Interventional Catheterization in Adult Congenital Heart Disease

Ignacio Inglessis, MD; Michael J. Landzberg, MD

Improved medical and surgical therapies for children with congenital heart disease have resulted in a growing population of patients reaching adulthood.1,2 Over this same time, the field of interventional cardiology has experienced significant growth, driven by technological improvements and better understanding of the mechanisms and intermediate-term results of individual procedures. Consequently, for adults with uncorrected or previously palliated congenital heart disease, percutaneous therapies have increasing acceptance as reasonable additions, alternatives, and treatments of choice when further surgical or medical intervention is contemplated (Table 1). Currently, interventional cardiology of adult congenital heart disease (ACHD) is a well-established field on its own and, programmatically, is a fundamental component of any center providing care for these patients.3 Although limited safety of interventional procedures for the ACHD population has been suggested in centers without ACHD global care programs,4 the wide variation in clinical presentation, novelty of cardiovascular pathologies (with similarity to as well as marked differences from both congenital and acquired conditions), and potential for concomitant multiple organ system pathology all contribute to situations atypical for standard adult or pediatric laboratories. These concerns, combined with a desire to centralize data collection to establish outcomes assessment for ACHD patients considered for interventional catheterization, lead to the recommendation that such procedures be performed in centers with ACHD expertise and established care programs.3

In this article, we review the most commonly performed percutaneous procedures in ACHD, including valvuloplasty, angioplasty, and device closures. We also include discussions concerning complex ACHD patients (Table 2) as well as future directions.

Valvuloplasty

Pulmonary Valve Stenosis

Pulmonary valve stenosis (PS) is almost always congenital in origin and usually results from commissural fusion of thin and pliable leaflets. Less frequently, the pulmonary valve is dysplastic with thickened and less mobile leaflets. In patients with complex malformations, such as tetralogy of Fallot or transposition of the great arteries, there may be additional obstruction at the infundibular or supravalvular level. Of note, mild PS does not appear to be associated with worsened gradients with age, and therefore most adults presenting with moderate or severe obstruction are likely undiagnosed during youth.

Percutaneous balloon pulmonary valvuloplasty (PPV) has become the treatment of choice for adult patients with isolated PS. The Second Natural History Study of Congenital Heart Defects revealed that pulmonary valve gradients >50 mm Hg were associated with poor outcomes from right ventricular infarction, ventricular arrhythmias, and sudden death.5 Conversely, gradients <30 mm Hg in the absence of subpulmonary ventricular systolic dysfunction or shunt-mediated cyanosis were associated with good prognosis and were unlikely to progress over the 2 to 3 decades to follow. However, as the ACHD population ages, concern may be raised regarding the even longer-term effects of mildly increased subpulmonary ventricular afterload. Consequently, given the low procedural risk and with the assumption that low postprocedural gradient carries low subsequent long-term risk, there is general agreement that PPV is indicated for catheter-based pulmonary valve gradients >40 mm Hg, irrespective of symptoms, or when gradients are ≤30 mm Hg but in the presence of symptoms of subpulmonary ventricular dysfunction or shunt-mediated cyanosis.6

PPV is highly technically successful and safe in the adult population with results comparable to those of surgical valvotomy. A significant reduction in gradient is obtained in up to 80% of procedures (influenced by annulus size, valve morphology, or operator technique), and most patients are free of events in the long term after a single procedure. Further reduction in residual gradients may be seen over time because of resolution of residual hypertrophic subvalvular stenosis. Long-term follow-up of adults who underwent PPV in their youth suggests that, similar to results with surgical valvotomy, late moderate or greater pulmonary regurgitation is increasingly recognized,7 and preprocedural counseling and surveillance for such are recommended. Although PPV has been attempted in subvalvular PS and in adults with dysplastic pulmonary valves, results are limited, and surgical valvotomy is usually indicated for these patients. The impact of
associated aneurysmal dilation of the main pulmonary (and potentially aortic) trunk in patients (and their relatives) with PS remains unclear.

Aortic Valve Stenosis
In contrast to PS, congenital valvar aortic stenosis (AS) secondary to bicuspid aortic valve disease is a progressive disorder in the adult. The bicuspid aortic valve typically becomes thickened and calcified by the fourth decade of life, becoming less suitable to balloon dilation.

Congenital cardiovascular practice guidelines for patients with AS have been established on the basis of valvular peak-to-peak gradients rather than echocardiographically estimated valve areas, in large part because of concerns regarding difficulties in accurately measuring systemic cardiac output and the uncommon presence of low output in pediatric

TABLE 1. Commonly Practiced Catheter-Based Interventions in ACHD: Indications and Level of Evidence

