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Society Guidelines

Canadian Cardiovascular Society 2022 Guidelines for Cardiovascular Interventions in Adults With Congenital Heart Disease*

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ABSTRACT

Interventions in adults with congenital heart disease (ACHD) focus on surgical and percutaneous interventions in light of rapidly evolving ACHD clinical practice. To bring rigour to our process and amplify the consensus of a Canadian panel comprised of multidisciplinary experts on this topic with a mandate to formulate disease-specific recommendations. These recommendations are aimed to provide a reasonable and practical approach to care for specialists and allied health professionals obliged with the duty of bestowing optimal care to patients and families, and can be subject to change as scientific knowledge and technology advance and as practice patterns evolve. The statement is not intended to be a substitute for physicians using their individual judgement in managing clinical care in consultation with the patient, with appropriate regard to all the individual circumstances of the patient, diagnostic and treatment options available and available resources. Adherence to these recommendations will not necessarily produce successful outcomes in every case.

RÉSUMÉ

Les interventions chez les adultes atteints de cardiopathie congénitale (AACC) sont axées sur des interventions chirurgicales et percutanées, tenant compte de l'évolution rapide de la pratique clinique dans ce

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*Dedicated to the memory of Gary D. Webb (1943-2021).

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‡These authors were co-chairs of this guideline update and contributed equally to this work.

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This statement was developed following a thorough consideration of medical literature and the best available evidence and clinical experience. It represents the

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cumulative nature of evidence ACHD care we used the ADAPTE process; we systematically adjudicated, updated, and adapted existing guidelines by Canadian, American, and European cardiac societies from 2010 to 2020. We applied this to interventions related to right and left ventricular outflow obstruction, tetralogy of Fallot, coarctation, aortopathy associated with bicuspid aortic valve, atrioventricular canal defects, Ebstein anomaly, complete and congenitally corrected transposition, and patients with the Fontan operation. In addition to tables indexed to evidence, clinical flow diagrams are included for each lesion to facilitate a practical approach to clinical decision-making. Excluded are recommendations for pacemakers, defibrillators, and arrhythmia-directed interventions covered in separate designated documents. Similarly, where overlap occurs with other guidelines for valvular interventions, reference is made to parallel publications. There is a paucity of high-level quality of evidence in the form of randomized clinical trials to support guidelines in ACHD. We accounted for this in the wording of the strength of recommendations put forth by our national and international experts. As data grow on long-term follow-up, we expect that the evidence driving clinical practice will become increasingly granular. These recommendations are meant to be used to guide dialogue between clinicians, interventional cardiologists, surgeons, and patients making complex decisions relative to ACHD interventions.

domaine. Afin d'apporter une certaine rigueur à notre démarche et d'amplifier la propension cumulative des données probantes concernant les AACC, nous avons utilisé le processus ADAPTE; nous avons systématiquement évalué, mis à jour et adapté les lignes directrices existantes des sociétés de cardiologie canadiennes, américaines et européennes de 2010 à 2020. Nous avons appliqué cette méthode aux interventions liées à l'obstruction du débit ventriculaire droit et gauche, à la tétralogie de Fallot, à la coarctation, à l'aortopathie associée à une dysfonction de la valve aortique bicuspide, aux anomalies du canal auriculo-ventriculaire, à l'anomalie d'Ebstein, à la transposition congénitale complète corrigée, et aux patients ayant subi une intervention de Fontan. En plus des tables indexées aux évidences, des diagrammes de flux cliniques sont inclus pour chaque affection afin de faciliter une approche pratique de la prise de décision clinique. En sont exclues : les recommandations concernant les stimulateurs cardiaques, les défibrillateurs et les interventions dirigées envers les arythmies, qui font l'objet de documents distincts. De la même façon, en cas de chevauchement avec d'autres directives sur les interventions valvulaires, il est fait référence à des publications parallèles. Il y a une pénurie d'évidences de haute qualité sous forme d'essais cliniques randomisés pour appuyer les lignes directrices concernant les AACC. Nous en avons tenu compte dans la formulation de l'amplitude des recommandations formulées par nos experts nationaux et internationaux. Au fur et à mesure que les données sur le suivi à long terme s'accumulent, nous nous attendons à ce que les preuves à la base de la pratique clinique deviennent de plus en plus granulaires. Ces recommandations sont destinées à guider la discussion entre les cliniciens, les cardiologues interventionnels, les chirurgiens et les patients qui doivent prendre des décisions complexes concernant les interventions chez les AACC.

The first Consensus Conference on the care of adults with congenital heart disease (ACHD) patients was led by Dr Gary Webb and held in Canada in 1996, with the proceedings published in l998.[1] We dedicate this guideline document to his memory. Without his lifelong contributions, we would not be here today assembling this body of knowledge.

The Canadian Adult Congenital Heart Network, known as the CACH Network, was recognized as a Canadian Cardiovascular Society (CCS) affiliate in 2010. Its current board members largely constitute the primary writing panel of these guidelines.

First-time empirical population-based measurements showing an increasing prevalence of ACHD were published using Canadian data sources.[2] Starting in 1985, there was a steep rise in the prevalence of ACHD, resulting in an equalization of the numbers of adults and children with congenital heart disease (CHD). By 2010, the number of adults with all forms of CHD exceeded those of children with CHD, with two-thirds of the population being adults.[3] In 2010, there were an estimated 257,138 patients living with CHD, of whom 166,428 were adults. The term, "geriatric adult congenital heart disease" was thus coined,[4] ushering in a growing body of data showing the lifelong complications of CHD occurring in parallel to increasing survival rates[5] and a shift in mortality from children to adults with CHD.[6] In Canada, cost containment for populations with chronic, lifelong morbidity challenges our ability to sustain delivery of high quality care.[7] In ACHD populations, significant increases in health services utilization have been shown during childhood,[8] during transitions in care,[9] in adulthood,[10] and into the geriatric years,[4] with national trends of increasing costs well shown using Canadian Institute for Health Information data for CHD populations.[11] International data sources have shown increasing health services utilization for a growing population of ACHD patients with heart failure (HF).[12]

With this set of guidelines, we turn our attention to the need for interventions occurring as a result of the mounting burden of comorbidities. Specifically excluded from this update are recommendations for arrhythmias, pacemakers, intracardiac cardioverter-defibrillators, cardiac resynchronization therapy, and specific arrhythmias or arrhythmia-directed surgical interventions because these have been comprehensively covered elsewhere in the field of ACHD with a dedicated group of experts.[13] Well established in our growing armamentarium of procedures, ACHD patients have benefited from catheter-based interventions for more than a decade[14] while improvements in advanced imaging capabilities have increased the reach of percutaneous procedures in CHD.[15] A growing need for valvular reinterventions particularly in adults will spur nimble adaptation of existing valvular interventions to a growing set of novel tools.[16-18] Even so, although the profile of surgical practice in ACHD is changing, the need for surgical reinterventions has remained significant.[19] The lag-time between the

clinical complications related to past interventions makes CHD surgery a challenge.[20] The risk stratification in ACHD patients undergoing cardiac surgery remains important but difficult.[21] The expectation is that individualized and validated risk-adjusted outcomes[22] would add counterpoint to the broad recommendations made in heterogeneous adult populations to mitigate morbidity observed during ACHD surgical admissions.[23]

Robust scientific inquiry is new to ACHD compared with other cardiovascular diseases. Increasingly heterogeneous in age, lesion subgroup, surgical history, and propensity to specific comorbidities, in an era that saw an explosion of clinical trials in adult cardiovascular medicine, ACHD patients were either systematically excluded from ongoing experimental analyses of medical or interventional therapies or failed to meet the subgroup sample size threshold needed to achieve meaningful data interpretation. With the exception of specific areas like pulmonary hypertension,[24] truly prospective randomized controlled trials (RCTs) are scant in ACHD even for common lesions and common medications.[25] For comparative purposes, over a 10-year period from 2007 to 2017, a Medline and PubMed search with uniformly applied concept filters in adults 18 years and older revealed > 2000 RCTs for coronary artery disease. During the same time frame, there were only 165 RCTs in ACHD patients, a number that fell to 15 after exclusion of trials related to pulmonary hypertension, bicuspid aortic valve (BAV), and Marfan syndrome, or trials only reporting "rationale and design."[26]

Whereas the class of recommendation reflects the expected size of the treatment effect, the level of evidence reflects the certainty of the expected treatment effect.[27] The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach defines the strength of a recommendation as the extent to which we can be confident that adherence to the recommendation will do more good than harm and the quality of evidence as a measure of the extent to which we can be confident that an estimate of effect is correct.[28] In ACHD guidelines, recommendations have largely been classified as class 1, although supported by a level of evidence that is B or C. Thus, relative to the treatment effect, recommendations are largely deployed with a mismatch between its expected size and the level certainty of the data supporting it. Despite enormous progress, at this time, as a field we lag significantly behind our adult colleagues in performing cardiovascular trials that would allow us to generate evidence comparable to that existing in non-CHD populations.

The current guidelines were developed for general cardiologists and the community of ACHD specialists. We involved a primary writing panel and subsequently engaged a secondary panel including interventionalists to review our recommendations in 2 rounds. Finally, we had our guideline reviewed by an international panel of experts. We used the rigourous process of the ADAPTE methodology to review previous recommendations as well as those of the American College of Cardiology/American Heart Association, accepting or rejecting a previous guideline and updating the recommendations where new evidence was available. Results of the ADAPTE process are presented in Supplemental Appendix S1. We sought a clear presentation of the material using tables and clinical decision diagrams for ease of reference. We specified applicability as necessary. Thus, our guideline adheres to the **A**ppraisal of **G**uidelines for **Re**search **E**valuation (AGREE) instrument[29] for assessing guidelines as adopted by the CCS.[30] Supplemental Appendix S2 shows the recommendations using class and GRADE.

Despite the persistent and substantial knowledge-to-evidence gap that continues to persist in ACHD care where small numbers harbor the difficulty in carrying out internally valid studies in a heterogeneous patient population, we have generated conservative guidelines focused on interventions. We recognize that the personalized application to individual patients remains in the hands of well trained, well informed clinicians functioning in multidisciplinary teams, where the range of perspectives gives depth to the complex decisions that must be made.

Atrial Septal Defect

Background

Atrial septal defect (ASD) is the most common type of congenital heart lesion presenting in the adult.[31] There are 4 types of inter-atrial communications: 2 "true" ASDs due to a deficiency in atrial septal tissue, the secundum ASD and the partial atrioventricular (AV) septal defect (AVSD; also known as primum ASD), and 2 other communications, the sinus venosus defect (superior and inferior), and the unroofed coronary sinus defect. Anatomy is important because there are differences in the natural history and indications for closure. Secundum ASD accounts for 80% of inter-atrial communications and management guidelines often focus on the secundum ASD (Fig. 1).

Clinical presentation

Presentation varies from asymptomatic patients to those with functional decline, arrhythmias, HF and/or, rarely, pulmonary arterial hypertension (PAH).[31] Patients whose inter-atrial communications are unrepaired, or repaired at a late age, have increased morbidity and mortality compared with an age-matched population.

Recommendations for intervention

Indications for closure are driven by presence of symptoms and/or evidence of a hemodynamically significant shunt in the absence of irreversible pulmonary vascular disease.[32,33] An ASD is considered hemodynamically significant if there is evidence of right ventricular (RV) enlargement and/or pulmonary flow (Qp):systemic flow (Qs) $\geq$ 1.5. Although this is the case for most hemodynamically significant shunts, exceptions might arise when PAH is present. The presence of pulmonary vascular disease is identified by assessing pulmonary pressures, vascular resistance, and shunt ratio between the pulmonary and systemic circulations. Patients with hemodynamically significant shunts who do not undergo closure have worse long-term outcomes compared with an age-matched population, with reduced functional capacity, more arrhythmias, progressive PAH, and increased mortality.[25,34-38] Closure before the age of 15-25 years is associated with improved patient survival.[39,40] Long-term benefits after closure in patients older than 40 years of age include improved functional capacity, favourable RV remodelling, reduction in

pulmonary pressures, and reduced arrhythmia burden. However, the evidence for improved survival is less robust.[25,41] Some patients might have other indications for closure such as prevention of recurrent paradoxical embolism, prophylaxis against paradoxical emboli in the presence of a permanent transvenous pacing electrode or indwelling catheter, or for treatment of orthodeoxia-platypnea syndrome. Considerations for closure need to be made in the context of the patient's clinical status, comorbidities, and risk associated with method of closure.

For secundum ASD, depending on size and anatomic features, percutaneous device or surgery may be used. For percutaneous closure, a secundum ASD typically should be smaller than 38 mm, with adequately-sized rims.[42] If anatomic features are favourable, percutaneous closure is preferred because it is associated with lower rates of mortality and major morbidity as well as shorter hospital stay compared with surgical closure.[43] In some patients with elevated pulmonary pressures, a fenestrated device may be considered. Percutaneous device closure requires technical expertise and equipment, with the best outcomes seen in higher-volume centres.[44] Surgical repair is generally required for primum ASD, sinus venosus defect, and unroofed coronary sinus defect, because these defects typically are not amenable to percutaneous closure, although emerging data indicate that some patients with sinus venosus defect might be suitable for percutaneous intervention.[45,46] Surgical repair of interatrial communications should be performed by operators with expertise in congenital heart surgery.[32]

For patients who do not meet criteria for closure, ongoing follow-up is recommended. When PAH is present, we recommend referral to a specialized centre to determine if medical therapy might be indicated to determine candidacy for closure.[32] In patients with small, hemodynamically insignificant shunts, overall prognosis might be favourable; however, intermittent follow-up long-term, and referral at least once to be seen by an ACHD specialist is warranted. (Table 1, Fig. 2).

Ventricular Septal Defect

Background

Ventricular septal defect (VSD) is one of the most commonly encountered congenital heart defects. There are 4 types of VSD: muscular, perimembranous, supracristal (outlet or conal [if located above the crista supraventricularis]) and AVSD (or inlet-type VSD) spectrum.[60] The type of VSD is important because there are differences in the natural history and indications for closure. Patients with an isolated VSD that is surgically repaired in childhood and those with small restrictive (without significant shunt) VSDs not requiring repair, have an excellent long-term prognosis, although they are not completely free from morbidity or mortality (Fig. 3).

Clinical presentation

Of patients with restrictive VSD deemed not to require surgical closure during childhood, long-term survival is expected and favourable.[60-62] Occasionally, isolated VSDs are not identified in childhood and might subsequently present in adulthood with left ventricular (LV) volume overload, infective endocarditis, progressive aortic regurgitation (AR), or PAH.

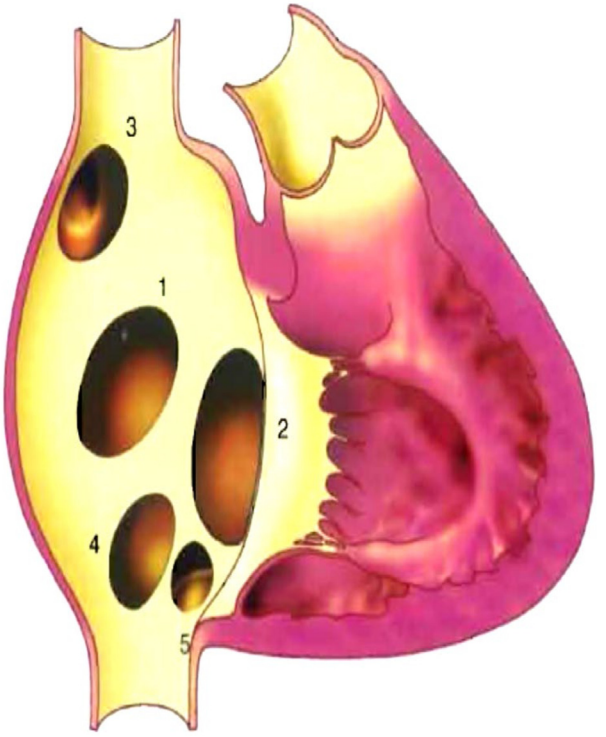


Figure 1. Various types of atrial septal defects. 1, type secundum; 2, type primum (incomplete atrioventricular septal defect); 3, type sinus venosus superior; 4, type sinus venosus inferior; and 5, unroofed coronary sinus defect. Reproduced from Popelová et al.[239] with permission of the Licensor through PLSclear. © 2008 Informa UK Ltd.

Recommendations for intervention

Conservative management is typical for patients with a small restrictive VSD.[63] Indications for closure derive from the presence of symptoms and/or evidence of a hemodynamically significant shunt in the absence of irreversible pulmonary vascular disease. A VSD is considered hemodynamically significant if there is evidence of LV volume overload and/or if there is a Qp:Qs $\geq$ 1.5 with no significant PAH.

