occur or residual problems (pulmonary hypertension, LV dysfunction, atrial fibrillation) may persist or develop. Patients with devices in situ should be followed periodically because the natural history of these devices is unknown.
Endocarditis prophylaxis is recommended for six months following PDA closure (surgical or device) or for life if any residual defect persists.
Class IIa, level B (40)

Endocarditis prophylaxis is not recommended in patients with an isolated PDA.
Class III, level B (40)

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