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Indication</th>
<th>Level of Evidence (ACC/AHA Format)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPV</td>
<td>Asymptomatic: Echo mean gradient/cath PSEG &gt;40 mm Hg</td>
<td>I:B</td>
</tr>
<tr>
<td></td>
<td>Symptomatic: Echo mean gradient/cath PSEG &gt;30 mm Hg, or less if RV dysfunction, or shunt-mediated cyanosis</td>
<td>I:B</td>
</tr>
<tr>
<td>Balloon aortic valvuloplasty</td>
<td>For catheterization Asymptomatic: Echo mean gradient &gt;40 mm Hg, or Doppler velocity &gt;4 m/s, or exercise-induced T-wave inversion</td>
<td>Ila:B</td>
</tr>
<tr>
<td></td>
<td>Symptomatic: Echo mean gradient &gt;30 mm Hg, or Doppler velocity &gt;3.5 m/s</td>
<td>I:B</td>
</tr>
<tr>
<td></td>
<td>For intervention Asymptomatic: PSEG &gt;60 mm Hg, or AVA ≤0.6 cm², with ≤moderate calcification and ≤moderate aortic regurgitation</td>
<td>Ila:B</td>
</tr>
<tr>
<td></td>
<td>PSEG &gt;50 mm Hg, or AVA ≤1.0 cm², with ≤moderate calcification and ≤moderate aortic regurgitation, when patient activities mandate potential marked augmentation of cardiac output (pregnancy, physical competitive sports)</td>
<td>Ila:C</td>
</tr>
<tr>
<td></td>
<td>Symptomatic: PSEG &gt;50 mm Hg, or AVA ≤1.0 cm², with ≤moderate calcification and ≤moderate aortic regurgitation</td>
<td>Ila:B</td>
</tr>
<tr>
<td>Aortic coarctation dilation</td>
<td>Discrete, postoperative, recurrent ≥20 mm Hg resting PSEG (30 mm with exercise) with radial-femoral pulse delay</td>
<td>I:B</td>
</tr>
<tr>
<td></td>
<td>≥10-20 mm Hg resting PSEG, LV dysfunction, radial-femoral pulse delay</td>
<td>Ila:C</td>
</tr>
<tr>
<td></td>
<td>Native ≥20 mm Hg resting PSEG (30 mm with exercise) with radial-femoral pulse delay</td>
<td>Ila:B</td>
</tr>
<tr>
<td></td>
<td>≥10-20 mm Hg resting PSEG, LV dysfunction, radial-femoral pulse delay</td>
<td>Ila:C</td>
</tr>
<tr>
<td>Balloon pulmonary angioplasty</td>
<td>RV pressure &gt;50% systemic levels, or RV pressure 25-50% systemic levels with either shunt-mediated cyanosis, RV dysfunction, &lt;20-25% of pulmonary flow to 1 lung, pulmonary hypertension in unaffected segments, or severe pulmonary regurgitation</td>
<td>Ila:B</td>
</tr>
<tr>
<td>(for peripheral PAS)</td>
<td>Conduit/baffle stenosis dilation RV pressure &gt;50% systemic levels, or RV pressure 25-50% systemic levels with either shunt-mediated cyanosis, RV dysfunction, or severe pulmonary regurgitation</td>
<td>Ila:B</td>
</tr>
<tr>
<td>ASD closure</td>
<td>RV volume overload, without additional etiology: pulmonary/systemic flow ≥1.5</td>
<td>I:B</td>
</tr>
<tr>
<td>PFO closure</td>
<td>Recurrent cryptogenic stroke despite therapeutic INR</td>
<td>Ila:B</td>
</tr>
<tr>
<td></td>
<td>Prevention of recurrent cryptogenic stroke or motor TIA within constraints of RCTs</td>
<td>Ila:B</td>
</tr>
<tr>
<td></td>
<td>Orthodeoxia-platypnea syndrome</td>
<td>I:B</td>
</tr>
<tr>
<td></td>
<td>Refractory migraines within constraints of RCTs</td>
<td>Ila:C</td>
</tr>
<tr>
<td>VSD closure</td>
<td>LV volume overload, without additional etiology, with pulmonary/systemic flow ≥1.5</td>
<td>Ila:B</td>
</tr>
<tr>
<td></td>
<td>Pulmonary/systemic flow &lt;1.5 with progressive aortic regurgitation or heart failure</td>
<td>Ila:B</td>
</tr>
<tr>
<td></td>
<td>Multiple recurrent endocarditis</td>
<td>Ila:B</td>
</tr>
<tr>
<td></td>
<td>Postoperative residual VSD with above criteria</td>
<td>Ila:B</td>
</tr>
<tr>
<td>PDA closure</td>
<td>LV volume overload without additional etiology or with severe pulmonary hypertension</td>
<td>Ila:B</td>
</tr>
<tr>
<td></td>
<td>Asymmetric, audible</td>
<td>Ila:B</td>
</tr>
</tbody>
</table>

ACC indicates American College of Cardiology; AHA, American Heart Association; AVA, aortic valve area; INR, international normalized ratio; LV, left ventricle; PA, pulmonary artery; PSEG, peak systolic ejection gradient; RCT, randomized controlled trial; RV, right ventricle; and TIA, transient ischemic attack.
patients. Data are few regarding timing and indications for intervention for adults with congenital AS, although current practice guidelines suggest that for symptomatic adults, either echocardiographic transvalvar Doppler velocity $>3.5$ m/s, mean gradient $>30$ mm, or ECG T-wave inversion (and in asymptomatic adults, mean gradient $>40$ mm Hg or transvalvar Doppler velocity $>4$ m/s) is an indication for catheterization and consideration of percutaneous aortic valvuloplasty (PAV). At catheterization, a peak-to-peak gradient $>60$ mm Hg without severe calcification and with less than moderate aortic insufficiency in adults without symptoms, as well as a peak-to-peak gradient $>50$ mm Hg in the presence of symptoms, is considered an indication for PAV in patients with congenital AS.

Although effective in reducing aortic valve gradients, PAV is associated with a 10% to 30% risk of significant residual aortic insufficiency (especially when a balloon/annulus ratio $>1$ is used). Balance should be considered at the time of balloon size selection between tolerating some residual stenosis and avoiding significant aortic insufficiency. PAV is associated with higher restenosis rates compared with PPV (averaging 50% to 60% event-free survival at 5 to 10 years of follow-up in young adults undergoing PAV). Risk and success of surgical repair for the uncommon patient sustaining avulsion of a valvular cusp during PAV do not appear compromised by attempted PAV, with periprocedural echocardiographic surveillance and timely surgical therapy. Although recommended in national guidelines for consideration as a first-line treatment in young and older adults with AS, PAV is best considered a palliative procedure, potentially delaying surgical valve replacement. Relative risks of surgical repair or replacement strategies should be counseled when PAV is considered. The impact of associated aneurysmal dilation of the ascending aorta (and potentially the pulmonary trunk) in patients with AS should be taken into consideration, as well. PAV has been attempted in patients with nondiscrete subaortic stenosis with limited success, and surgical intervention is generally recommended. Catheter-based percutaneous balloon valvuloplasty has been offered as a shorter-termed alternative to surgical repair of more discrete subaortic stenosis when catheter-based gradient or mean echo gradient is $>50$ mm Hg and either symptoms develop or the ability to