There is significant morbidity and mortality if surgical closure of a VSD is attempted in patients with pulmonary vascular disease.[54] If the pulmonary artery (PA) systolic pressure is $>$ 2/3 systemic, pulmonary vascular resistance (PVR) is $>$ 2/3 systemic vascular resistance, and/or there is net right-to-left shunting across the VSD (Eisenmenger physiology), the surgical risk is prohibitive.[55,64] Even more contemporary attempts to intervene in this patient population continue to show a significantly high rate of morbidity and mortality.[65] Therefore, closure of a VSD in patients with important and irreversible pulmonary vascular disease remains contraindicated. Patients in this category should undergo vasoreactivity testing (pure oxygen, inhaled nitric oxide, or inhaled prostanoids) because there is evidence that those who

Table 1. Recommendations for intervention in adults with ASDs

	Recommendations	GRADE		References
		Strength	Quality	
1	We recommend closure of an ASD (secundum ASD, partial AVSD, sinus venosus defect, or unroofed coronary sinus) in a symptomatic patient with a net left-to-right hemodynamically significant shunt (RV enlargement and/or Qp:Qs ≥ 1.5*) when the PAP is < 50% of systemic pressure, and/or PVR is < 1/3 SVR.	Strong	Moderate	34,36-38,47-50
2	We suggest that closure of an ASD (secundum ASD, partial AVSD, sinus venosus defect, or unroofed coronary sinus) is reasonable in an asymptomatic patient with a net left-to-right hemodynamically significant shunt (RV enlargement and/or Qp:Qs ≥ 1.5*) when the PAP is < 50% of systemic pressure, and/or PVR is < 1/3 SVR.	Weak	Low	34,36,38,48
3	We recommend percutaneous device closure of secundum ASD as the method of choice if expertise is available and the defect is amenable to device closure.	Strong	Moderate	43
4	We recommend surgical closure of a partial AVSD, sinus venosus defect, or unroofed coronary sinus defect. We recommend that surgery be performed by a cardiac surgeon with expertise in congenital heart surgery.	Strong	Moderate	37,50
6	We suggest that closure of an ASD may be considered in the presence of elevated pulmonary pressures, when the net shunt is left-to-right and PAP is < 2/3 of systemic pressure, and/or the PVR is < 2/3 SVR. Such patients should be assessed and cared for by a multidisciplinary team with expertise in CHD and PAH.	Weak	Moderate	51-53
7	We do not recommend closure of an ASD in patients with PAP > 2/3 systemic, PVR > 2/3 systemic, and/or a net right-to-left shunt. Such patients should receive care from specialists with expertise in CHD and PAH.	Strong	Low	54,55
8	We suggest that an ASD may be considered for closure in patients who have had a stroke, TIA, or systemic embolism of unknown cause, and paradoxical embolism is suspected.	Weak	Low	56
9	We suggest that an ASD may be considered for closure in patients with orthodeoxia-platypnea.	Weak	Low	57,58
10	We suggest that closure of an ASD in patients with transvenous pacing electrodes or chronic indwelling venous catheters is reasonable to diminish the risk of paradoxical embolism.	Weak	Low	59

ASD, atrial septal defect; AVSD, atrioventricular septal defect; CHD, congenital heart disease; GRADE, Grading of Recommendations Assessment, Development and Evaluation; PAH, pulmonary arterial hypertension; PAP, pulmonary artery pressure; PVR, pulmonary vascular resistance; Qp, pulmonary flow; Qs, systemic flow; RV, right ventricular; SVR, systemic vascular resistance; TIA, transient ischemic attack.

*For closure of an ASD in the patient with a net left-to-right hemodynamically significant shunt and RV enlargement, a Qp:Qs measurement might not be necessary in decision-making.

can achieve PVR < 5 Wood units and a Qp:Qs ≥ 1.5 might still be candidates for closure after multidisciplinary consultation with a PAH specialist.[66]

The risk of infective endocarditis is higher in patients with an open VSD than after surgical closure.[67] Although a reduction in the risk of endocarditis is not by itself sufficient to justify closure of a small defect, after infective endocarditis, closure of the defect might be warranted to prevent recurrence.[68] Similarly, patients with transvenous pacemaker leads and an open intracardiac shunt have a twofold increase in the risk of systemic thromboemboli compared with those without transvenous leads in place. Thus, closure of VSDs might be considered before implantation of transvenous pacing systems.[59] VSD closure might be indicated to prevent progressive AR, especially in patients with supracristal VSDs, in whom there is an increased risk of developing AR secondary to aortic valve prolapse.[69,70] In a subset of patient with supracristal VSDs who do not have progressive AR, cautious surveillance might be reasonable.[71]

Surgical closure of a VSD has been the gold standard of management, with low operative mortality.[72] An increasing number of techniques, ranging from fully percutaneous procedures to minimally invasive and hybrid techniques are now available. Some are in widespread use because of favourable safety profiles and patient preference.[73,74] Percutaneous options were initially thought to be prudent only for the management of muscular VSDs, because of the reported high incidence of complete heart block and valvular complications after percutaneous closure of perimembranous and supracristal (outlet) VSDs.[75] More recent studies suggest that these risks were likely overestimated and that device closure is safe and effective for most VSDs.[6,76] The decision regarding method of VSD closure should be on the basis of local expertise, patient preference, and other anatomic considerations including aortic valve prolapse. VSD closure should be performed in a high-volume centre by interventionalists and/or surgeons trained in CHD[77] (Table 2, Fig. 4).

Patent Ductus Arteriosus

Background

Patent ductus arteriosus (PDA) represents a spectrum of severity from a small, nonsignificant ductus to a large shunt lesion.[79] In the average full-term neonate, the ductus arteriosus closes soon after birth. The incidence of a persistent PDA is approximately 1 per thousand. Although surgical closure has been performed since 1939, percutaneous techniques have proven effective in large case series. More recently, patient preference and cost-effectiveness have led to percutaneous device closure performed by congenital interventionalists becoming the preferred method of closure (Fig. 5).

Clinical presentation

A large patent ductus, if left untreated, can result in LV volume overload, PAH eventually leading to right-to-left shunting, and reduction in life expectancy.[79]

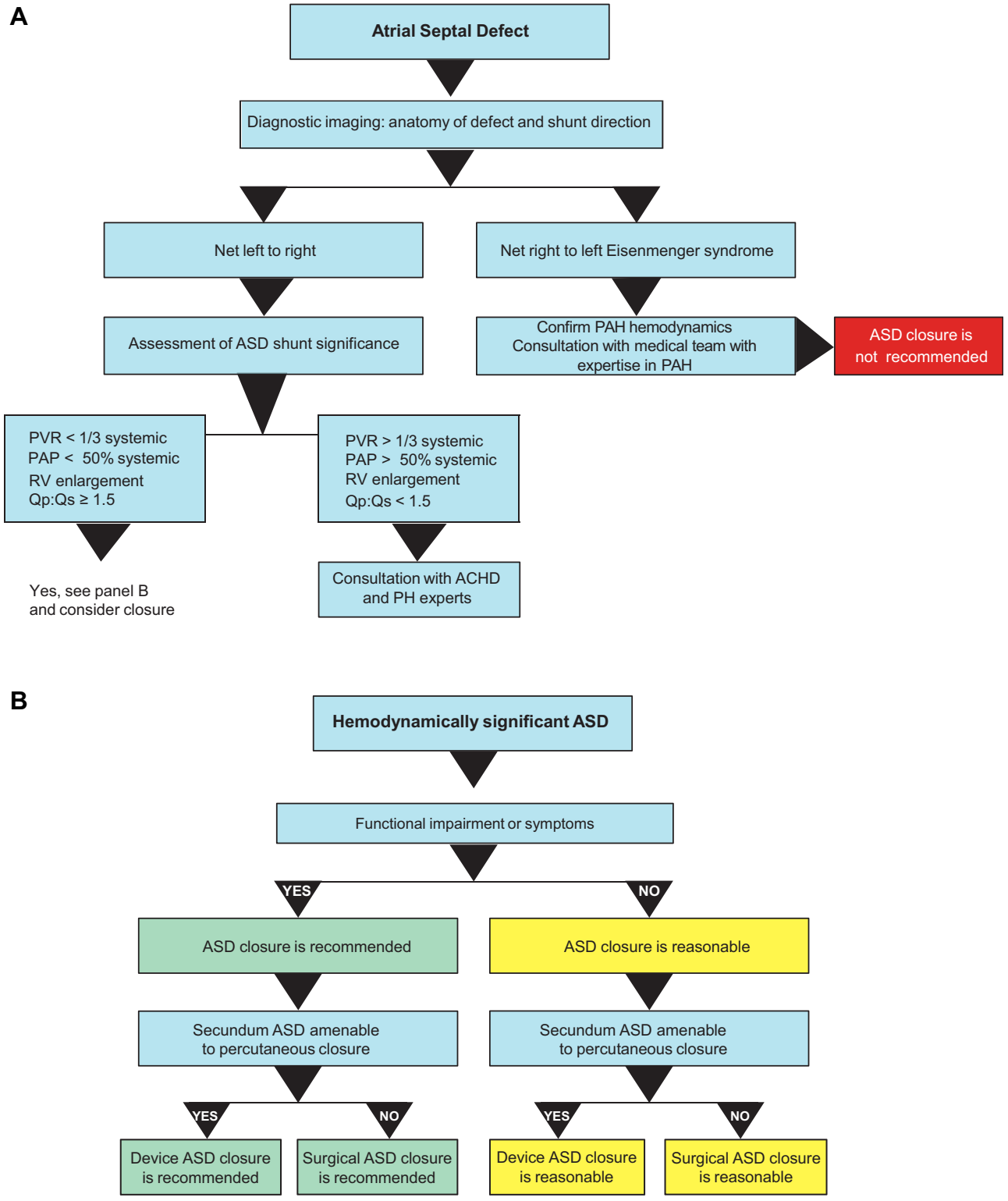


Figure 2. (**A**) ASD intervention pathway. (**B**) ASD intervention pathway (continued). ACHD, adults with congenital heart disease; ASD, atrial septal defect; PAH, pulmonary arterial hypertension; PAP, pulmonary artery pressure; PH, pulmonary hypertension; PVR, pulmonary vascular resistance; RV, right ventricular; Qp, pulmonary flow; Qs, systemic flow.

Recommendations for intervention

The decision to close a PDA or monitor expectantly depends on its hemodynamic significance. A hemodynamically significant PDA results in LV volume overload and closure has been shown to decrease LV end-diastolic volume.[80] Similar to other shunt lesions, the presence of significant

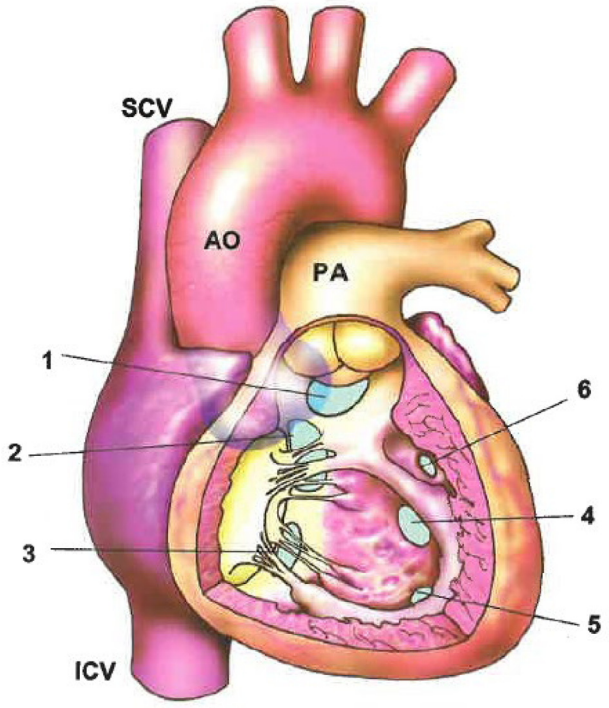


Figure 3. Various types of ventricular septal defects (VSDs). Anatomic location of VSDs, viewed from the right ventricle. 1, Outlet VSD; 2, perimembranous VSD; 3, inlet VSD; 4, muscular central VSD; 5, muscular apical VSD; and 6, muscular marginal VSD. AO, aorta; ICV, inferior caval vein; PA, pulmonary artery; SCV, Superior caval vein. Reproduced from Popelová et al.[239] with permission of the Licensor through PLSclear. © 2008 Informa UK Ltd.

PAH (systolic pulmonary artery pressure [PAP] > 2/3 systemic pressure and/or PVR > 2/3 systemic vascular resistance) is a contraindication to closure.[54] Closure may be considered in those with moderate PAH with evidence of reversibility.[81] In the presence of a history of endarteritis, closure may be considered to prevent recurrent endarteritis[82] (Table 3, Fig. 6).

Atrioventricular Septal Defect

Background

The term, AVSD, embraces the obsolete terms, AV canal defect and endocardial cushion defect that are sometimes used interchangeably to describe the spectrum of anomalies caused by abnormal development of the endocardial cushions. The defect might be limited to the atrial level (ostium primum ASD) or might include an inlet-type VSD. The AV valves are characteristically abnormal, derived by varying degrees of development and fusion of the right anterosuperior, right inferior, superior bridging, inferior bridging, and left mural leaflets.[31] This might result in separate right and left AV valves with a "cleft" at the junction of superior and inferior zone of apposition, or a common valve. Collectively, the various forms of AVSD occur with a prevalence of 0.21/1000 adults, which is approximately one-quarter of the prevalence of the more commonly seen ASD and VSD lesions. An AVSD might coexist with other cardiac and noncardiac lesions. It can be encountered in patients with chromosomal abnormalities and various genetic syndromes, the most common association being with trisomy 21 (Down syndrome). Anatomic variants include: *partial AVSD:* primum ASD, intact ventricular septum, cleft left AV valve, 2 separate AV valve annuli; *intermediate AVSD:* primum ASD, restrictive VSD, cleft left AV valve, fused anterior and posterior bridging leaflets resulting in distinct left and right AV valve components; and *complete AVSD:* nonrestrictive inlet-type VSD, common AV orifice, usually with primum ASD, though, rarely, the atrial septum is intact.

Clinical presentation

Clinical presentation of a partial AVSD depends not only on the size of the atrial shunt but also, and most commonly, on the degree of associated mitral regurgitation when present. Most adults with a complete AVSD will have undergone surgical repair in childhood, although some might have had palliation with PA banding. Adults with complete AVSD not repaired in infancy will have developed pulmonary vascular obstructive disease with Eisenmenger physiology. Adults with partial or intermediate AVSD might occasionally present with unrepaired defects. Symptoms can reflect HF, pulmonary vascular disease, and/or arrhythmias.[31]

In adults who underwent surgical repair, common long-term complications include left AV valve regurgitation and, less frequently, stenosis, LV outflow tract (LVOT) obstruction, atrial arrhythmias, and AV block. Favourable results have been reported in cohorts of selected adults with primary AVSD repair[87,88] or previously operated AVSD and subsequent surgery for residual defects.[88-97] Although the left AV valve in AVSD is not identical to a mitral valve, it is reasonable to extrapolate recommendations for surgical intervention related to mitral regurgitation, in the absence of evidence-based criteria more specific to AVSD.[98-100] However, anatomical differences between a left AV valve in AVSD and a mitral valve could affect the technical feasibility of valve repair. Additionally, complications of surgery, including AV block are more frequent.[101-105] In patients with AVSD and LVOT obstruction (LVOTO), factors associated with less favourable outcomes include a mean LVOT Doppler gradient ≥ 40 mm Hg, symptoms of HF, and accompanying moderate or severe left AV valve or AR.[106,107]

Recommendations for intervention

The recommendations summarized in Table 4 and corresponding flow diagram (Fig. 7) emphasize the prohibitive morbidity and mortality associated with shunt repair of an AVSD in patients with Eisenmenger physiology but recognize that there are some adults with an AVSD and elevated PAP who have net left-to-right shunts in whom shunt closure might prevent worsening of PAH.[54,55,108] Such cases must be carefully evaluated by a multidisciplinary team including ACHD and PAH specialists. Surgical closure is recommended when anatomic considerations preclude percutaneous interventions most commonly with associated AV canal defect, sinus venosus ASD, or unroofed coronary sinus defect.

Table 2. Recommendations for intervention in adults with VSDs

	Recommendations	GRADE Strength	GRADE Quality	References
1	We recommend closure of a hemodynamically significant VSD (evidence of LV volume overload and/or Qp:Qs ≥ 1.5) with no significant PAH (PAP < 50% systemic and/or PVR < 1/3 SVR).	Strong	Moderate	55,72,78
2	We suggest that closure of a hemodynamically significant VSD may be considered in the setting of moderate PAH (PAP ≥ 50% systemic and/or PVR > 1/3 SVR but Qp:Qs ≥ 1.5 at baseline or in response to vasodilator challenge). Such patients should be assessed and cared for by a multidisciplinary team with expertise in CHD and PAH.	Weak	Low	66
3	We do not recommend closure of a hemodynamically significant VSD in the setting of significant PAH (PAP > 2/3 of systolic blood pressure, PVR > 2/3 SVR, net right-to-left shunt). Such patients should receive care from specialists with expertise in CHD and PAH.	Strong	Low	54,55,64
4	We suggest that closure of a hemodynamically insignificant VSD with no evidence of PAH is reasonable after repeated episodes of infective endocarditis.	Weak	Low	67,68
5	We suggest closure of a hemodynamically insignificant VSD with no evidence of PAH is reasonable if there is a requirement for transvenous pacing or chronic indwelling venous catheter(s).	Weak	Low	59
6	We suggest that closure of a hemodynamically insignificant perimembranous or supracristal VSD is reasonable in the setting of progressive aortic regurgitation secondary to aortic cusp prolapse and in the absence of PAH.	Weak	Low	69,70,78
7	We recommend that the method of VSD closure should be determined by local expertise and performed in a high-volume centre by interventionalists and/or surgeons trained in CHD. Although surgical closure of VSD remains the gold standard, percutaneous closure may be an alternative in select cases.	Strong	Moderate	74-77

CHD, congenital heart disease; GRADE, Grading of Recommendations Assessment, Development and Evaluation; LV, left ventricular; PAH, pulmonary arterial hypertension; PAP, pulmonary artery pressure; PVR, pulmonary vascular resistance; Qp, pulmonary flow; Qs, systemic flow; SVR, systemic vascular resistance; VSD, ventricular septal defect.