<table>
<thead>
<tr>
<th>Defect</th>
<th>Symptomatology</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetralogy of Fallot</td>
<td>RV dysfunction</td>
<td>ASD closure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RV outflow tract dilation/stent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PAS dilation/stent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Residual VSD closure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Percutaneous pulmonary valve implantation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Right coronary artery intervention</td>
</tr>
<tr>
<td>LV dysfunction</td>
<td></td>
<td>Residual aorta–pulmonary artery shunt closure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Residual VSD closure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Left coronary artery intervention</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Percutaneous aortic valve implantation</td>
</tr>
<tr>
<td>D-TGA (atrial switch)</td>
<td>Systemic venous congestion or subpulmonary ventricular failure</td>
<td>Systemic venous baffle obstruction dilation/stent</td>
</tr>
<tr>
<td></td>
<td>Pulmonary venous congestion or subaortic ventricular failure</td>
<td>Pulmonary venous baffle obstruction dilation/stent</td>
</tr>
<tr>
<td></td>
<td>Cyanosis</td>
<td>Baffle leak closure</td>
</tr>
<tr>
<td>D-TGA (arterial switch operation)</td>
<td>Chest pain/ventricular failure</td>
<td>Percutaneous coronary intervention</td>
</tr>
<tr>
<td></td>
<td>RV dysfunction</td>
<td>Pulmonary artery obstruction dilation/stent</td>
</tr>
<tr>
<td></td>
<td>Semilunar valve regurgitation</td>
<td>Percutaneous valve implantation</td>
</tr>
<tr>
<td>Fontan</td>
<td>Volume retention/fatigue</td>
<td>Baffle obstruction or thrombosis dilation/stent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pulmonary artery obstruction dilation/stent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Systemic venous–pulmonary venous connection closure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Systemic arterial–pulmonary venous connection closure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Systemic arterial–systemic venous connection closure</td>
</tr>
<tr>
<td></td>
<td>Cyanosis</td>
<td>Pulmonary arteriovenous fistulae closure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intramural/baffle leak closure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Systemic venous–pulmonary venous connection closure</td>
</tr>
</tbody>
</table>

D-TGA indicates (S,D,D) transposition of the great arteries; LV, left ventricle; and RV, right ventricle.

<table>
<thead>
<tr>
<th>Defect</th>
<th>Symptomatology</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyanosis</td>
<td></td>
<td>Pulmonary arteriovenous fistulae closure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intramural/baffle leak closure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Systemic venous–pulmonary venous connection closure</td>
</tr>
</tbody>
</table>

D-TGA indicates (S,D,D) transposition of the great arteries; LV, left ventricle; and RV, right ventricle.

TABLE 2. Potential Interventions in Complex ACHD Patients

(averaging 50% to 60% event-free survival at 5 to 10 years of follow-up in young adults undergoing PAV). Risk and success of surgical repair for the uncommon patient sustaining avulsion of a valvular cusp during PAV do not appear compromised by attempted PAV, with periprocedural echocardiographic surveillance and timely surgical therapy. Although recommended in national guidelines for consideration as a first-line treatment in young and older adults with AS, PAV is best considered a palliative procedure, potentially delaying surgical valve replacement. Relative risks of surgical repair or replacement strategies should be counseled when PAV is considered. The impact of associated aneurysmal dilation of the ascending aorta (and potentially the pulmonary trunk) in patients with AS should be taken into consideration, as well. PAV has been attempted in patients with nondiscrete subaortic stenosis with limited success, and surgical intervention is generally recommended. Catheter-based percutaneous balloon valvuloplasty has been offered as a shorter-termed alternative to surgical repair of more discrete subaortic stenosis when catheter-based gradient or mean echo gradient is $>50$ mm Hg and either symptoms develop or the ability to
Aortic Coarctation

Aortic coarctation in the adult is typically located just distal to the origin of the left subclavian artery, although various degrees of obstruction can also occur throughout the aortic arch. The presence of cystic medial necrosis in the aortic wall adjacent to the coarctation site is believed to predispose to wall rupture and aneurysm formation after surgical and percutaneous interventions. Indications for relief of obstruction even in the asymptomatic patient have included clinically determined radial-femoral arterial pulse delay or catheter-derived peak-to-peak gradient of ≥20 mm Hg at rest or ≥30 mm Hg after exercise. However, relief of aortic coarctation may still be indicated in the presence of lower gradients if there is a large collateral network or subaortic ventricular systolic or diastolic dysfunction or if concomitant anatomic (aortic valve, aortic aneurysm, coronary or carotid atherosclerosis) procedures are being considered.

There is general agreement that percutaneous balloon angioplasty with or without stent implantation is a preferred treatment modality for recurrent postsurgical aortic coarctation. The procedure is successful in reducing the gradient to <20 mm Hg in ∼80% of interventions, with a 1.5% incidence of late aneurysm formation (with low incidence of aneurysm formation potentially the result of either postsurgical periaortic fibrosis or removal of most of the abnormal aortic wall tissue at the time of surgery).

Percutaneous balloon angioplasty of the unoperated aortic coarctation in the adult is more controversial, especially in the absence of standardization of indication for repair, technique, end points, and postprocedural follow-up. A higher incidence of late aneurysm formation and restenosis compared with surgically treated patients has been suggested but not universally confirmed. The procedure is successful in reducing the gradient to <20 mm Hg in 85% of patients, with a restenosis rate of ∼8%. Acute dissection has been observed and may be related to failure to recognize aortic nondistensibility during balloon inflation. Death from aortic rupture is a rare complication and highlights the need for onsite catheter-based and surgical support (see below). The incidence of late aneurysm formation is higher than in postsurgical patients, with wide variance reported (from 8% to 35%) in different series. The suspected mechanism for late aneurysm formation is intimal tear at the site of cystic media necrosis, although current literature does not support a relationship between balloon size, coarctation diameter, and the incidence of late aneurysm formation. The overall long-term clinical impact of such aneurysms is unclear because most aneurysms tend to be small and have not required further treatment.

Stent implantation may theoretically overcome some of the shortcomings of balloon dilatation for aortic coarctation because metal scaffolding may reduce the incidence of acute elastic recoil as well as late restenosis due to more complete elimination of gradient in the high-velocity flow arterial system (Figure 1). Additionally, stents may reduce the incidence of residual intimal tears and subsequent aneurysm formation by allowing both the use of smaller dilation balloons (especially in the presence of mild anatomic stenosis) as well as graded inflations in staged procedures. Intra-vascular stent implantation may carry greater potential in adult patients than in children because patient growth is less of a problem, and the aging aorta is potentially more fragile. Preliminary data on the use of stents for aortic coarctation suggest a lower residual stenosis, lower restenosis rate, and lower rate of late aneurysm formation (<5%) compared with balloon angioplasty alone. Aortic rupture has been seen in stent implantation procedures, especially when lack of compliance of the aorta has not been recognized. The risk of subacute stent thrombosis is believed to be low, and although periprocedural antiplatelet or anticoagulant regimens are standardly prescribed, their use remains unsubstantiated.

Stent implantation has rapidly become a recommended procedure for the treatment of unoperated aortic coarctation in many institutions, despite the lack of available multicenter long-term registry data regarding risks or benefits of this procedure. Covered stents should be readily available in the cardiac catheterization laboratory for the emergency therapy of acute aortic dissection or rupture complicating endovascular procedures. This technology has also been considered for...
treatment of late aortic aneurysms after endovascular or surgical repair of aortic coarctation and for subatretic native aortic coarctation. Caution should be exercised, however, in regard to differing risks attributed to covered stents, including stent thrombosis, in-stent restenosis, and inability to redilate such stents at future settings.

**Pulmonary Artery Stenosis**

Pulmonary artery stenosis (PAS) in patients with congenital heart disease may occur anywhere in the pulmonary vascular tree from the main pulmonary artery to the distal-most branches. PAS is typically associated with other cardiac defects or syndromes, such as presence of ventricular septal defect (VSD), tetralogy of Fallot, Williams syndrome, or Alagille syndrome or after in utero rubella infection; however, it can also occur in isolation. Additionally, PAS may result as sequelae of surgical interventions (including systemic-pulmonary shunts, homograft or conduit implantation, pulmonary artery banding, or pulmonary arterioplasty or after arterial switch operation) or may be a residue of acquired diseases (including chronic thromboembolic disease, tumor infiltration or compression, inflammatory arteritis, perivascular fibrosis, or postsurgical scarring after lung resection and reanastomosis).

Although unilateral PAS typically presents asymptptomatically in the otherwise normal adult, in persons with abnormal pulmonary resistance, isolated branch obstruction can result in pulmonary hypertension, increased subpulmonary ventricular afterload, pulmonary valve insufficiency, or sufficient perfusion-ventilation imbalance that may lead to symptoms. Quantitative radiographic assessment of lung perfusion and ventilation should be part of the diagnostic algorithm and should be used as a tool to evaluate the results of dilation procedures in such patients. Surgical access and correction of PAS may be cumbersome and limited. Consequently, after joint medical-surgical discussion of goals and risks, and in appropriate centers, percutaneous therapy may be a preferred treatment method to restore pulmonary blood flow and balance and to decrease resistance for patients with PAS. Indication for balloon pulmonary angioplasty has included presence of right ventricular pressure >50% of systemic levels or lesser pressure in the setting of symptoms, shunt-mediated cyanosis, subpulmonary ventricular dysfunction, pulmonary flow imbalance with <20% to 25% total flow to a single lung, pulmonary hypertension in unaffected lung arterial segments, or severe pulmonary regurgitation.

Ballon angioplasty for PAS is successful (defined as increase of >50% of predilation vessel diameter or 20% decrease in systolic subpulmonary ventricle to aortic pressure ratio) in ~75% of cases when high-pressure balloons are used (Figure 2). Complications have included arterial rupture, unilateral or segmental pulmonary edema, thrombosis, and hemothysis. The restenosis rate approaches 15%, and there is a 3% to 4% incidence of aneurysm formation. Certain PAS lesions treated with balloon angioplasty alone have worse outcome, such as highly elastic proximal main branch narrowing, postsurgical stenoses, long segments, and external compressions. Balloon angioplasty has been performed in patients with distal chronic thromboembolic ob-

Figure 2. Dyspnea and volume retention in this patient with tetralogy of Fallot/pulmonary atresia after right ventricular to pulmonary artery conduit repair led to nuclear lung scintigraphy, revealing 80% flow to the left lung, and echocardiography, suggesting right ventricular hypertension >50% systemic levels and moderate pulmonary regurgitation, with normal right ventricular volume. Angiography (A) confirmed tight proximal stenosis of the proximal branch right pulmonary artery at the anastomotic site with the right ventricular to pulmonary artery conduit, which was relieved (B) after high-pressure balloon angioplasty. Post-procedural right ventricular pressure was 30% systemic, and nuclear lung scintigraphy returned to 55% flow to the right lung.

struction with the use of a smaller balloon-lesion ratio, with promising results.

Similar to the treatment of aortic coarctation, intravascular stent deployment may be more practical in the adult patient with PAS than in the pediatric population because patient growth is less of an issue. Stent deployment appears to have improved the outcomes of balloon pulmonary angioplasty because its use is associated with a larger postprocedure lumen and less occurrence of restenosis, which may be treated effectively with redilation. Certain lesions remain problematic for stent therapy, such as proximal main pulmonary stenosis close to the pulmonary valve and bifurcation stenoses. Stents have been proven to be cost-effective compared with either percutaneous angioplasty methods or surgical intervention. Innovations in stent technology are likely to expand the future indications of stent therapy for PAS.
To date, optimal postimplantation antiplatelet or anticoagulant strategies remain undefined.