Aortopathy in Patients Wth Bicuspid Aortic Valve

Background

BAV is the most common congenital anomaly, occurring in 1%-2% of the general population, with male predominance.[109] BAVs might become stenotic or regurgitant with time. Dilation of the aorta occurs in approximately 50% of patients with BAV. The dilation usually occurs at the level of the mid ascending aorta although the sinuses of Valsalva are sometimes involved. Flow rheology as well as genetic mutations are thought to contribute to the aortic dilation in this

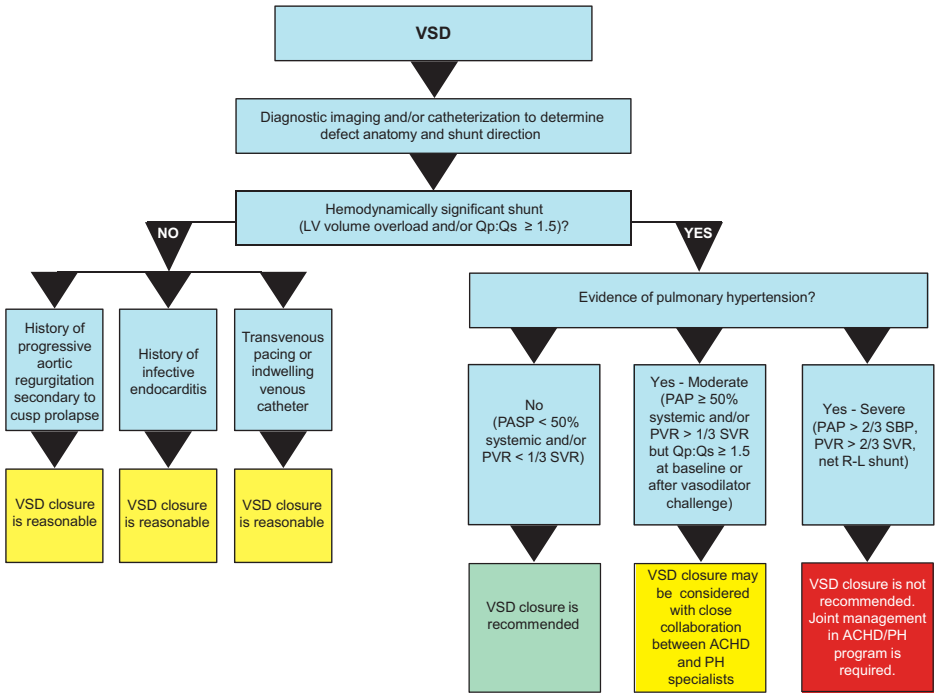


Figure 4. Ventricular septal defect (VSD) intervention pathway. ACHD, adults with congenital heart disease; L, left; LV, left ventricle; PAP, pulmonary artery pressure; PASP, pulmonary arterial systolic pressure; PH, pulmonary hypertension; PVR, pulmonary vascular resistance; Qp, pulmonary flow; Qs, systemic flow; R, right; SBP, systolic blood pressure; SVR, systemic vascular resistance.

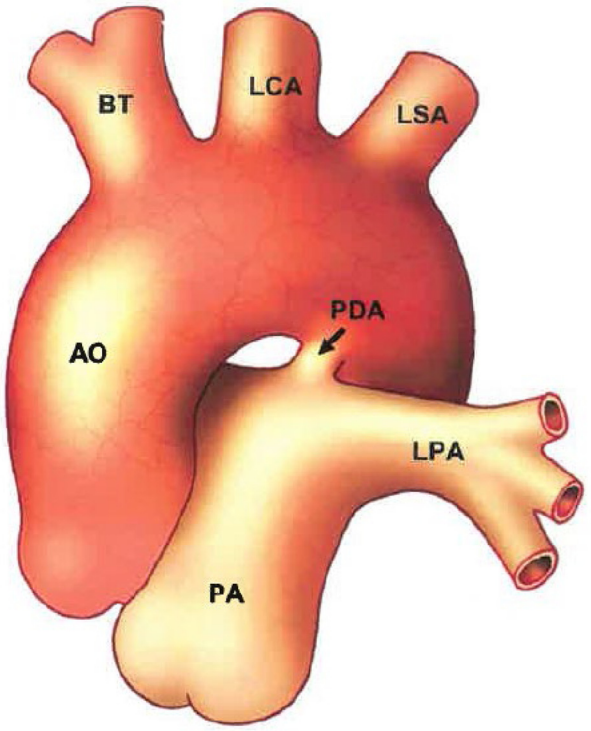


Figure 5. Patent ductus arteriosus (PDA). AO, aorta; BT, brachiocephalic trunk; LCA, left carotid artery; LPA, left branch of pulmonary artery; LSA, left subclavian artery; PA, pulmonary artery. Reproduced from Popelová et al.[239] with permission of the Licensor through PLSclear. © 2008 Informa UK Ltd.

group of patients. BAV might also be associated with syndromes such as Turners syndrome.

Clinical presentation

In the patient with BAV and an aortopathy, aortic dissection can present as chest pain and can mimic a myocardial infarction.[109] In approximately 10% of cases, aortic dissection is painless. Other presentations include neurologic deficits (hemiparesis, hemianaesthesia, Horner syndrome), syncope, or congestive HF in patients who develop severe AR. Measurements of the aorta are most accurate when assessed using contrast-enhanced computed tomography (CT) or cardiac magnetic resonance imaging (CMR).[110]

Recommendations for intervention

In patients with BAV aortopathy, medical management with β-blockers, angiotensin converting enzyme inhibitors, or statins has not been proven to be effective.[111-113] The optimal timing for surgical aortic replacement is controversial. An ascending aorta measuring 50 mm at its widest diameter had previously been cited to be an indication for surgery.[114] However, in more recent consensus statements, a maximum diameter of 55 mm has been suggested.[115,116] If high-risk features are present, such as family history of dissection or rapid annual growth (> 3-5 mm per year), then prophylactic replacement of the dilated aorta should be considered at 50 mm.[115,116] Additionally, a cross-sectional area/height ratio of $\geq$ 10 cm^2/m, measured using CMR or CT, has been associated with adverse outcomes.[117,118] In patients with Turner syndrome, prophylactic aorta replacement should be considered when the aorta measures > 2.5 cm/m^2.[119] Timing of aorta replacement in such cases should follow published guidelines.[114]

Management of BAV lesions should follow published valvular and CHD guidelines.[32,33,99,100,120,121] In patients with severe aortic stenosis or AR needing an aortic valve replacement (AVR), this should be considered when the aorta is > 45 mm.[122] Aortic valve-sparing surgery can be considered in patients undergoing aorta replacement, assuming the BAV has no more than moderate AR or moderate AS[123] (Table 5, Fig. 8).

Subaortic Stenosis and Supravalvular Aortic Stenosis

Background

Subaortic stenosis. Subaortic stenosis (SubAS) can take different forms, including a discrete, "membrane-like" or long "tunnel-like" obstruction.[109] If discrete, it is often an isolated lesion and can be treated surgically with a low recurrence rate. If "tunnel-like" it is often associated with other lesions of the left heart such as aortic coarctation, interrupted aortic arch, Shone complex (with multilevel left heart obstructive lesions),[109] or in the context of an AVSD. Management of tunnel-like SubAS often requires more complex surgery such

Table 3. Recommendations for intervention in adults with PDA

	Recommendations	GRADE Strength	GRADE Quality	References
1	We recommend closure of a PDA if LV enlargement is present and attributable to the PDA with net left-to-right shunt, PAP < 50% systemic and PVR < 1/3 systemic.	Strong	Low	80,83
2	We suggest that PDA closure may be considered in the presence of a net left-to-right shunt even if PAP is ≥ 50% systemic, and/or PVR is 1/3-2/3 systemic.	Weak	Moderate	81
3	We do not recommend PDA closure in patients with a net right-to-left shunt or PAP > 2/3 systemic or PVR > 2/3 systemic. Such patients should receive care from specialists with expertise in CHD and PAH.	Strong	Low	54
4	We suggest that closure of a small PDA is reasonable after an episode of endarteritis.	Weak	Low	82
6	We recommend device closure as the preferred method for treatment of an isolated PDA.	Strong	Moderate	84-86

CHD, congenital heart disease; GRADE, Grading of Recommendations Assessment, Development and Evaluation; LV, left ventricular; PAH, pulmonary arterial hypertension; PAP, pulmonary artery pressure; PVR, pulmonary vascular resistance; PDA, patent ductus arteriosus.

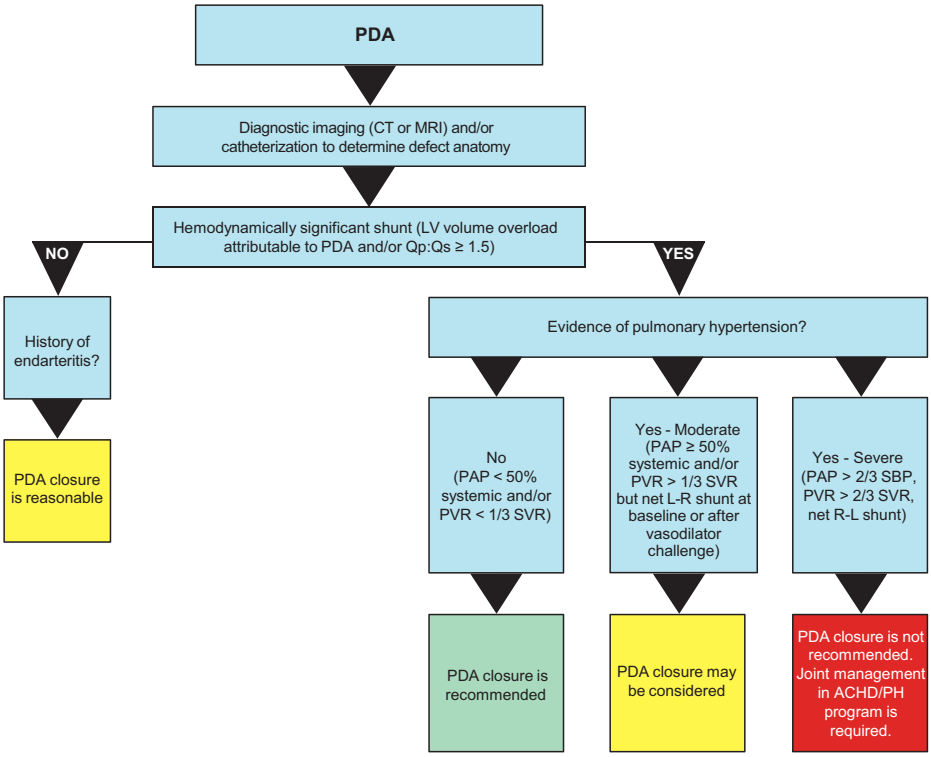


Figure 6. Patent ductus arteriosus (PDA) intervention pathway. ACHD, adults with congenital heart disease; CT, computed tomography; L, left; LV, left ventricle; MRI, magnetic resonance imaging; PAP, pulmonary artery pressure; PH, pulmonary hypertension; PVR, pulmonary vascular resistance; Qp, pulmonary flow; Qs, systemic flow; R, right; SBP, systolic blood pressure; SVR, systemic vascular resistance.

as the Konno (reconstruction of the LVOT) procedure and the recurrence rate is approximately 40%.[125] In both forms of SubAS, AR might develop from damage to the aortic valve resulting from turbulent flow in the LVOT.

Supravalvular aortic stenosis. Supravalvular aortic stenosis (SupraAS) is a rare form of LVOTO.[109] It can be discrete or diffuse (hourglass deformity) and is usually located at the level of the sinotubular junction, although it might involve the coronary ostia. Its occurrence has been associated with a mutation of the elastin gene that causes obstructive arteriopathy. SupraAS is often associated with Williams syndrome and PA stenosis.

Clinical presentation

SubAS. In patients with SubAS, symptoms are dependent on the severity of the obstruction and the associated valve lesions.[109] The symptoms associated with SubAS are similar to those of valvar aortic stenosis, including syncope, angina, and/or HF.

Table 4. Recommendations for intervention in adults with AVSDs

	Recommendations	GRADE Strength	GRADE Quality	References
1	We recommend surgery in patients with an AVSD for primary repair or for a residual left-to-right shunt (Qp:Qs ≥ 1.5), if the PAP is < 50% systemic, and/or PVR is < 1/3 systemic.	Strong	Low	25,87,89-91,93,108
2	We recommend that patients with AVSD and severe left-sided AV valve regurgitation undergo valve surgery as per valve guideline-directed recommendations for mitral valve regurgitation.	Strong	Low	96,98-104
3	We suggest that in patients with AVSD and discrete LVOT obstruction surgical repair is reasonable if the mean Doppler gradient is ≥ 40 mm Hg, if the LVOT obstruction is < 40 mm Hg and there are symptoms of heart failure or if there is concomitant moderate or severe left AV valve or aortic regurgitation.	Weak	Low	96,97,106,107
4	We suggest that surgery may be considered in patients with AVSD for primary repair or for a residual left-to-right shunt (Qp:Qs ≥ 1.5), if the PAP is ≥ 50% systemic, and/or the PVR is 1/3-2/3 systemic.	Weak	Low	54,55
5	We do not recommend surgical closure of an AVSD or a residual shunt if there is a net right-to-left shunt, the PAP is > 2/3 systemic, or the PVR is > 2/3 systemic.	Strong	Moderate	54,55

AV, atrioventricular; AVSD, atrioventricular septal defect; GRADE, Grading of Recommendations Assessment, Development and Evaluation; LVOT, left ventricular outflow tract; PAP, pulmonary artery pressure; PVR, pulmonary vascular resistance; Qp, pulmonary flow; Qs, systemic flow.

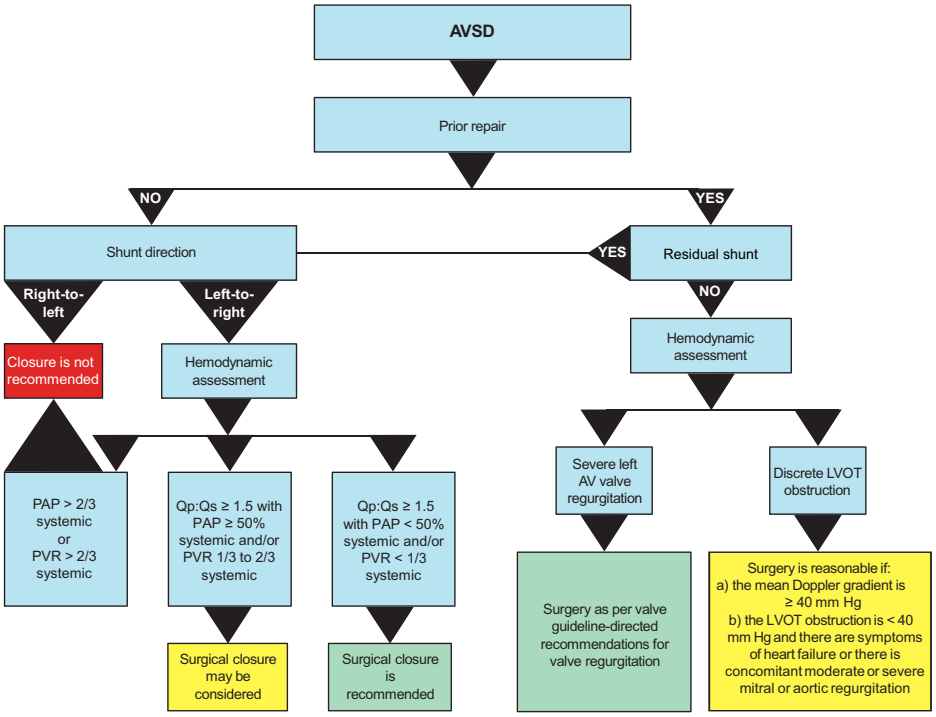


Figure 7. Atrioventricular septal defect intervention (AVSD) pathway. AV, atrioventricular; LVOT, left ventricular outflow tract; PAP, pulmonary artery pressure; PVR, pulmonary vascular resistance; Qp, pulmonary flow; Qs, systemic flow.