Conduit and Baffle Stenosis
Extracardiac conduits may be used to connect the subpulmonary ventricle to the pulmonary arteries in patients with complex congenital disease. These conduits can develop obstruction secondary to severe angulation, calcification, sternal compression, or tissue proliferation, most notably at anastomotic sites. Balloon angioplasty procedures offer little improvement, and restenosis is common. Stent implantation has demonstrated better long-term outcome (predominantly measured as freedom from reoperation), albeit with recognized risk. Stent fracture has been observed in up to 16% of cases. Stent implantation at anastomotic sites may limit the ability of future surgical conduit replacement and may result in severe regurgitation in valved conduits. Finally, the potential for coronary compression (coursing of coronary artery sufficiently adjacent to the conduit) by stent implantation has been reported, with catastrophic potential, and must be assessed before intervention.

Conduit stenosis can be observed after Glenn or Fontan operations (Figure 3). Similarly, systemic baffle obstruction is observed in up to 15% of patients undergoing atrial switch (Mustard or Senning) procedures. Balloon angioplasty occasionally results in long-term relief; however, stent deployment has been highly successful in relieving obstruction, with low complication rates and superior results, especially when performed in the superior portion of the systemic venous baffle after atrial switch operations. Systemic anticoagulation has been recommended for at least 6 months after stenting of the low-velocity flow baffles, without supportive data.

Device Closure

Interatrial Communications
Interstitial communications can be classified as atrial septal defect (ASD) or patent foramen ovale (PFO), each having different clinical and anatomic implications.

The left-to-right shunt in an ASD is driven by compliance differences, with low to nil transatrial pressure gradients. Morbidities related to aging may lead to decreased left ventricular compliance, contributing to increased left-to-right shunt.

Of all the interventions for adults with congenital heart disease, the greatest consensus appears regarding the indication for and method of secundum ASD closure. The standard for intervention has been promulgated as the imaging-based presence of right ventricular volume overload (usually associated with sustained pulmonary to systemic flow ratio [Qp/Qs] > 1.5, the threshold associated with the potential for right ventricular dysfunction, progressive pulmonary vascular disease, and atrial arrhythmia development, even in asymptomatic patients). Right-to-left shunting may be present in such patients as evidence of streaming or elevation of pulmonary vascular resistance, with closure still being considered provided that net Qp/Qs is > 1.5 (typically with pulmonary vascular resistance < 8 to 10 indexed Wood units and pulmonary/systemic resistance < 0.2 to 0.4), although increased long-term risk due to residual pulmonary vascular disease likely persists. Intracatheterization ASD test occlusion with observation of resultant hemodynamics may aid in observing the acute hemodynamic effects of closure, although studies assessing the longer-term predictive nature of such testing have not been performed. Complex strategies utilizing concomitant pulmonary vascular therapies or customized "fenestrated" closure devices have been reported in patients with large-volume left-to-right shunting and moderate to severe pulmonary hypertension.

Even though there are no randomized trials comparing percutaneous versus surgical closure of ASDs, most centers favor percutaneous closure if the anatomy is suitable. Percutaneous closure of ASDs has been reported in nonrandomized uncontrolled fashion to be associated with improvement in right ventricular anatomy, function, and left ventricular interaction, as well as in exercise capacity as measured by cardiopulmonary exercise testing. ASDs can be classified as ostium secundum, ostium primum, sinus venosus, and coronary sinus septal defects, depending on location in the interatrial septum. Occasionally, multiple defects can be observed, especially associated with a thin, hypermobile septum primum. Multiple devices have been used for percutaneous ASD closure since the technique was first attempted in the mid-1970s. The basic device design is of a dual-disc structure joined at a waist, with each disc deployed in either side of the septum. An atrial septum rim > 5 mm around the majority of the defect is required for the safe use of any closure device, although more deficient

Figure 3. Development of peripheral edema led to cardiac magnetic resonance imaging in this patient with tricuspid atresia after intracardiac cavopulmonary anastomosis/Fontan palliation, with relatively diffuse left pulmonary artery stenosis. Catheterization confirmed stenosis (A) with minimal gradient, which was relieved by stent implantation (B). Reduction in systemic venous pressures and marked improvement in cardiac output and diuresis ensued.
anterior superior aortic rim is typical and does not preclude percutaneous closure.

The only currently available devices for clinical use worldwide are the Amplatzer septal occluder (AGA Medical), the CardioSEAL device (NMT Medical), and the Helex septal occluder (W.L. Gore and Associates) (Figure 4). At present, 2 devices (Amplatzer septal occluder and CardioSEAL device) are approved in the United States for closure of different types of atrial defects, with the largest worldwide experience with the use of the Amplatzer septal occluder (Figure 5).

Each of the aforementioned devices has its own advantages and disadvantages. The Amplatzer septal occluder is a self-centering and retrievable device up to the point of full release; however, it has a larger profile once deployed, and rare cases of late cardiac perforations and erosions (as late as 3 years after implantation) causing serious or catastrophic events have been reported and remain a source of concern and indication for further study. The CardioSEAL device typically has a lower profile favoring rapid and more extensive endothelialization. However, only its STARFlex modification (NMT Medical) is a self-adjusting device. As well, retrieval is more complicated after right atrial disk deployment, and the risk of device arm fracture (6%) and device-related thrombosis appears higher than with the Amplatzer septal occluder. Incidence of device-associated supraventricular tachycardia after implantation of either of these devices is under prospective study.

The Amplatzer device allows for closure of ostium secundum ASDs with \(36\) to \(40\) mm of nominal balloon stretched diameter, whereas the CardioSEAL can only be used in off-label fashion for moderate-sized defects (\(18\) mm). Both devices are successful in closing ASDs, with procedural success (almost complete or complete closure and absence of major complications) reported for the Amplatzer device at \(>95\%\) at 3 months. Although earlier nonrandomized studies reported greater safety and efficacy with the use of the Amplatzer device compared with the Clamshell (C.R. Bard Inc) and CardioSEAL devices, the self-adjusting STARFlex modification has been reported to have procedural success equal to the Amplatzer septal occluder with fewer complications.

Although fluoroscopic guidance alone is possible and used by some, most operators prefer echocardiographic guidance for percutaneous ASD closure because it offers a more complete and accurate evaluation of the interatrial septum and surrounding structures. Both transesophageal and intracardiac echocardiography have proven to be useful and effective in guiding procedures, with most operators preferring transesophageal echocardiography for large or multiple defects.
Although elevation of procoagulation markers has been reported after percutaneous ASD closure,\textsuperscript{31} there remains no consensus on the appropriate anticoagulation or antiplatelet regimen after percutaneous ASD closure; most operators recommend aspirin alone or a combination of aspirin and clopidogrel for at least 6 months, in large part because of regimens used in ongoing multicenter randomized trials utilizing related devices. Antibiotic prophylaxis is generally recommended for up to 12 months after device implantation.

PFO, present in $\approx 25\%$ of the adult population, has been associated with various disease processes, including paradoxical emboli causing cryptogenic strokes or other systemic arterial occlusion events, systemic hypoxemia from right-to-left shunt, decompression sickness in divers, and migraine headaches. To date, causal mechanisms for these associations have not been well established; associations appear strongest in younger populations, in which prevalence of additional known risks for disease occurrence is less.

The treatment options for patients with PFO and cryptogenic stroke currently include medical therapy (anticoagulation or antiplatelet drugs) and surgical or percutaneous PFO closure. Two PFO closure devices, the CardioSEAL occluder (February 2000) and the Amplatzer PFO occluder (April 2002), were approved in the United States, via Humanitarian Device Exemption (each limited to $<4000$ implants yearly), for implantation in patients with recurrent cryptogenic stroke due to presumed paradoxical embolus despite use of conventional drug therapy, defined as therapeutic international normalized ratio with the use of oral anticoagulation.\textsuperscript{32,33} As of the fall 2006, these Humanitarian Device Exemptions are no longer applicable under Food and Drug Administration regulations, having been replaced by specific corporate and institutional research protocols. At the present time, for the greater population of patients with PFO and cryptogenic stroke after the index event, despite promulgation of general care guidelines and desire for further study of this problem, there is no consensus on best treatment strategies because no randomized studies evaluating the available options have been completed.\textsuperscript{34} However, available nonrandomized, uncontrolled data analyzed within systematic review suggest that approximately two thirds of recurrent thromboembolic events may be prevented by percutaneous PFO closure compared with medical therapy, corresponding to a 4% absolute reduction in annual events.\textsuperscript{35} As a result of increasingly widespread support, several large-scale multicenter randomized controlled trials (Evaluation of the STARFlex Septal Closure System in Patients With a Stroke or Transient Ischemic Attack due to Presumed Paradoxical Embolism Through a PFO [CLOSURE 1], Randomized Evaluation of Recurrent Stroke Comparing PFO Closure to Established Current Standard of Care Treatment [RESPECT], and a United States Randomized Clinical Trial of the Cardia Star Patient Foramen Ovale Closure System [CARDIA STAR trial]) evaluating the safety and efficacy of PFO closure contrasted with best medical therapies in younger-aged patients for prevention of recurrent cryptogenic stroke are actively recruiting patients, and trial results are expected to shed further light on the relative appropriateness of these therapies.\textsuperscript{36}

Figure 6. Profound dyspnea on standing led to recognition of orthodeoxia-platypnea after 2 years of symptoms. Right-to-left transatrial angiographic passage (A) is eliminated by Cardio-SEAL PFO closure (B), accompanied by total relief of symptomatology.

PFO closure has been performed successfully in patients with positional oxygen-unresponsive systemic hypoxemia (orthodeoxia-platypnea syndrome), resulting from right-sided compliance abnormalities leading to positional right-to-left shunt across the PFO\textsuperscript{37} (Figure 6). Care should be exercised to exclude low pulmonary venous oxygen saturation caused by poor oxygen exchange, concomitant right ventricular systolic dysfunction, and excessive pulmonary vascular resistance in such patients before catheter-based PFO closure.

The association between PFO and migraine headaches has been suggested, especially for migraine with aura. Currently there is no indication to close PFO for migraine occurrence. The complexity of headache assessment and recognition of large-scale placebo benefits achieved in past trials led to Migraine Intervention With STARFlex Technology (MIST I), the first double-blinded, randomized, sham procedure–controlled trial comparing PFO closure with medical therapy in patients with refractory migraines performed in the United Kingdom. MIST I has been completed recently, trial data are pending detailed review, and results of additional larger trials being performed worldwide are expected to further elucidate...
the relative risks and benefits of such therapy in patients with refractory migraines.

Ventricular Septal Defects
VSDs are classified as inflow, muscular, or perimembranous depending on location in the septum. Patients with sizable VSD can develop cardiac left-sided volume overload, subsequent ventricular failure, and pulmonary hypertension, typically at younger ages than patients with atrial-level defects. Consequently, most patients with large enough defects requiring therapy are usually diagnosed and treated in childhood. VSD closure in the adult is usually recommended either when left ventricular volume overload, unexplained by alternative mechanism, is present, correlating with \( Qp/Qs > 1.5 \), in the presence of multiple recurrences of otherwise unexplained bacterial endocarditis, or when accompanied by progressive aortic regurgitation.