SupraAS. Progressive SupraAS might occur in adulthood. Those with severe outflow tract obstruction might present with syncope, angina, or HF.[109] SupraAS might be associated with significant ostial coronary stenosis, PA stenosis, and/or progressive AR, and symptoms correspond to the associated lesions. Williams syndrome is a nonfamilial variant of SupraAS characterized by distinctive facies and voice, short stature, developmental delay, friendly temperament, and other vascular anomalies including renal artery stenosis.

Recommendations for intervention

SubAS. In patients with SubAS, indications for surgical management depend on symptoms, degree of LVOTO, and/or the degree of AR.[32,33,120,126] Symptomatic patients with severe LVOTO (mean Doppler gradient $\geq$ 40 mm Hg) should undergo surgical relief of the obstruction. Symptomatic patients with moderate LVOTO should be considered for surgical relief if the symptoms are attributable to the outflow tract obstruction, or if there is severe AR or LV dysfunction.[32,33,120,121] Symptomatic patients with severe LVOTO (mean Doppler gradient $\geq$ 40 mm Hg) and moderate or severe AR might benefit from relief of LVOTO and AVR.[32,33,120,121] Surgical repair of SubAS carries a 10%-15% risk of complete heart block, and usually becomes apparent in the immediate postoperative period. Lifelong follow-up is recommended to monitor for the development of symptoms from progressive SubAS or recurrence of SubAS post resection (Table 6, Fig. 9).

Table 5. Recommendations for intervention in adults with bicuspid valve aortopathy

	Recommendations	GRADE Strength	GRADE Quality	References
1	We recommend that patients with BAV and stenotic or regurgitant valve lesions should have valve repair or replacement according to published valve guidelines.	Strong	Moderate	32,33,99,100,120,121
2	We recommend that patients with BAV and an ascending aorta diameter $\geq$ 55 mm (widest diameter) undergo surgical aorta replacement.	Strong	Moderate	115,116
3	We suggest that it is reasonable that patients with BAV and an ascending aorta $\geq$ 50 mm (widest diameter) with high-risk features (family history of dissection, rapid progression [> 3-5 mm per year], or maximum cross-sectional area/height ratio $\geq$ 10 cm^2/m), undergo surgical aorta replacement.	Weak	Moderate	114-116
4	We suggest that in patients with Turner syndrome, prophylactic aorta replacement is reasonable when the aorta measures > 2.5 cm/m^2.	Weak	Moderate	124
5	We suggest that in patients with severe aortic stenosis or regurgitation needing an aortic valve replacement, prophylactic aortic replacement is reasonable when the aorta is > 45 mm.	Weak	Moderate	122

BAV, bicuspid aortic valve; GRADE, Grading of Recommendations Assessment, Development and Evaluation.

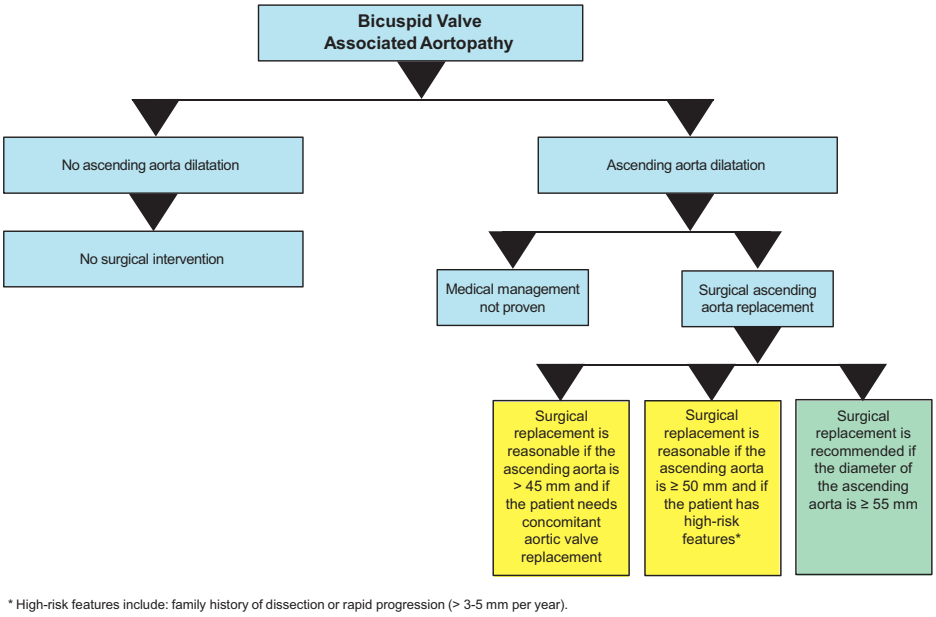


Figure 8. Bicuspid aortic valve aortopathy intervention pathway.

SupraAS. Indications for intervention in patients with SupraAS depend on the symptom status of the patient, the severity of obstruction, ventricular systolic function, involvement of the coronary ostia, and aortic or pulmonic valve involvement. Symptomatic patients with a mean Doppler gradient $\geq$ 40 mm Hg should undergo surgical relief of the obstruction. Asymptomatic patients with a mean Doppler gradient on echocardiography $\geq$ 40 mm Hg might benefit from surgical relief of the obstruction, especially if the surgical risk is low. Patients with a mean Doppler gradient $<$ 40 mm Hg and symptoms or LV dysfunction attributable to the obstruction should undergo surgery.[32,33,120,121] Patients with significant concomitant coronary ostial stenosis (left main stenosis $\geq$ 50% or proximal right coronary stenosis $\geq$ 70%) should undergo coronary bypass surgery at the time of surgical relief of SupraAS. Coronary ostioplasty has also been successful and should be considered in younger adults. In patients with progressive AR, especially if more than moderate, concomitant AVR might be required at the time of surgical relief of SupraAS. At the time of surgery for SupraAS, aortic valve intervention may be considered as indicated.

Various surgical techniques exist to repair SupraAS. A 1-patch technique (the McGoon elliptical patch or the Doty pantaloons-shaped technique) or a 3-patch technique (Brom technique) can be used. The choice depends on the underlying anatomy.[127-129] Percutaneous catheter-based interventions are not appropriate for the treatment of SupraAS. Reoperation for re-stenosis, AR, or PA restenosis is required in approximately 25% of patients over a 25-year follow-up.[127-129] These patients need lifelong surveillance (Table 7, Fig. 10).

Coarctation of the Aorta

Background

Coarctation of the aorta (CoA) is defined as a narrowing of the aorta usually at the level of the ductus arteriosus.[130] It can be discrete just distal to the left subclavian artery or more

Table 6. Recommendations for intervention in adults with subaortic stenosis

	Recommendations	GRADE		References
		Strength	Quality	
1	We recommend that patients with symptomatic severe LVOTO (mean Doppler gradient $\geq$ 40 mm Hg) should undergo surgical intervention.	Strong	Moderate	32,33,120,121
2	We suggest that in symptomatic patients with moderate LVOTO (mean Doppler gradient of 20-40 mm Hg) and moderate or greater AR surgical intervention including relief of LVOTO and aortic valve intervention is reasonable.	Weak	Low	32,33,120,121
3	We suggest that in asymptomatic patients with severe LVOTO (mean Doppler gradient $\geq$ 40 mm Hg) and 1 or more of: a) Moderate or severe AR b) Decrease in BP in response to exercise c) LVH or LV dysfunction surgical intervention consisting of relief of LVOTO with or without aortic valve intervention is reasonable.	Weak	Low	32,33,120,121

AR, aortic regurgitation; BP, blood pressure; GRADE, Grading of Recommendations Assessment, Development and Evaluation; LV, left ventricular; LVH, left ventricular hypertrophy; LVOTO, left ventricular outflow tract obstruction.

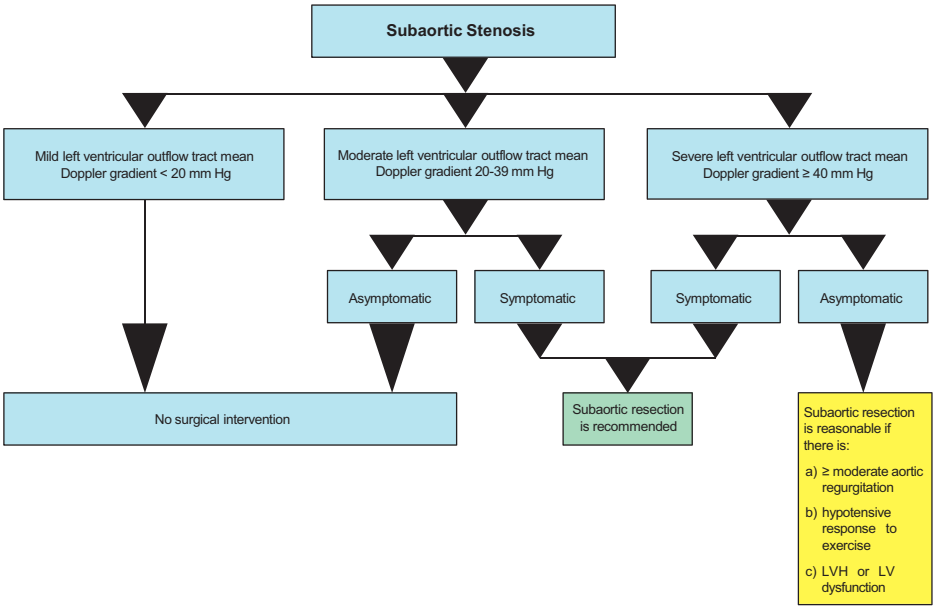


Figure 9. Subaortic stenosis intervention pathway. LV, left ventricular; LVH, left ventriular hypertrophy.

diffuse encompassing the aortic arch and isthmus. CoA can be associated with BAV, Shone complex (multiple levels of left-sided obstruction such as BAV, SubAS, mitral valve stenosis due to parachute mitral valve, and supravalve mitral stenosis), VSD, PDA, and intracranial aneurysm (Fig. 11).

Clinical presentation

The spectrum of clinical presentation is variable.[130] At one extreme is severe coarctation characterized by marked anatomical narrowing, presence of collateral arteries, high gradient, and upper body hypertension; at the other extreme is mild coarctation, characterized by mild aortic hypoplasia, absence of collaterals, little or no gradient, and no hypertension. In a patient with hemodynamically significant CoA, presentation in adolescence or adulthood might be with upper body hypertension, differential systolic arm-leg blood pressure (highest arm blood pressure exceeds leg blood pressure by $\geq$ 20 mm Hg), faint femoral pulses, murmur, leg fatigue on exertion, dyspnea, or angina. Rarely, patients present with intracerebral hemorrhage.

In the absence of extensive collateral circulation, a significant CoA can be defined as the presence of upper limb hypertension with an associated significant gradient at catheterization (simultaneous peak to peak gradient $\geq$ 20 mm Hg). Catheterization hemodynamics might be inaccurate if performed with a patient under sedation or taking multiple antihypertensive medications. A significant CoA can also be defined on CMR as $>$ 50% lumen narrowing of the CoA segment compared with the aortic diameter at the diaphragm.[131] Although echocardiographic Doppler assessment of coarctation is often used as a screening tool, it is subject to error and significant CoA must be established using catheterization and/or alternative cardiac imaging such as CMR.

If significant CoA is left untreated, patients might die prematurely from HF, aortic rupture/dissection, endocarditis, cerebral hemorrhage, coronary artery disease, or concomitant aortic valve failure (in the context of BAV).

Long-term complications after interventions might include systemic hypertension or premature coronary artery disease despite adequate relief of the obstruction. Re-CoA occurs in 10%-20% of patients. Possible additional long-term complications include true aneurysm formation at the site of the intervention (especially after patch repair or subclavian flap technique). Regular follow-up with CMR (possibly every 5 years) should be considered for these patients. Aneurysm or

Table 7. Recommendations for intervention in adults with SupraAS

	Recommendations	GRADE		References
		Strength	Quality	
1	We recommend that symptomatic patients with a mean Doppler gradient $\geq$ 40 mm Hg should undergo surgical relief of the obstruction.	Strong	Moderate	32,33,120,121
2	We suggest that asymptomatic patients with a mean Doppler gradient $\geq$ 40 mm Hg may be considered for surgical relief of the obstruction, especially if the surgical risk is low.	Weak	Low	32,33,120,121
3	We recommend that patients with a mean Doppler gradient $<$ 40 mm Hg and symptoms or LV dysfunction attributable to the obstruction, undergo surgical relief of the obstruction.	Strong	Moderate	32,33,120,121
4	We recommend that at the time of surgical relief of SupraAS, patients with significant ostial coronary stenosis undergo surgical ostioplasty or coronary artery bypass surgery.	Strong	High	32,33,120,121

GRADE, Grading of Recommendations Assessment, Development and Evaluation; LV, left ventricular; SupraAS, supravalvular aortic stenosis.

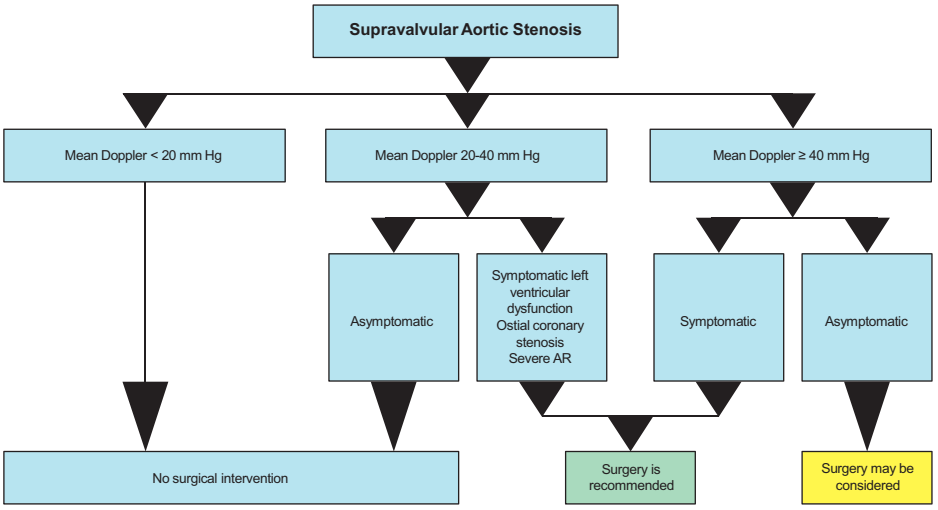


Figure 10. Supravalvular aortic stenosis intervention pathway. AR, aortic regurgitation.

pseudoaneurysm can develop at the site of previous surgical repair or transcatheter intervention.

Recommendations for intervention

A patient with CoA should have an intervention if there is concomitant systemic hypertension attributable to the CoA at rest or with exercise. In patients with CoA and significant LV dysfunction or collaterals, the peak to peak gradient at catheterization might underestimate the severity of CoA and one should place more weight on CMR imaging. In normotensive patients with a significant CoA confirmed using cardiac catheterization, intervention may be considered when technically feasible.

When an intervention is considered, detailed imaging of the coarctation site using CT or CMR is recommended. For a discrete CoA, a transcatheter stent is usually performed.[32,33,120,121,132,133] Balloon dilation solely without a stent is not preferred because of its potential for intimal tear and long-term risks of aneurysm formation. The type of stent used will depend on the operator's preference and technical specifications.[134] If the CoA site is long and tubular or if there is concomitant diffuse arch hypoplasia, a surgical approach is usually favoured because of concerns about perfusion and injury to spinal arteries. Surgical repair can be done by end-to-end anastomosis (most frequent), graft interposition, Dacron patch repair, subclavian flap repair or, rarely, ascending aorta to descending aorta bypass with a conduit. The type of surgery needs to be tailored to the patient's underlying anatomy.[135]

When the patient needs a concomitant AVR, a staged procedure can be performed,[135] namely a stent to address the coarctation if the anatomy is suitable followed by a surgical AVR at a later date. In the context of diffuse hypoplasia of the aortic arch and coarctation, a combined surgical approach for the coarctation and the AVR is preferred.

Guidelines for intervention for recurrent coarctation are the same as for native coarctation. Pseudoaneurysm formation might require surgical or transcatheter intervention with a covered stent. A patient with an aneurysm at the site of a coarctation repair requires multidisciplinary review by an ACHD specialist and congenital heart surgeon, and, if an immediate intervention is not provided, careful ongoing ACHD follow-up (Table 8, Fig. 12).

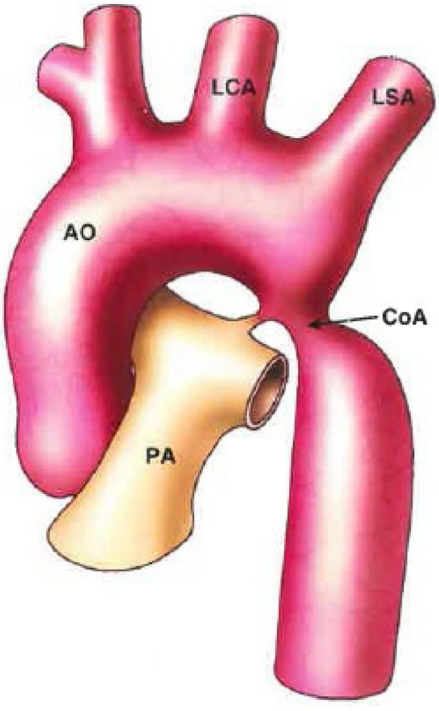


Figure 11. Coarctation of the aorta (CoA). AO, aorta; LCA, left carotid artery; LSA, left subclavian artery; PA, pulmonary artery. Reproduced from Popelová et al.[239] with permission of the Licensor through PLSclear. © 2008 Informa UK Ltd.