Percutaneous closure of congenital or acquired (post–myocardial infarction septal rupture) muscular VSD is a particularly attractive therapeutic option because surgical closure of these defects may carry increased risk of morbidity and mortality. Transcatheter VSD closure is generally technically more challenging than ASD closure, with intravascular passage through the VSD with the use of a balloon-tipped catheter (to ensure passage via the largest lumen) from the left ventricular side, snaring a guidewire in the pulmonary artery, formation and externalization of a venous-arterial-venous vascular loop, and subsequent device deployment based on a pathway allowing maximal device arm–septal apposition, without interference with adjacent intracardiac structures. Although this technique may be highly successful in achieving clinical improvement as defined by risk scales designed for this population, recent reports have highlighted the complexity and morbidities encountered in such high-risk patients undergoing percutaneous VSD closure with earlier double-umbrella devices as well as the current CardioSEAL occluder (the 1 device approved in the United States for this indication). Early results with the Amplatzer muscular VSD occluder, although encouraging, have not included outcome data related to longer-term clinical improvement. Percutaneous closure of perimembranous VSD is even more challenging because of the proximity of the aortic and tricuspid valve, as well as the conduction system, with postprocedural complete heart block observed on occasion, even with asymmetrical devices. Increased data collection and design modifications have potential to improve safety and efficacy.

Patent Ductus Arteriosus
A patent ductus arteriosus (PDA) is an abnormally persistent arterial connection after birth between the descending aorta and the pulmonary artery, most commonly to the junction of the main and left pulmonary artery branches. As is the case for VSD, patients with large PDA may develop left-sided volume overload and pulmonary hypertension at younger ages, leading to diagnosis early in life. It is not uncommon that the diagnosis of PDA is made in adulthood by means of physical examination and presence of the continuous murmur typical of PDA or as an incidental finding on echocardiography. Additional problems associated with PDA include infectious endarteritis, aneurysm formation, calcification, and rare rupture. Large PDA with significant left-to-right shunt should be closed to reduce occurrence of the sequelae of subaortic ventricular failure or pulmonary arterial hypertension. In adults, the treatment of small anatomic PDAs with associated small-quantity shunting remains controversial. The standard to advise PDA closure in an asymptomatic adult patient, with an audible murmur but without other indication, has come under increasing debate due to lack of supportive data for such interventions.

Percutaneous closure of PDA has been performed for >20 years with several generations of devices and is the preferred mode of therapy worldwide given increasing surgical risk with age because of PDA calcification and potential for intraoperative recurrent laryngeal nerve damage. Currently, in adults with PDA, the Amplatzer ductal occluder is the most commonly used device (Figure 7), typically implanted during an outpatient procedure, with coil embolization reserved for PDA measuring <2 to 3 mm or for residual leaks. Complete closure has been reported in >95% of patients at 6 months with both techniques, with device embolization being rarely encountered. Contrary to PDA closure in children, left pulmonary artery obstruction is not a concern in adults. The postimplantation antplatelet regimen remains unsubstantiated, although it is typically recommended for 3 to 4 months.

Figure 7. This 80-year-old subject had progressive fatigue and dyspnea at walking 1 block. By echocardiography, global left ventricular dysfunction (ejection fraction 30%) and right ventricular pressures estimated that 50% systemic levels were present, and a 4- to 5-mm PDA was noted with left-to-right flow. Catheterization noted unobstructed epicardial coronary arteries. Lateral angiography (A) confirmed a long conical tunnel-type PDA with minimal diameter 5 mm (B), which was closed with an Amplatzer PDA occluder (C) on an outpatient basis. Three months later, the patient had returned to walking 2 miles daily, with echocardiographic left ventricular ejection fraction 45%.
and patients continue to receive antibiotic prophylaxis against subacute bacterial endocarditis for 12 months after device implantation.

Fontan Fenestrations and Atrial Switch Baffle Leaks
Patients after Fontan operation may have spontaneous or surgically created residual fenestrations that may lead to right-to-left shunt and consequent systemic oxygen desaturation, systemic emboli, and exercise incapacity. These fenestrations can be closed with the use of the CardioSEAL or Amplatzer septal occluder devices. However, given the non-pulsatile circulation and prothrombosis encountered in patients with Fontan palliation, we favor use of the lower-profile CardioSEAL (the only device currently approved in the United States for fenestration closure). Patients typically receive long-term anticoagulation and prophylaxis against subacute bacterial endocarditis. Transient balloon test occlusion of the fenestration has been correlated with successful longer-term outcomes after closure and, given such, should be performed before permanent closure.42

Up to 25% of patients undergoing Mustard or Senning operations will demonstrate late baffle leaks, likely as the result of suture dehiscence. Although many of these shunts are hemodynamically unapparent and do not require therapy, closure is indicated for large defects resulting in significant intracardiac shunting. Percutaneous closure has been reported with the use of both CardioSEAL and Amplatzer devices as alternatives to surgery.

Coil Embolization
Aortopulmonary Arterial Collaterals
Aortopulmonary collaterals may be observed in patients with congenital malformations associated with decreased pulmonary flow, including pulmonary atresia, as well as variations of single-ventricle physiology or after Glenn shunt or Fontan palliation. These collaterals can arise from any systemic artery and connect directly to the pulmonary arteries at the lung hilum or at the periphery. Resulting left-to-left systemic arterial to pulmonary arterial shunting may cause pulmonary vascular disease, elevation of systemic ventricular filling pressure, systemic ventricular volume loading, and ultimate failure. Residual surgically created systemic to pulmonary arterial shunts share the same pathophysiological sequelae.

In addition to the aforementioned factors, aortopulmonary collateral embolization is indicated before the final stage of surgical subpulmonary ventricle to pulmonary artery connection because left-to-right shunt directly into the pulmonary arteries complicates cardiopulmonary bypass, and dual supply to vascular branches leads to overcirculation and development of pulmonary arterial hypertension. Embolization is typically performed in those collaterals that share significant flow from the main or additional unifocalized pulmonary arteries to avoid lung infarction. Embolization is typically performed with coils; however, the Amplatzer vascular plug has recently become available for occlusion of larger collaterals, with similar success reported.