Table 8. Recommendations for intervention in adults with coarctation of the aorta

	Recommendations	GRADE Strength	GRADE Quality	References
1	We recommend that patients with significant native or recurrent coarctation of the aorta (simultaneous peak to peak gradient at catheterization ≥ 20 mm Hg* or > 50% narrowing of the aorta compared with the diaphragmatic aorta on magnetic resonance images) should have an intervention if there is concomitant systemic hypertension.	Strong	Moderate	32,33,120,121,132,133
2	We recommend that if native or recurrent coarctation is significant and discrete, repair with a transcatheter stent should be performed when technically feasible.	Strong	Moderate	32,33,120,121,132,133
3	We recommend that if the coarctation site is long and tubular or if there is concomitant diffuse arch hypoplasia, a surgical approach be favoured.	Strong	Moderate	134

GRADE, Grading of Recommendations Assessment, Development and Evaluation.

*Some patients with significant left ventricular dysfunction or with collaterals might not have a significant peak to peak gradient at the time of catheterization and still require intervention.

Right Ventricular Outflow Tract Obstruction and Tetralogy of Fallot

Valvular pulmonary stenosis, supravalvar pulmonary stenosis, double-chambered right ventricle

Background. Right ventricular outflow tract obstruction (RVOTO) can occur at subinfundibular, infundibular, valvular, or supravalvular levels.[136] Valvular pulmonary stenosis is the most common form of RVOTO, and is typically congenital in origin. Pulmonary valve (PV) stenosis often occurs in isolation. In contrast, supravalvular RVOTO might involve narrowing of the main PA, PA bifurcation, and/or PA branches and seldom occurs in isolation. Supravalvar RVOTO might occur in the context of tetralogy of Fallot (TOF), Williams syndrome, Noonan syndrome, Alagille syndrome, and congenital rubella syndrome. Subinfundibular RVOTO arises as a result of muscular hypertrophy and can result in a double-chamber right ventricle, where excessive hypertrophy of septal, parietal, and moderator bands result in a high-pressure inlet chamber and a low-pressure outlet chamber. The archetypal infundibular RVOTO lesion is TOF (discussed below).

Severity of RVOTO can be classified according to peak Doppler gradients as follows: mild < 36 mm Hg (< 3 m/s), moderate 36-64 mm Hg (3-4 m/s), and severe > 64 mm Hg (> 4 m/s). The echocardiographic assessment of RVOTO will usually incorporate an estimation of RV systolic pressure by tricuspid regurgitation (TR) velocity. When the RV pressure is greater than two-thirds of the systemic pressure it is considered significant. Importantly, Doppler measurements across the narrowed segment might be unreliable in some settings, such as a long segment of narrowing or multilevel obstruction.

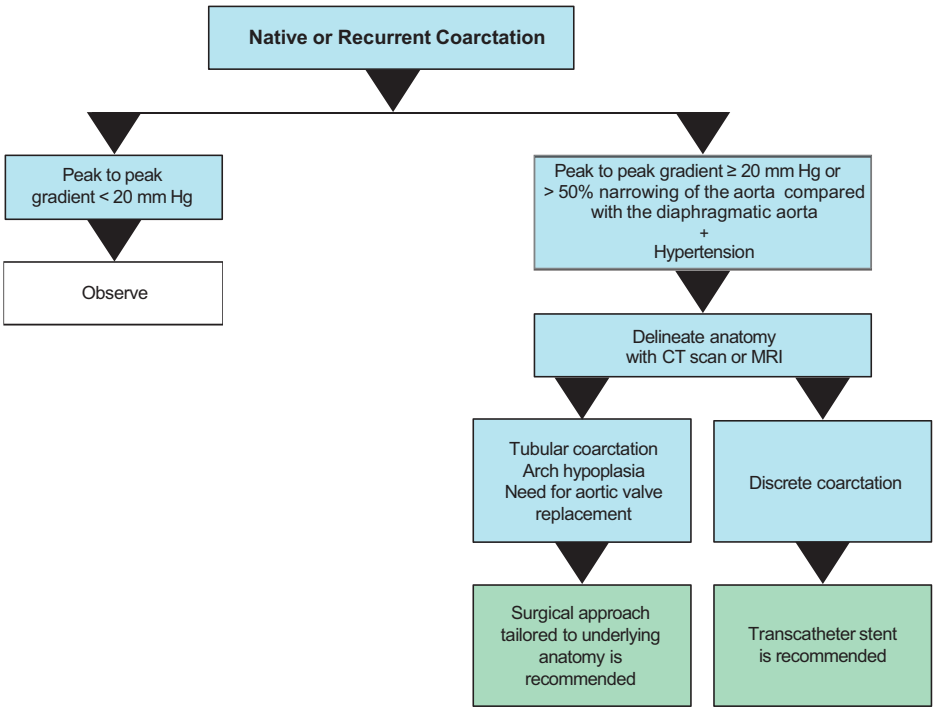


Figure 12. Coarctation of the aorta intervention pathway. CT, computed tomography; MRI, magnetic resonance imaging.

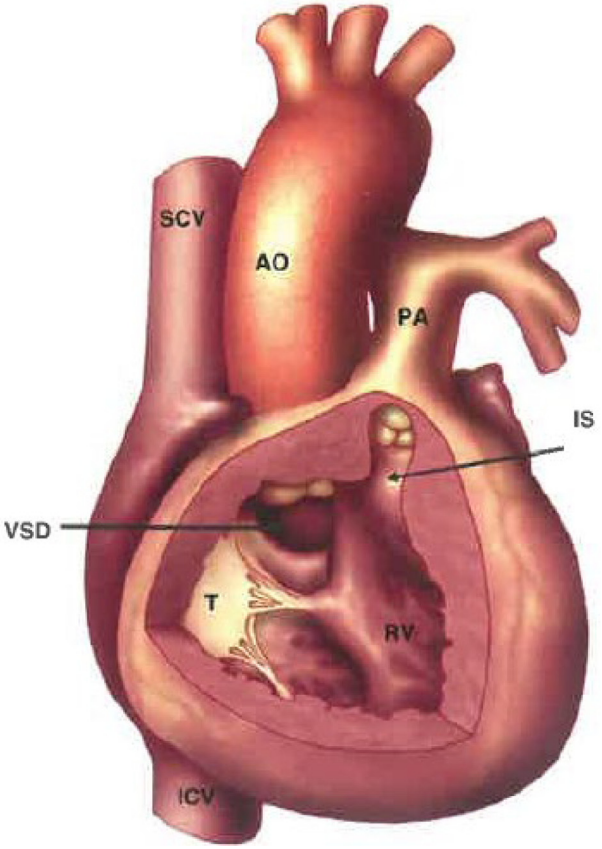


Figure 13. Tetralogy of Fallot. AO, aorta; ICV, inferior caval vein; IS, infundibular septum; PA, pulmonary artery; RV, right ventricle; SCV, superior caval vein; T, tricuspid value; VSD, ventricular septal defect. Reproduced from Popelová et al.[239] with permission of the Licensor through PLSclear. © 2008 Informa UK Ltd.

Clinical presentation. Patients with mild pulmonary stenosis or RVOTO will have a reassuring natural history and are unlikely to require intervention.[136] Those with severe stenosis will often have intervention in childhood and those with moderate obstruction have a more variable clinical course. Undiagnosed RVOTO in the adult might manifest as right-sided HF or tachyarrhythmia.

Recommendations for intervention. Percutaneous intervention is first-line therapy for valvular pulmonary stenosis. Specifically, balloon valvuloplasty is recommended for symptomatic patients with moderate or severe PV stenosis and may be considered for asymptomatic patients with severe PV stenosis. Surgical intervention is generally recommended in the context of significant obstruction at the supravalvular or subinfundibular levels, marked PV dysplasia/annular hypoplasia, or more than moderate pulmonary regurgitation (PR). PR might occur as a sequela of intervention for pulmonary stenosis. Surgical PV replacement or transcatheter PV replacement is recommended in the presence of cardiovascular symptoms/signs and may be considered with accompanying RV enlargement/dysfunction and/or decline in exercise capacity.[137]

Tetralogy of Fallot

Background. TOF is the most common cyanotic congenital heart defect.[138] Four characteristic features of TOF derive from the fundamental anatomic anomaly of anterior and superior deviation of the infundibular septum: malalignment of the VSD; RVOTO at the infundibular and often also valvular and supravalvular levels; dextroposition of the aorta; and RV hypertrophy (secondary to the RV hypertension, particularly if repair is delayed). Adult survival has steadily improved, reflecting evolution of surgical repair strategies. Primary repair now tends to be performed in the first year of life. Unrepaired TOF in the adult is uncommonly discovered but is generally amenable to surgical repair in the absence of irreversible pulmonary vascular disease (Fig. 13).

Clinical presentation. Residual and sequelae after TOF repair include PR, pulmonary stenosis, TR, RV dilation or dysfunction, LV dysfunction, aortic dilation and/or AR and arrhythmias. Adults might present with progressive exercise intolerance, right- or left-sided HF, tachyarrhythmias, and/or sudden death. Chronic PR is a very common finding in the adult after successful repair in early childhood, and typically results in a cascade of RV dilation, ventricular dysfunction, and exercise intolerance.[138] Assessment of PR severity and RV size/function can be difficult using echocardiography alone and therefore is best achieved using CMR imaging, which is considered the reference standard for right heart measurements. Although PV replacement for chronic PR is the most common reason for intervention in the adult population after TOF repair, some patients might require interventions (surgical or catheter-based) for valvar or peripheral PA stenosis, tricuspid valve surgery, or electrophysiology procedures.

Table 9. Recommendations for intervention in adults with right ventricular outflow tract obstruction

	Recommendations	GRADE Strength	GRADE Quality	References
1	We recommend that adults with symptomatic moderate or severe PV stenosis be referred for percutaneous balloon valvuloplasty. We recommend surgical valvotomy in those in whom percutaneous intervention has failed or are not eligible for percutaneous intervention.	Strong	Moderate	137,150,151
2	We suggest that in asymptomatic adults with severe PV stenosis, percutaneous or surgical intervention is reasonable in the presence of RV dysfunction.	Weak	Low	150,151
3	We recommend that symptomatic adults with severe PR and RV dilation with or without dysfunction resulting from intervention for isolated pulmonary stenosis be referred for PV replacement, which may be surgical or transcatheter.	Strong	Very Low	137

GRADE, Grading of Recommendations Assessment, Development and Evaluation; PR, pulmonary regurgitation; PV, pulmonary valve; RV, right ventricular.

Table 10. Recommendations for intervention in adults with tetralogy of Fallot

	Recommendations	GRADE Strength	GRADE Quality	References
1	We recommend PV replacement in patients with rTOF and severe PR* and cardiovascular symptoms not otherwise explained.	Strong	Moderate	146,147,152
2	We suggest that PV replacement is reasonable in asymptomatic patients with rTOF and severe PR and RV enlargement† with or without RV systolic dysfunction, significant RVOTO,‡ or a decrease in objective exercise capacity.	Weak	Moderate	142-145,147
3	We suggest that PV replacement is reasonable for adults with severe PR who require intervention for other lesions of hemodynamic significance.	Weak	Low	141
4	We suggest that PV replacement is reasonable in addition to arrhythmia management in patients with severe PR and sustained ventricular tachyarrhythmia.	Weak	Low	140

CMR, cardiac magnetic resonance imaging; GRADE, Grading of Recommendations Assessment, Development and Evaluation; PR, pulmonary regurgitation; PV, pulmonary valve; rTOF, repaired tetralogy of Fallot; RV, right ventricular; RVEDVi, right ventricular end-diastolic volume indexed; RVESVi, right ventricular end-systolic volume indexed; RVOTO, right ventricular outflow tract obstruction.

*Defined as severe PR on echocardiography or a regurgitation fraction > 25% on CMR.

†RVEDVi ≥ 160 mL/m^2 or RVESVi ≥ 80 mL/m^2 on CMR.

‡Significant RVOTO is defined as an RV systolic pressure > 2/3 of systemic pressure.

Recommendations for intervention. Surgical PV replacement to address residual PR is the most common procedure in the adult population with repaired TOF (rTOF). PV intervention is recommended in a patient with significant PR (defined as severe PR on echocardiography or a regurgitation fraction > 25% on CMR imaging) and attributable symptoms. In the asymptomatic patient with significant PR, PV replacement may be considered in the presence of an enlarged right ventricle (right ventricular end-diastolic volume indexed ≥ 160 mL/m^2 or right ventricular end-systolic volume indexed ≥ 80 mL/m^2 on CMR imaging), RV dysfunction (particularly if interval deterioration is shown on serial testing), significant RVOTO, or a decrease in objectively assessed exercise capacity.

LV dysfunction might occur as a result of ventricular-ventricular interactions in association with significant RV dilation and might be ameliorated after PV replacement.[139] PV replacement can be considered in addition to arrhythmia management in adults with greater than moderate PR and sustained

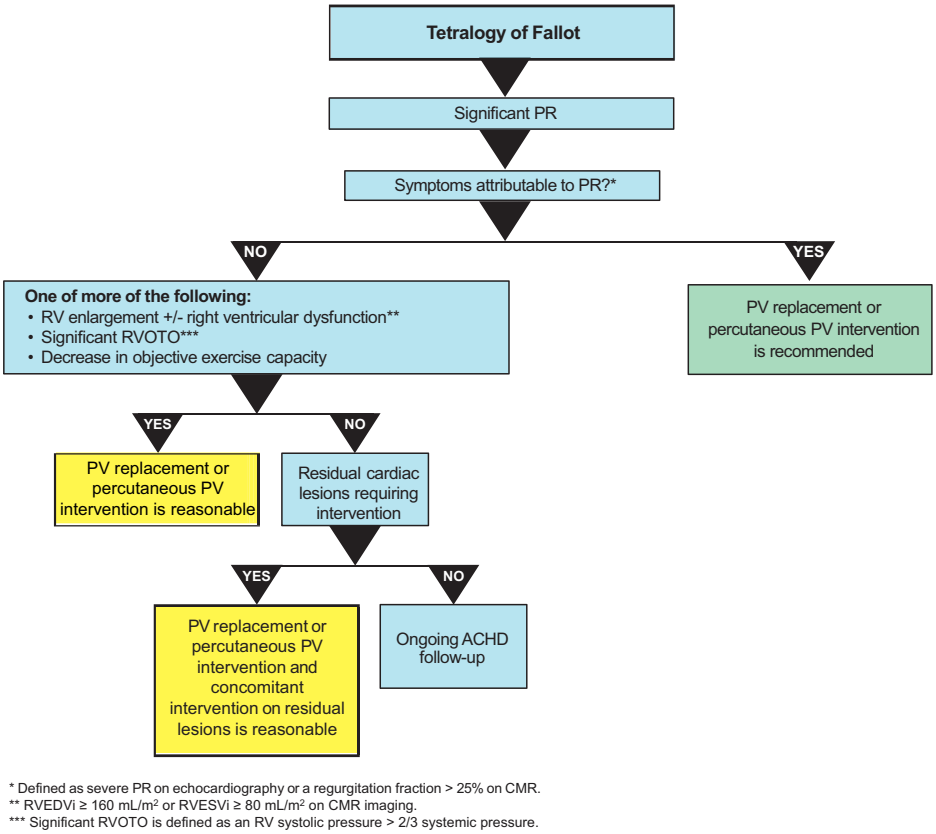


Figure 14. Tetralogy of Fallot intervention pathway. ACHD, adults with congenital heart disease; CMR, cardiac magnetic resonance; PR, pulmonary regurgitation; PV; pulmonary valve; RV, right ventricular; RVEDVi, right ventricular end-diastolic volume indexed; RVESVi, right ventricular end-systolic volume indexed; RVOTO, right ventricular outflow tract obstruction.

Table 11. Recommendations for intervention in adults with Ebstein anomaly

	Recommendations	GRADE Strength	GRADE Quality	References
1	We recommend tricuspid valve surgery (repair or replacement) in the symptomatic adult (NYHA class $\geq$ 2) with Ebstein anomaly and severe tricuspid regurgitation.	Strong	Moderate	159,160
2	We suggest tricuspid valve surgery (repair or replacement) is reasonable in the asymptomatic adult with Ebstein anomaly and severe tricuspid regurgitation in the presence of progressive RV dilation and/or progressive RV systolic dysfunction on CMR, objective evidence of declining exercise capacity, desaturation (< 90%) due to right-to-left shunting, paradoxical embolism, or refractory atrial arrhythmias.	Weak	Moderate	165-167
3	We suggest a bidirectional cavopulmonary anastomosis may be considered at the time of tricuspid valve surgery in the presence of severe RV dilation and/or moderate to severe RV systolic dysfunction.	Weak	Moderate	159,163,164
4	We suggest that in the presence of cyanosis (SO_2 < 90%) or paradoxical emboli device closure of an interatrial shunt may be considered after very careful hemodynamic evaluation.	Weak	Low	159,163,164
5	We do not recommend closure of an ASD or PFO if unfavourable hemodynamics are noted during test occlusion (increase in filling pressures and/or decrease in cardiac output).	Strong	Moderate	158,165,166

ASD, atrial septal defect; CMR, cardiac magnetic resonance imaging; GRADE, Grading of Recommendations Assessment, Development and Evaluation; NYHA, New York Heart Association; PFO, patent foramen ovale; RV, right ventricular; SO_2, oxygen saturation.

ventricular tachyarrhythmia[140] or in those who require intervention for other lesions of hemodynamic significance.[141] Referral for PV intervention on the basis of RV volumes is predicated on the observation that normalization of RV size is unlikely to occur if right ventricular end-diastolic volume indexed is > 160 mL/m^2 or right ventricular end-systolic volume indexed is > 80 mL/m^2 on CMR imaging before PV replacement. However, the longer-term implications of complete vs incomplete remodelling on quality of life and long-term survival are ill-defined.[142-146] There are no randomized trials that have compared the effect of PV replacement on mortality in patients with severe PR who received PV replacement compared with those who did not receive PV replacement. A meta-analysis of 10 cohort studies comprising 657 patients showed that PV replacement in patients with rTOF and severe PR was associated with improvement in functional status and RV volume but had no effect on mortality.[147] Concomitant tricuspid valve repair/replacement and residual VSD closure might be required in some cases.

Thresholds for intervention are likely to continue to evolve as novel percutaneous strategies emerge with broader applicability within the surgically modified right ventricular outflow tract (RVOT) and with development of new CMR techniques for evaluation of myocardial function.[148,149]

In patients with PR after valvuloplasty for isolated PV stenosis evidence is lacking to support PV intervention. The clinician should be cautious about directly extrapolating from the rTOF literature to isolated PR because the risk-benefit profile is likely to be different (Tables 9 and 10, Fig. 14).

Ebstein Anomaly

Background

Ebstein anomaly is a syndrome including a dysplastic tricuspid valve, myopathy of the right and LV myocardium, and abnormalities of the conduction system that have a wide

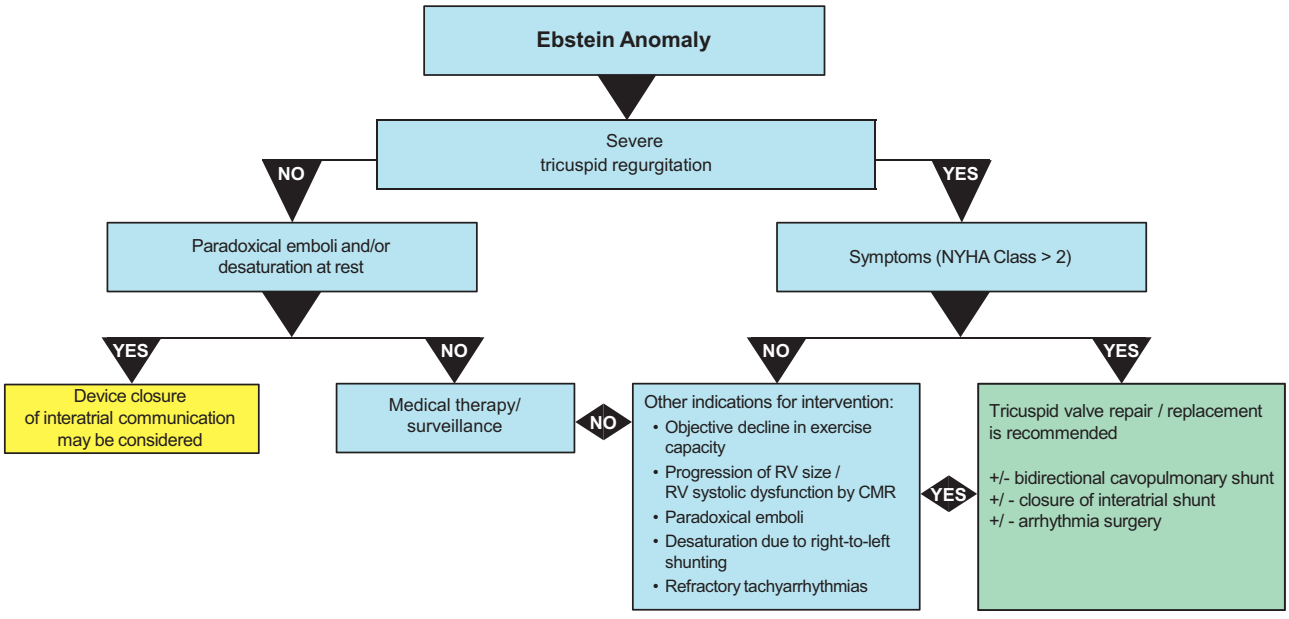


Figure 15. Ebstein anomaly intervention pathway. CMR, cardiac magnetic resonance; NYHA, New York Heart Association; RV, right ventricular.

Table 12. Recommendations for intervention in adults with complete transposition of the great arteries and atrial or arterial switch operations

	Recommendations	GRADE Strength	GRADE Quality	References
Atrial switch operation				
1	We suggest that in symptomatic patients with severe systemic TR and adequate ventricular function (RVEF ≥ 45%), surgical replacement of the tricuspid valve is reasonable.	Weak	Low	177
2	We recommend that patients with symptoms from stenosis or obstruction of the pulmonary venous baffle undergo surgical repair or percutaneous intervention.	Strong	Low	178
3	We recommend that patients with symptoms from stenosis or obstruction of the systemic venous baffle undergo surgical repair or percutaneous intervention.	Strong	Low	178,179
4	We suggest that in asymptomatic patients with stenosis of the systemic venous baffle who require implantation of transvenous pacemaker/defibrillator leads, it is reasonable to undergo percutaneous correction of the stenosis before lead implantation.	Weak	Low	178,179
5	We recommend that patients with symptoms from interatrial baffle leaks undergo percutaneous intervention.	Strong	Low	179
6	We suggest that in asymptomatic patients with interatrial baffle leaks that result in a significant left to right shunt (Qp:Qs ≥ 1.5), percutaneous closure is reasonable.	Weak	Very low	177,178
7	We suggest that in asymptomatic patients with interatrial baffle leaks who require implantation of a transvenous pacemaker/defibrillator lead, percutaneous closure to prevent paradoxical embolism is reasonable.	Weak	Low	179
8	We recommend that patients with symptoms secondary to severe systemic right ventricular dysfunction who are refractory to medical and interventional therapy be referred to a heart transplant team with expertise in ACHD transplantation.	Strong	Very low	181
Arterial switch operation				
9	We recommend that patients with coronary obstruction causing symptoms or a significant burden of ischemia undergo revascularization.	Strong	Very low	
10	We recommend that patients with symptoms due to right ventricular outflow tract obstruction undergo intervention.	Strong	Very low	
11	We suggest that in asymptomatic patients with severe right ventricular outflow tract obstruction (peak Doppler gradient > 64 mm Hg, peak velocity > 4 m/s or RVSP ≥ 2/3 of systemic blood pressure) and those with RVOTO and worsening right ventricular function (where gradients might be lower because of impaired RV contractility), intervention is reasonable.	Weak	Very low	
12	We recommend aortic valve repair or replacement for patients with severe aortic regurgitation and symptoms or left ventricular dysfunction (LVEF < 50%).	Strong	Very low	198
13	We suggest that in asymptomatic patients with severe aortic regurgitation with significant left ventricular dilation (LVESD > 50 mm or LVEDD > 65 mm), aortic valve repair or replacement is reasonable.	Weak	Very low	198
14	We suggest that in patients who have aortic root or ascending aortic dilation ≥ 55 mm, repair of the aorta is reasonable.	Weak	Very low	199
15	We suggest that in patients with an aortic diameter ≥ 45 mm, it is reasonable to undergo concomitant aortic root replacement at the time of aortic valve surgery.	Weak	Very low	32,199

ACHD, adults with congenital heart disease; GRADE, Grading of Recommendations Assessment, Development and Evaluation; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; Qp, pulmonary flow; Qs, systemic flow; RV, right ventricular; RVEF, right ventricular ejection fraction; RVOTO, right ventricular outflow tract obstruction; RVSP, right ventricular systolic pressure; TR, tricuspid regurgitation.

variation in severity.[153] The key anatomic feature is incomplete delamination and rotational displacement of the dysplastic septal with or without posterior tricuspid valve leaflets toward the apex (apical displacement of the septal leaflet > 8 mm/m^2) and elongation of the anterior leaflet. This typically results in a varying degree of TR.[154,155] As a consequence of the apical displacement of the tricuspid valve, part of the right ventricle is "atrialized," yielding 3 components of the right heart: the morphologic right atrium, the atrialized portion of the right ventricle, and the functional right ventricle. An interatrial communication (patent foramen ovale [PFO] or secundum ASD) is commonly associated. Multiple accessory pathways are also common. LV noncompaction might be found.[156,157] The RV response to volume load is specific to Ebstein anomaly and therefore RV volume thresholds recommended for intervention in other right heart volume overload conditions such as TOF are not applicable. CMR is the imaging modality of choice for evaluation of chamber dimensions, volumes, and ventricular systolic function.

Clinical presentation

The broad spectrum of manifestations of Ebstein anomaly is determined by severity of tricuspid valve disease, associated congenital heart defects, presence of accessory pathways, and the inherent cardiomyopathy.[153] Ebstein anomaly in its milder form might be diagnosed incidentally in an asymptomatic adult. A supraventricular tachycardia mediated by an accessory pathway can be the reason for first presentation. Adults with moderate and severe forms of Ebstein anomaly and severe TR present with fatigue, reduced exercise tolerance, dyspnea on exertion, cyanosis due to right-to-left shunting across an interatrial defect, tachyarrhythmias, and/or HF. Severe dilation of the true right atrium and atrialized portion of the right ventricle predispose to refractory tachyarrhythmias. Progressive oxygen desaturation and atrial arrhythmias are ominous findings that might reflect hemodynamic worsening due to progressive TR, ventricular dysfunction and associated increased right-to-left shunt across a secundum ASD, or a stretched PFO. Most adults with Ebstein anomaly

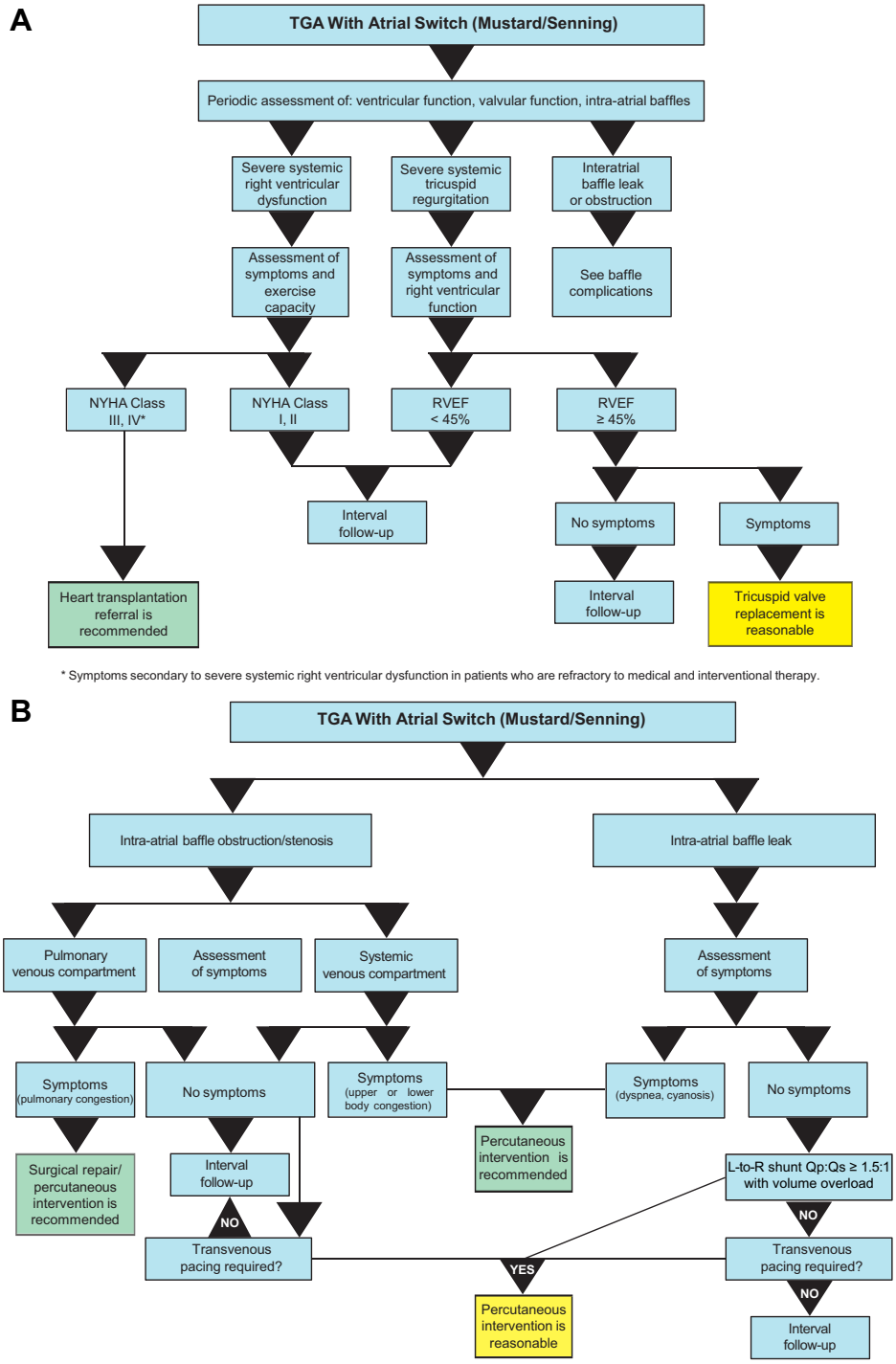


Figure 16. (**A**) Atrial switch operation for complete transposition of the great arteries (TGA) intervention pathway. (**B**) Atrial switch operation for complete TGA intervention pathway: baffle obstruction and baffle leak. L, left; NYHA, New York Heart Association; Qp, pulmonary flow; Qs, systemic flow; R, right; RVEF, right ventricular ejection fraction.

will not have undergone surgical repair or replacement of the tricuspid valve during pediatric care.

Recommendations for intervention

The wide anatomic and clinical spectrum of Ebstein anomaly poses unique challenges when offering guidelines for intervention. Attributable cardiovascular symptoms are usually an indication for intervention. Timing of tricuspid valve surgery is a challenge because the surgical risk is relatively high compared with that in other congenital heart operations. However, perioperative survival and long-term results are usually favourable in large-volume centres with expertise. When systolic function of the functional right ventricle is

moderately to severely reduced, and/or LV systolic dysfunction develops, surgical risks escalate considerably.[158-160] Surgery is generally very complex, but benefits can outweigh risks even in older patients if surgery is performed in experienced centres.[161] Cone repair of the tricuspid valve is preferable, might result in favourable ventricular remodelling, but the operation has a steep learning curve.[162] Closure of an interatrial communication (PFO/ASD) at the time of tricuspid valve surgery requires careful consideration because shunt closure might have a negative effect on the maintenance of cardiac output. Surgical reduction of the size of the atrialized portion of the right ventricle and right atrium, and arrhythmia surgery are frequent concomitant procedures. In a patient with an accessory pathway a preoperative electrophysiology study with ablation is recommended. Creation of a bidirectional cavopulmonary anastomosis is a decision usually made intraoperatively to reduce the load on a myopathic right ventricle, which might fail when faced with increased afterload expected when tricuspid valve competence is achieved.[159,163,164] Device closure of an interatrial communication as an isolated procedure may be considered to address paradoxical embolic events in the absence of indications for additional procedures (eg, severe TR), but requires careful hemodynamic evaluation, because shunt closure might decrease cardiac output. Long-term oral anticoagulation is available as alternative therapy. Percutaneous ASD closure can be offered to carefully selected patients with resting cyanosis or exercise desaturation with the goal of symptomatic improvement after careful hemodynamic evaluation and consideration of the risk of low cardiac output after elimination of the right-to-left shunt[159,163,164] (Table 11, Fig. 15).

Complete Transposition of the Great Arteries

Background

In patients with complete transposition of the great arteries (TGA) there is AV concordance and ventriculoarterial discordance (ie, the right atrium connects to the morphological right ventricle, which gives rise to the aorta, and the left atrium connects to the morphological left ventricle, which gives rise to the PA).[168] In the anatomic designation of TGA, when the aorta is anterior and to the right (or dextro, "d") of the PA, it is referred to as d-TGA. Approximately two-thirds of patients have no associated anomaly ("simple d-TGA") whereas one-third have associated anomalies ("complex d-TGA") especially VSD, LVOTO, and coarctation. In the physiologic designation of TGA, d-TGA is also referred to as "complete TGA" to contrast it with congenitally corrected TGA (ccTGA). The morphologic tricuspid valve is a systemic AV valve (SAVV).