Coronary Fistulae
Coronary fistulae can originate from all major epicardial coronary arteries, and drainage usually occurs to the coronary sinus, right atrium, right ventricle, or pulmonary artery. These collaterals can become markedly enlarged and can lead to significant left-to-right shunting with right-sided volume overload and effective coronary arterial steal leading to ischemia. Embolization has been reported predominantly with coils; however, other devices such as ASD closure devices or the Amplatzer vascular plug have been used successfully, as well.43 Long-term effects of intravascular fistula occlusion have yet to be demonstrated.

Other Forms of Collaterals
Collaterals from the systemic to the pulmonary veins (venous-venous collaterals) can occur in patients with single-ventricle physiology, especially after Glenn or Fontan operations, in part because of chronically elevated systemic venous pressures. Pulmonary arteriovenous fistulae may also present late after Glenn anastomosis, as well as in patients with chronic liver failure or with hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu syndrome). In both instances, there is right-to-left shunt with various degrees of cyanosis. Both types of abnormal connections can be treated successfully with coil embolization or Amplatzer closure devices44 provided that right-to-left shunt is not of hemodynamic benefit as potential relief of subpulmonary ventricular afterload due to the presence of severe pulmonary arterial hypertension. Nevertheless, recurrence of collaterals is not uncommon unless the underlying physiology driving their development is modified significantly.

Miscellaneous Procedures
As the ACHD population ages, epicardial coronary disease is becoming more prevalent. Thus, coronary angiography is indicated at the time of catheterization in all patients older than 40 years or in younger patients with significant risk factors for atherosclerosis (in particular, all men aged >35 years). Epicardial coronary stenting should be performed, if indicated, by operators with expertise in percutaneous coronary revascularization techniques. Additionally, coronary angiography should be performed before any percutaneous procedure with potential for coronary compromise, such as stenting of a right ventricular to pulmonary conduit.

Balloon atrial septoplasty has been used to create or enlarge existing ASDs in patients with severe pulmonary hypertension and right ventricular failure as means for providing a “pop-off” valve to the failing right ventricle. However, this approach must be balanced against excessive decreases in systemic oxygen saturations from increased right-to-left shunting. Restenosis of the interatrial septum is common, and fenestrated closure devices are becoming available with the hope of improving long-term patency.

Baffle fenestrations are performed increasingly at the time of Fontan surgery because they reduce the incidence of postoperative effusions. These fenestrations can become occluded in the early postoperative period, leading to rapid hemodynamic deterioration from increased pulmonary vascular resistance and low cardiac output. Balloon angioplasty
of the fenestration usually restores patency; however, there is risk of thrombus embolization to the left heart. Rarely, the fenestration cannot be proved with a catheter, and wire and baffle puncture with a transseptal needle is required.

Cardiac arrhythmias are frequent in the complex ACHD patient, resulting in unpredictable and variable degrees of hemodynamic compromise. Electrophysiology procedures, such as programmed stimulation and temporary pacing, are performed frequently in conjunction with simultaneous hemodynamic measurements, allowing for accurate diagnosis and development of treatment strategies.

Future Directions

Percutaneous Valve Replacement

Percutaneous valve replacement has substantive potential for ACHD patients who have been subjected to multiple operations and may have premature aging of multiple organ systems, raising the risk of recurrent surgeries. The largest group to potentially benefit from such advances, at present, includes patients with tetralogy of Fallot with postoperative residual pulmonary insufficiency. Early reports of percutaneous pulmonary valve replacement in this population are encouraging. Nevertheless, unresolved issues remain, including valve durability, stent fracture, device embolization, adjacent structure impingement, limited valve size, recurrent regurgitation and stenosis, and the need for large catheters for delivery, although most initial results are encouraging in limited centers. Larger-scale multicenter trials with percutaneous pulmonary valve stent implantation are expected, and, if found to be of benefit, it is hoped that they will extend the potential for more widespread applications.

Hybrid Procedures

As collaboration between congenital cardiovascular surgeons and interventional cardiologists expands, hybrid procedures, involving both teams simultaneously or in temporally staged fashion, may increase clinical application of technological applications, with the potential to extend the clinical well-being of ACHD patients. Examples of such hybrid interventions include intraoperative pulmonary artery dilation in preparation for pulmonary valve or homograft placement, percutaneous closure of apical or muscular VSDs under direct vision in the operating department, and percutaneous closure of aortopulmonary collaterals or completion of conduit placement as Fontan palliation.

Conclusion

The ACHD patient, at baseline or in need of intervention, presents unique challenges to caregivers. Life demands (including sudden needs for augmentation in cardiac output, such as with exercise or pregnancy) and altered anatomy coupled with increasing potential for exercise incapacity and progressive extracardiac comorbidity contribute to physiological occurrences, risks, and complications encountered less frequently in typical pediatric or adult catheterization laboratories. As witnessed in the advancement of pediatric congenital cardiovascular care, it is highly likely that catheterization-based interventions planned and performed in conjunction with appropriate surgical and medical caregivers in centers expert in such care, with centralized data collection and outcome assessments, will likewise assist in the further advancement of adults with congenital heart disease and its sequelae.

Disclosures

Dr Inglessis is on the Speakers’ Bureau for Boston Scientific and is a consultant for Medtronic. Dr Landzberg has received research grants from and served as a consultant for NMT Medical, AGA Medical, Actelion, and Nitrox. He has also received a grant from Myogen.

References


Interventional Catheterization in Adult Congenital Heart Disease
Ignacio Inglessis and Michael J. Landzberg

Circulation. 2007;115:1622-1633
doi: 10.1161/CIRCULATIONAHA.105.592428
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2007 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/115/12/1622

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/