Clinical presentation

Three types of adult survivors with d-TGA might be seen. Those who originally underwent surgical repair had an atrial switch procedure to redirect blood at the atrial level, in the form of a Senning (using atrial flaps) or Mustard operation (with a baffle composed of Dacron or pericardium) to achieve physiological correction.[169] After an atrial switch procedure, the right ventricle is the systemic ventricle. As of 1985, atrial switch procedures were being replaced by the arterial switch operation whereby blood is redirected at the great artery level by switching the aorta and PA and reimplanting the coronary arteries. After an arterial switch operation, the left ventricle is the systemic ventricle. A small proportion of patients with a VSD and LVOTO have been repaired with a Rastelli operation, or other strategies (ventricular level repair or Nikaidoh procedures), to redirect blood flow at the ventricular level. After a Rastelli operation, the left ventricle is the systemic ventricle.

Recommendations for intervention

A. Complete TGA with atrial switch. After Mustard or Senning operations, long-term survival cohorts show reduced survival due to HF and arrhythmias.[170-173] One of the potential late complications is the development of PAH.[174] CMR, cardiopulmonary exercise testing, Holter monitoring, and brain natriuretic peptide levels are useful in the follow-up of these patients, in addition to clinical monitoring and echocardiography.[175]

TR can be a marker of systemic RV failure. TR secondary to ventricular dysfunction and annular dilation should be treated conservatively. Occasionally, TR is due to an intrinsic abnormality of the tricuspid valve. In these cases, TR might be analogous to primary mitral regurgitation in the left ventricle, and surgical repair to reduce volume overload on the right ventricle might have a role in preventing worsening of ventricular function and reducing rates of HF.[176]

Obstruction of or leak through the interatrial baffles might occur after atrial switch procedures. Obstruction of atrial baffles might be challenging to detect using echocardiography, and CMR or CT imaging are helpful to define the anatomy. Stenosis or obstruction of the pulmonary venous baffle is an uncommon cause of symptoms of pulmonary venous congestion in an adult with TGA. Surgery or a hybrid procedure is usually required, because the pulmonary venous compartment is not easily amenable to percutaneous intervention. Obstruction of the superior vena cava (SVC) and/or inferior vena cava (IVC) limbs of the systemic venous baffle is not uncommon and might be tolerated because of adequate collateral circulation through the azygous and hemi-azygous systems. SVC stenosis in particular, present in up to 25% of patients after the Mustard operation, is often benign and usually does not require intervention. Patients with symptoms from systemic venous baffle obstruction (venous congestion of the upper half of the body causing headache, facial swelling, and fullness or of the lower half of the body causing leg swelling, ascites, hepatic congestion, and cirrhosis) should be considered for intervention. Percutaneous intervention is often feasible for systemic venous baffle obstruction and successful in improving symptoms and/or facilitating nonobstructing access for transvenous pacemaker or defibrillator leads.[177,178]

Leaks in the interatrial baffles are more common than clinically suspected, detectable in up to 65% of patients using echocardiography with saline contrast.[179] Transesophageal echocardiography is helpful to identify the size and location of the interatrial communication. Baffle leaks might be a mechanism for right-to-left shunting (causing cyanosis at rest or with exertion and allowing paradoxical embolism) or left-to-right shunting that might lead to volume overload

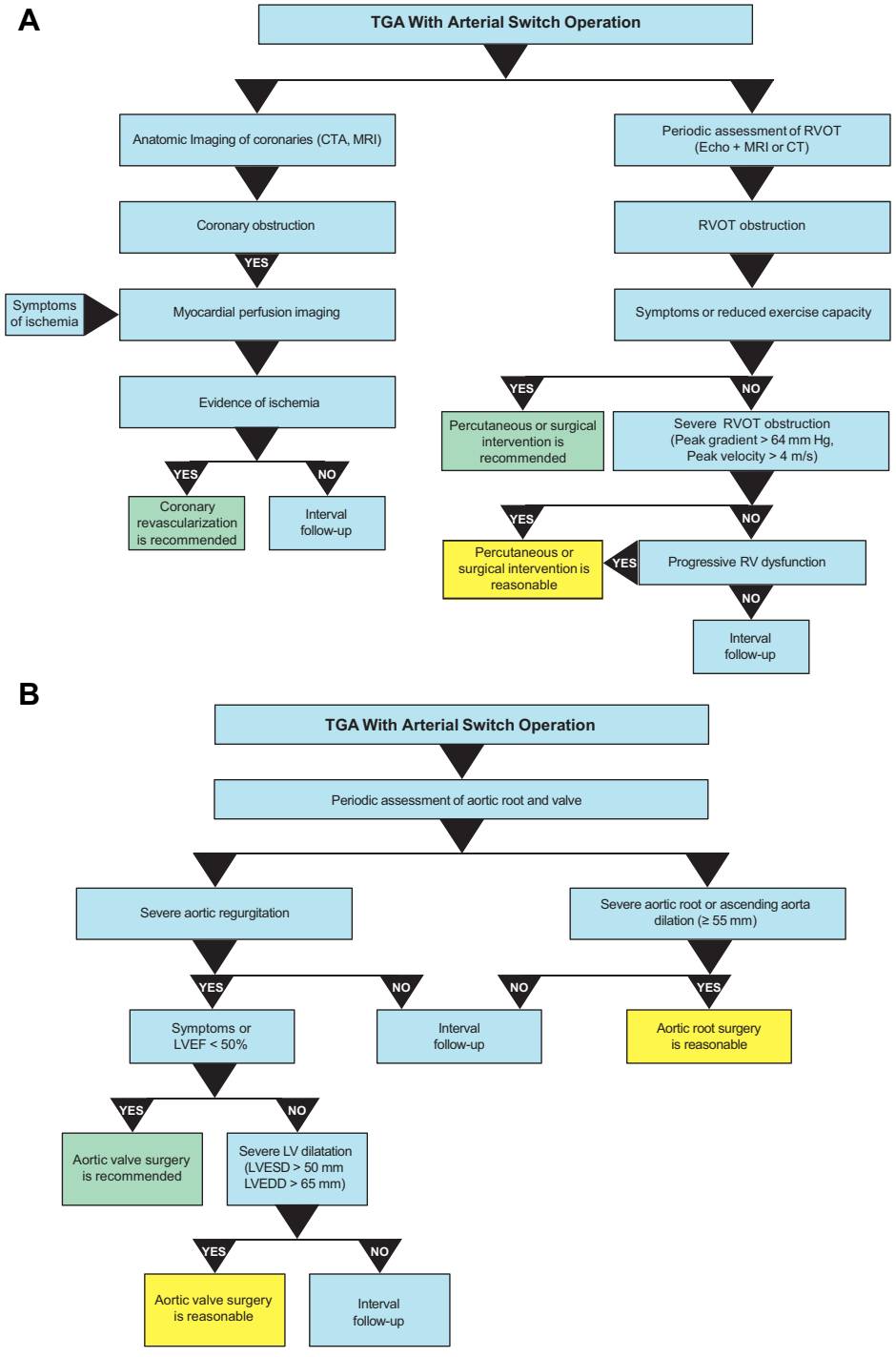


Figure 17. (**A**) Arterial switch operation for complete transposition of the great arteries (TGA) intervention pathway: coronary disease and RVOT obstruction. (**B**) Arterial switch operation for complete TGA intervention pathway: aortic and aortic valve interventions. CTA, computed tomography angiography; Echo, echocardiography; LV, left ventricular; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; MRI, magnetic resonance imaging; RV, right ventricular; RVOT, right ventricular outflow tract.

(causing exercise intolerance or rarely HF). Baffle leaks that cause symptoms should be closed. Percutaneous closure might be feasible using either an occluder device or a covered stent, with surgery reserved for leaks not amenable to device closure. Baffle leaks that result in a significant left-to-right shunt (Qp/Qs > 1.5) associated with volume overload may be considered for closure in the absence of symptoms to prevent ventricular dilation and dysfunction or PAH. In addition, if a baffle leak is found before implantation of a transvenous pacemaker/defibrillator electrode, percutaneous device closure of the leak should be considered to prevent paradoxical embolism.

After atrial switch procedures, patients might remain stable for decades despite ventricular dysfunction.[172] Markers associated with an increase in mortality in d-TGA after atrial

Table 13. Recommendations for intervention in adults with congenitally corrected transposition of the great arteries

	Recommendations	GRADE Strength	GRADE Quality	References
1	We recommend SAVV (SAVV, morphologic tricuspid valve) replacement in symptomatic patients who have severe regurgitation and preserved or mildly impaired systemic RV dysfunction.*	Strong	Moderate	204,205
2	We suggest SAVV replacement is reasonable in asymptomatic patients who have severe regurgitation associated with systemic RV dilation or mildly impaired RV dysfunction.*	Weak	Low	205
3	We suggest that in symptomatic patients with a failing LV to PA conduit,† conduit repair may be considered.‡	Weak	Moderate	206
4	We recommend that patients with symptoms secondary to severe systemic RV dysfunction who are refractory to medical and interventional therapy be referred to an advanced heart failure team with expertise in ACHD heart transplantation.	Strong	Very low	

ACHD, adults with congenital heart disease; GRADE, Grading of Recommendations Assessment, Development and Evaluation; LV, left ventricular; PA, pulmonary artery; PR, pulmonary regurgitation; RV, right ventricular; RVEF, right ventricular ejection fraction; SAVV, systemic atrioventricular valve.

*There should be caution in proceeding with valve replacement in patients with severe SAVV regurgitation accompanied by significant systemic RV dysfunction (RVEF $< 40\%$) because some of these patients might develop postoperative RV failure.

†Failing conduit is defined as an LV to PA conduit with a peak Doppler gradient > 64 mm Hg, peak velocity > 4 m/s, pulmonary ventricle pressure $\geq 2/3$ of systemic blood pressure, or severe PR.

‡When conduit repair is contemplated for a failing LV to PA conduit, the potential worsening of SAVV regurgitation (through septal shift with leaflet tethering) should be considered in decision-making.

switch include atrial tachycardia, prolonged QRS duration, ventricular dysfunction, PAH, fibrosis on CMR imaging, elevated brain natriuretic peptide level, poor exercise tolerance, and increasing age.[180] Late after an atrial switch operation for d-TGA, PA banding can be applied to retrain the left ventricle with the eventual goal of performing an arterial switch operation and Mustard/Senning takedown. This has been shown to be feasible in children younger than the age of 12 years,[181] and possibly even in adults when performed at experienced centres.[182] However, there is insufficient clinical experience to recommend it routinely for the failing systemic right ventricle in an adult with TGA post atrial switch.

Cardiac transplantation remains the definitive long-term treatment for systemic RV dysfunction.[180] The role of ventricular assist devices in this patient population is unclear, but they have been used as a bridge to transplant,[183] and may be considered in those who are not candidates for transplantation. Heart transplantation in this population is complex, requiring takedown of the interatrial baffle, complex cannulation techniques, and challenges with anastomosis of the great vessels; hence the surgery should be performed by surgeons with expertise in CHD (Table 12, Fig. 16).

B. Complete TGA with arterial switch. Long-term survival cohorts after the arterial switch operation are emerging[184-187] and have shown that intervention might be needed to address complications in 3 recognized areas: obstruction of the reimplanted coronary arteries, complications related to the RVOT, and dilation of the neoaortic root with or without AR.

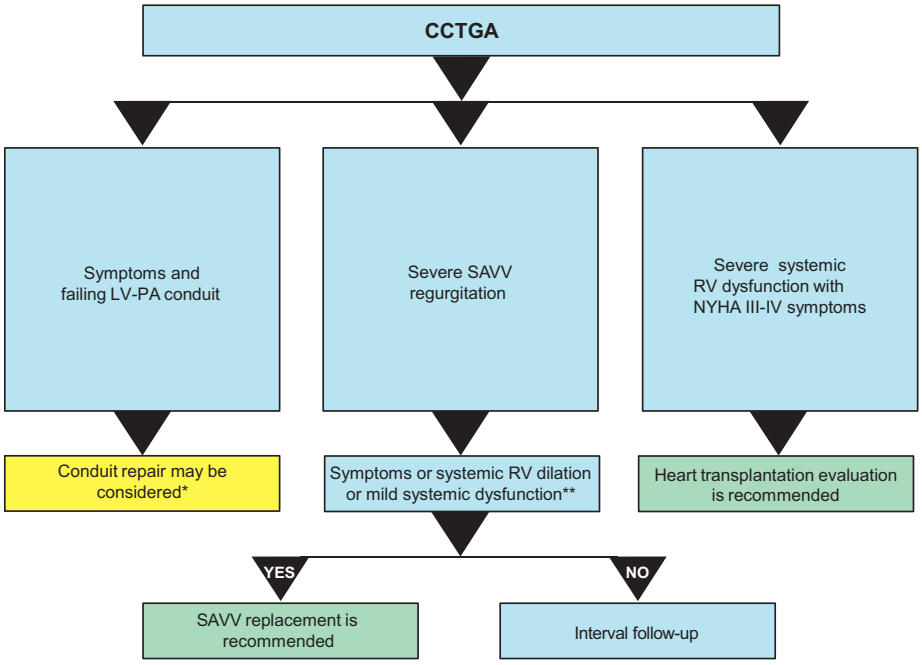
1. Coronary artery obstruction. Coronary sequelae after the arterial switch operation are found in approximately 7% of patients with d-TGA who undergo routine coronary imaging.[187,188] Most coronary events occur early in infancy or childhood after the arterial switch operation, but coronary obstruction can occur late, be clinically silent, and not be detected in routine tests such as electrocardiogram, exercise testing, or echocardiography.[188,189] For this reason, it is reasonable to perform anatomic evaluation of coronary patency in asymptomatic adults with d-TGA after the arterial switch operation.[32,188] CT coronary angiography is the preferred imaging modality, because of its high resolution yielding detailed anatomic information, including coronary arterial origins, course, and relation to adjacent structures that can elucidate the mechanism of coronary obstruction.[190,191]

If coronary obstruction is detected, and/or if the patient has symptoms, testing for myocardial ischemia should be performed. There is greater clinical experience with nuclear perfusion imaging[192] than stress echocardiography. Because the mechanism of coronary obstruction might be related to abnormal coronary ostia, course or impingement by adjacent structures such as aortic sinus or PA, stress modalities that increase cardiac output are likely to be more sensitive than vasodilator stress in detecting ischemia.

It is reasonable to perform revascularization for coronary obstruction causing symptoms or a large ischemia burden. Decisions regarding revascularization should be made by ACHD cardiologists, interventionalists, and congenital heart surgeons familiar with the anatomy after the arterial switch. Because of the nature of the coronary obstruction, surgical revascularization is usually required.[187] The need for such surgery in the adult is rare[193] and the surgery might be complex, requiring takedown of the PA to access the coronaries in the posterior aortic root, hence it should be performed by surgeons with expertise in CHD.

The benefits of intervening for coronary obstruction without documentation of reversible ischemia might be outweighed by procedure-related risks, because collateral circulation might have developed over time to augment myocardial perfusion. Indeed, late sudden death after arterial switch for d-TGA appears to be very rare and has not been definitively attributed to coronary obstruction.[187]

2. RV outflow tract complications. Right ventricular outflow tract obstruction is the most common reason for reintervention in adults with d-TGA after the arterial switch operation[184,185] and periodic imaging should be performed to screen for RVOT complications. If echocardiography suggests elevation of RV systolic pressure, additional tomographic imaging using



* In some cases, failing LV-PA conduits can be addressed percutaneously, otherwise surgical replacement will be required. When intervention is contemplated for the failing LV to PA conduit, the potential worsening of SAVV regurgitation (through septal shift with leaflet tethering) should be considered in decision making.

** There should be caution in proceeding with valve replacement in patients with severe SAVV regurgitation accompanied by significant systemic RV dysfunction (RVEF < 40%) as some of these patients may develop post-operative RV failure.

Figure 18. Congenitally corrected transposition of the great arteries (CCTGA) intervention pathway. LV, left ventricular; NYHA, New York Heart Association; PA, pulmonary artery; RV, right ventricular; RVEF, right ventricular ejection fraction; SAVV, systemic atrioventricular valve.

cardiac CT or CMR is helpful to define the anatomy. RVOTO is mild in most cases, but 10%-25% have moderate or severe obstruction,[184,185] with the incidence of RVOTO increasing with age.[186] Scarring at the anastomotic suture line between the neopulmonary root and the PA is the most common site of RVOTO, although obstruction can occur at any level. Other factors that can contribute to RVOTO are small neopulmonary root (particularly in the setting of a VSD), shrinkage of the patch needed to repair the neopulmonary root after translocation of the coronary arteries, and stretching of the branch PAs with somatic growth, especially if the pulmonary root is rightward or the aortic root is dilated.[194]

The decision to intervene for RVOTO depends on the degree of obstruction and presence of symptoms.[32] Intervention should be performed for patients with symptoms and moderate (peak Doppler gradient 36-64 mm Hg, peak velocity 3-4 m/s) or severe (peak Doppler gradient $>$ 64 mm Hg, peak velocity $>$ 4 m/s or right ventricular systolic pressure $\geq$ 2/3 systemic blood pressure) outflow tract obstruction. It is reasonable to consider intervention in asymptomatic patients who have severe RVOTO after the arterial switch and those with moderate RVOTO and RV dysfunction (gradients might be lower because of impaired RV contractility). Either percutaneous (balloon dilation with or without stenting) or surgical intervention can be used to address RVOTO and branch PA stenosis. The form of intervention depends on the anatomical substrate and local expertise.

Although much less common than PA stenosis, PR has been observed after the arterial switch operation.[184-187] PV replacement should be performed in patients with symptoms and severe PR associated with RV dilation or dysfunction. Decreased exercise capacity can be taken as a surrogate for symptoms. PV replacement may be considered in asymptomatic patients with severe PR who have severe or progressive RV dilation or dysfunction.

3. Aortic root dilation and AR. Aortic root dilation is present in 76% of patients with d-TGA after the arterial switch,[195] and might progress with aging leading to AR.[186,195-197] Echocardiography is the first-line of imaging and usually sufficient to grade AR and measure the aortic root.

Significant (moderate or severe) AR is found in approximately 20% of patients with simple d-TGA 20 years after the arterial switch,[196] and in up to 40% of patients with complex d-TGA at 25 years.[197] AR has been related to size discrepancy between the aortic and pulmonary roots before the arterial switch operation,[197] PA banding before the arterial switch procedure that distorts the neoaortic root, abnormal neoaortic root geometry, as well as increased arterial stiffness in d-TGA.

Patients with d-TGA and severe AR with symptoms or LV dysfunction (LV ejection fraction $<$ 50%) should be referred for surgery. In the absence of specific data for this patient population it is reasonable to extrapolate existing recommendations for

Table 14. Recommendations for intervention in adults with Fontan operations

	Recommendations	GRADE Strength	GRADE Quality	References
1	We suggest that a percutaneous intervention is reasonable in patients with Fontan circulation dysfunction* and 1 or more of the following: a) Obstruction to systemic venous return in the Fontan circuit b) Obstruction of branch pulmonary arteries c) Obstruction of pulmonary venous return d) Veno-venous collaterals or pulmonary atriovenous malformation e) Residual shunt secondary to a previous palliative surgical shunt or residual ventricle-to-PA connection causing a hemodynamically significant volume or pressure load f) Residual ASD or fenestration resulting in significant right-to-left shunt in absence of elevated PVR.	Weak	Low	208-216
2	We suggest that surgical intervention may be considered in patients with Fontan circulation dysfunction* and 1 or more of the following, in the absence of significant ventricular dysfunction: a) Significant (moderately severe or greater) SAVV regurgitation b) LVOTO with a significant gradient.	Weak	Low	208-216
3	We suggest that Fontan conversion surgery, including arrhythmia surgery and epicardial pacemaker implantation as indicated, may be considered for patients with recurrent atrial tachyarrhythmias refractory to pharmacological therapy and catheter ablation.	Weak	Moderate	217-230
4	We recommend early referral to an advanced heart failure centre with expertise in ACHD transplantation for patients with refractory protein-losing enteropathy, failing Fontan circulation, and/or symptomatic heart failure refractory to medical or interventional therapy.	Strong	Moderate	231-238

ACHD, adults with congenital heart disease; ASD, atrial septal defect; GRADE, Grading of Recommendations Assessment, Development and Evaluation; LVOTO, left ventricular outflow tract; PA, pulmonary artery; PVR, pulmonary vascular resistance; SAVV, systemic atrioventricular valve.

*Fontan circulatory dysfunction is defined as impaired flow dynamics in the Fontan pathway.

the management of AR[99,100] and to consider surgery in asymptomatic patients with severe AR and significant LV dilation (left ventricular end-systolic diameter > 50 mm or left ventricular end-diastolic diameter > 65 mm). Either AVR or aortic valve repair might be appropriate, depending on clinical factors, the mechanism of AR, and local expertise.

Addressing concomitant aortic root dilation should be considered at the time of aortic valve surgery if the aortic root diameter equals or exceeds 45 mm, according to established practice.[114] Although data are scarce on the risk of aortic complications with d-TGA, reports of aortic dissection exist.[198] Hence it is reasonable to extrapolate existing recommendations for aortic dilation and repair the neoaortic root in d-TGA after the arterial switch at a diameter ≥ 55 mm.[33,114]

Aortic root or valve surgery requires transection of the pulmonary trunk to access the posterior aortic root, hence should be performed by surgeons with expertise in CHD (Table 12, Fig. 17).

C. Complete TGA with Rastelli-type repair. Adult patients with d-TGA with a VSD and LVOTO might have undergone Rastelli repair. This surgery involves patching the VSD so as to redirect blood flow at the ventricular level to the aorta via an intraventricular tunnel, and connecting the right ventricle to the PA by means of a valved RV-PA conduit. After a Rastelli operation, need for reintervention is frequent, usually related to deterioration of the RV-PA conduit. Other structural complications that might need to be addressed after Rastelli repair include subaortic obstruction and residual VSD. Indications for intervention on the RV-PA conduit are addressed in the section of this guideline on RVOT obstruction. Indications for intervention for subaortic obstruction are addressed in the section on LVOTO. For indications for intervention on a residual VSD, see the VSD section of this guideline.

Congenitally Corrected Transposition

Background

ccTGA is characterized by double discordance (AV and ventriculoarterial discordance).[200] Systemic venous return to the right atrium enters the morphologic left ventricle across a morphological mitral valve and is pumped across the PV to the PA. Pulmonary venous return from the left atrium enters the morphologic right ventricle across a morphological tricuspid valve, and is ejected across the aortic valve into the aorta. This arrangement provides a "corrected" physiology but with the morphological right ventricle supporting the systemic circulation. Other terms for this condition are levo-TGA, ventricular inversion, and double discordance.

Most patients with ccTGA have associated congenital cardiac anomalies, whereas a small percentage of patients have isolated ccTGA. Common associated cardiac anomalies in patients with ccTGA include VSD (most are perimembranous), pulmonary stenosis (most are associated with a VSD), and tricuspid valve (SAVV) anomalies (most are Ebstein-like malformations).

Clinical presentation

Patients with isolated ccTGA might go unrecognized until adulthood because of lack of symptoms, and survival into advanced age without intervention has been reported.[200] However, many adult patients develop symptoms associated with progressive systemic ventricular dysfunction and SAVV regurgitation. Adults might also present with heart block. Survival is better in the absence of associated anomalies but remains reduced compared with the general population. Usual causes of death are sudden (presumed arrhythmic) and progressive systemic ventricular dysfunction with SAVV regurgitation. Imaging with CMR is considered the gold standard

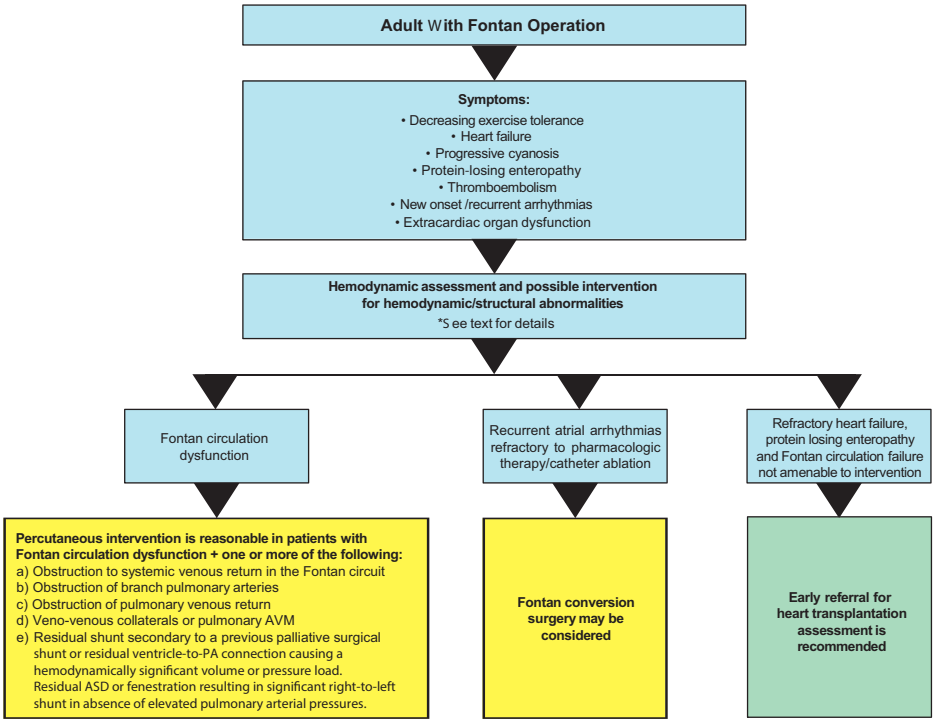


Figure 19. Fontan operation intervention pathway. ASD, atrial septal defect; AVM, arterial venous malformation; PA, pulmonary artery.

for assessment of morphologic RV function in patients with ccTGA.

Recommendations for intervention

These will vary on the basis of the underlying anatomy and symptoms as well as the presence or absence of previous surgical interventions. Relevant to adults, an older surgical approach for ccTGA in childhood was to repair the associated lesions but leave the morphologic right ventricle as the systemic ventricle at the end of the procedure (so-called physiologic repair).[201] Depending on the baseline anatomy, surgery typically consisted of (in isolation or in combination): closure of a VSD, placement of an LV to PA conduit, or replacement of the SAVV. Since the 1990s, some centres have adopted a surgical strategy in childhood that results in the morphologic left ventricle becoming the systemic ventricle (so-called anatomic repair).[202] This requires a "double-switch" consisting of an atrial switch with an arterial switch, or an atrial switch with a Rastelli-type procedure, depending on the baseline anatomy.

Long-term complications in patients who received the surgery depend on the procedure done. In the subset of patients who had placement of a LV to PA conduit, conduit stenosis and eventual failure of the conduit valve will need to be addressed. When percutaneous intervention or surgical replacement for a failing LV to PA conduit is contemplated, potential worsening of SAVV regurgitation postprocedure (as a result of adverse septal shift with leaflet tethering) should be considered in decision-making.[202]

In adult patients with ccTGA, without previous surgery in childhood, interventions typically centre on addressing SAVV regurgitation and the failing systemic right ventricle. Late anatomic surgical repair in adulthood has led to poor results and should not be undertaken.[203] Intervention on the SAVV is usually performed when there is severe regurgitation associated with symptoms, objective exercise dysfunction, or adverse systemic RV remodelling. In some patients with severe SAVV regurgitation who have significant RV dysfunction, surgical risk for SAVV replacement might be prohibitive because of likely postsurgical systemic RV failure. These patients are best managed with advanced HF therapies. When SAVV replacement is performed, prosthetic valves should be used, and the choice of valve type is at the discretion of the patient, cardiologist, and cardiac surgeon[176] (Table 13, Fig. 18).

Fontan Operation

Background

The Fontan operation is a procedure performed in patients with a functionally or anatomically single ventricle or complex malformation unsuitable for biventricular repair. The Fontan operation was originally performed in patients with tricuspid atresia and was designed to divert IVC and SVC blood directly to the PAs, bypassing the right ventricle. Although initially for tricuspid atresia, the operation has now been extended to most forms of single-ventricle physiology such as mitral atresia, double-inlet left ventricle, and hypoplastic left ventricle or right ventricle.

The bidirectional cavopulmonary ("Glenn") anastomosis, which connects the SVC to the PA, or other palliate procedures to increase or decrease pulmonary blood flow, are commonly performed in infancy. This procedure is then followed by the Fontan completion. There have been numerous

variations in the Fontan operation over the years, leading to a variety of Fontan configurations in adult patients.[207]

The most common types of Fontan operation encountered in adults include: (1) the atriopulmonary Fontan (direct right atrium to PA connection); (2) the lateral tunnel (SVC to PA and IVC to PA through a tunnel using the lateral wall of the RA); (3) the extracardiac conduit (SVC to PA and IVC to PA via an external conduit); (4) the intra-atrial conduit (SVC to PA and IVC to PA via a conduit within the atria, preferred in certain anatomical situations [eg, dextrocardia] to avoid compression of an extracardiac conduit); and (5) RA-RV connection through a conduit or connecting flap to the RVOT. In addition, the Fontan might be fenestrated by a surgically created ASD or connection to the pulmonary venous atrium to permit limited right-to-left shunting as a means of enhancing systemic output.

Clinical presentation

Although the Fontan operation has dramatically decreased mortality in children born with a univentricular heart, the downside is exposure of the individual to an obligatory high-pressure central venous circulation and relatively low cardiac output with suppressed capacity to increase it to meet physiologic demands over a lifetime. Well recognized factors associated with accelerated medium-term morbidity and mortality in the Fontan population include: ventricular dysfunction, significant SAVV regurgitation, thromboembolism, and recurrent arrhythmias. Fontan circulation dysfunction can present insidiously over years manifesting in many ways including progressive symptoms, declining exercise capacity, progressive cyanosis, protein-losing enteropathy, HF, and extracardiac organ dysfunction.[207]

Recommendations for intervention

The cornerstone of Fontan patient care is vigilant surveillance for Fontan circulation dysfunction or factors that could lead to or accelerate Fontan circulation dysfunction. When observed, evaluation of and intervention on reversible precipitants and complications should be pursued, provided that the potential benefits outweigh potential risks.[159-167,170] The evidence supporting these multiple possible interventions in this heterogeneous population is limited, nonetheless important to consider. It is essential that the Fontan circuit allow for unobstructed flow into the pulmonary circulation. Obstruction of a total cavo-pulmonary conduit due to thrombus or other mechanism might require thrombectomy, percutaneous angioplasty, and stenting or surgical revision.[159-161] In the case of thrombus, a therapeutic trial of anticoagulation or thrombolysis could be considered. Treatment of obstruction should be considered even if there is a low or no measurable pressure gradient, because an obstruction can suppress flow and not manifest as a measurable pressure difference across it. Similarly, obstruction at the level of the pulmonary arteries should be considered for intervention. Pulmonary venous obstruction is detrimental to flow through the Fontan circuit and its presence might require repair of anomalous pulmonary venous return. Increased systemic ventricular pressure should be addressed, and in the presence of significant SAVV regurgitation, consideration given to AV valve repair or replacement, keeping in mind that in a patient with a Fontan circulation these are high-risk procedures especially if ventricular function is impaired.[162] Intervention for hemodynamically significant LVOTO should also be considered. Veno-venous collaterals can lead to progressive cyanosis, and transcatheter occlusion of these collaterals can be considered after careful hemodynamic assessment, although it is of questionable benefit.[163] Similarly, pulmonary arteriovenous fistulas can be addressed percutaneously or, in the case of a classic Glenn shunt, reconstitution of discontinuous PAs by conversion to a bidirectional cavopulmonary connection. Residual shunts secondary to a previous palliative surgical shunt or residual ventricle-to-PA connection causing a hemodynamically significant volume or pressure load should be considered for closure via transcatheter occlusion or surgery. A persistent fenestration can be a reason for progressive cyanosis and imparts risk of paradoxical thromboembolism; therefore, consideration can be given to transcatheter occlusion of the fenestration after careful hemodynamic assessment.[164-167,170] In contrast, patients with protein-losing enteropathy can be considered for creation of a fenestration in the atrial septum to decrease systemic venous pressure and improve cardiac output, at the expense of cyanosis.

When HF, protein-losing enteropathy, or Fontan circulation failure are refractory to pharmacologic management and interventions, early referral for heart transplantation assessment should be undertaken.[171-184] This should be to a centre with expertise in heart transplantation in the Fontan population. Decision-making around the appropriate timing for transplantation and consideration of multiorgan transplantation is challenging. Patients with the Fontan procedure pose particular surgical challenges including increased fibrosis and adhesions resulting from previous surgeries, collateral formation increasing bleeding risk, allosensitization in the context of previous surgeries and blood product transfusions, and liver and kidney dysfunction.

Special consideration should be given to Fontan conversion in the setting of refractory atrial tachyarrhythmias, extensive thrombus within the Fontan and/or pulmonary venous obstruction.[185-192] Atrial tachyarrhythmias are highly prevalent in the adult Fontan population and are associated with significant morbidity and mortality because of the negative hemodynamic consequences on the Fontan circulation and increased risk of systemic/peripheral thromboembolism.[193,194] As such, atrial tachyarrhythmias need to be addressed promptly with the goal of rhythm control while undertaking thorough investigations to rule out potential precipitants. Conversion of an older-type Fontan circuit to a total cavo-pulmonary conduit, in combination with arrhythmia surgery, should be considered in patients with atrial tachyarrhythmias refractory to pharmacologic and catheter ablation therapies. Patients being considered for Fontan conversion must have excellent hemodynamics and no evidence of end organ dysfunction (Table 14, Fig. 19).

Conclusions

Interventions in ACHD focus on surgical and percutaneous ACHD clinical practice. The writing group used a novel method, the ADAPTE process, to systematically adjudicate, update, and adapt existing guidelines. In addition to tables indexed to evidence, clinical flow diagrams are included for each lesion to facilitate a practical approach to clinical-

decision making. These recommendations are meant to be used to guide dialogue between clinicians, interventional cardiologists, surgeons, and patients making complex decisions relative to ACHD interventions.

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Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at www.onlinecjc.ca and at https://doi.org/10.1016/j.cjca.2022.03.021.