**Special Report**

**Pathophysiology of Congenital Heart Disease in the Adult, Part II**

**Simple Obstructive Lesions**

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With the successes in cardiothoracic surgery over the past 3 decades, adults with congenital heart disease (CHD) outnumber, for the first time, their pediatric counterparts. As a result, adult patients with CHD are beginning to appear more frequently in the practices of adult cardiologists. This series is designed to provide a review of the pathophysiology and natural history of common congenital heart problems that are now being seen by adult cardiologists. In the first part, simple shunt lesions were reviewed. This section will examine the physiology and natural history of some of the more common congenital obstructive lesions that may be seen by adult cardiologists, as well as indications for intervention. Principally, these lesions will include ventricular outflow obstructions that may or may not have undergone prior intervention. Congenital obstructions of systemic and pulmonary venous return, congenital intra-atrial obstructions, and congenital atrioventricular valve stenosis will not be included in this review because they are far less common and present clinically predominantly in childhood.

**Congenital Obstructive Lesions**

In the normal circulation, the ventricular outflow tracts, semilunar valves, and great arteries present no obstruction to flow. Congenital narrowing of any of these pathways increases ventricular afterload and in more distal lesions causes maldistribution of flow (see individual defects below). In response to the increased afterload, physiological ventricular hypertrophy occurs, which results in thicker chamber walls, reduced chamber compliance, and higher filling pressures in the atrium. With severe noncompliance (diastolic dysfunction) venous congestion may occur, with exertion or even at rest, which limits cardiac output and physical activity in this population. A reduced stroke volume may also be a direct consequence of increased afterload and may be particularly important in the face of increased demands.

All patients with hemodynamically significant obstructions of large ventriculoarterial pathways will present with a heart murmur, the result of the turbulent flow created as blood passes, under pressure, through the stenosis. For lesions of the outflow tracts, valves, and proximal great arteries, echocardiography generally remains the diagnostic modality of choice to establish both the site and the severity of the obstruction. Magnetic resonance imaging (MRI) and computed tomography are superior for imaging the more distal anatomy of the aortic arch and the branch pulmonary arteries (PAs).

Symptoms, in general, are related to the severity of obstruction. The pressure gradient across the lesion reflects the degree of obstruction, as estimated either by Doppler or by MRI techniques or as measured directly in the catheterization laboratory; however, this value cannot be used in isolation. The pressure drop is a reflection of both the degree of pathway narrowing and the amount of flow across the narrowed portion (Ohm’s law: pressure=flow/resistance). The degree of obstruction could be underestimated significantly by the pressure gradient alone, for example, in a patient with low cardiac output or in a patient with a shunt lesion that removes blood from a chamber proximal to the obstruction. Similarly, small resting gradients may increase substantially with exercise or any other state that produces a physiological increase in flow across the lesion.

**Conditions With Increased Right Ventricular Afterload**

Congenital obstruction may occur in the outlet portion of the right ventricle (RV) proximal to the pulmonary valve (subvalvar stenosis), at the valve itself (valvar pulmonary stenosis), distal to the valve in the main pulmonary artery (MPA; supravalvar stenosis), or more peripherally in the branch PAs. In the absence of left-sided disease, PA pressure is normal distal to the obstructive lesion. With increased afterload, the RV hypertrophies, and right atrial filling pressures rise. Mild proximal obstructions and isolated distal lesions are tolerated easily without symptoms. In more severe cases in which there is RV noncompliance but normal systolic performance, patients are well at rest but may experience substantial increases in right atrial filling pressures with transient venous conges-
Obstruction within the RV outflow tract is rare in isolation. Most often, isolated subvalvar pulmonary obstruction in adults is a residuum of earlier surgical intervention (ie, for tetralogy of Fallot), but it can be seen in adult patients with CHD who have not undergone surgery.

Severe subvalvar obstruction can present de novo in adults with a double-chambered RV. In the double-chambered RV, a muscular band obstructs the RV outflow tract, dividing the chamber into a high-pressure inflow portion (proximal to the obstruction) and a low-pressure outflow chamber (distal). The diagnosis presents most frequently in childhood as a complex that includes the subvalvar muscular obstruction and a perimembranous ventricular septal defect. Membranous subaortic stenosis will also be present in a small percentage of patients. When the subpulmonary obstruction is relatively mild, the child presents with an asymptomatic heart murmur; however, as patients with a double-chambered RV age, the degree of muscular obstruction tends to progress, whereas the ventricular septal defect often closes spontaneously. For patients with access to regular medical care, the harsh systolic murmur associated with the outflow obstruction should bring them to attention long before the increasing afterload reaches critical levels. However, if not diagnosed previously, these patients may present with exercise intolerance as young adults due to RV systolic or diastolic dysfunction. With more severe obstruction and hypertrophy, ventricular arrhythmia, syncope, and sudden cardiac death may be the first presenting sign.

**Indications for Intervention**

Patients with clinical symptoms, patients with RV systolic pressures approaching that of the aortic pressure, and those with global RV hypertrophy, especially with reduced systolic function, should be considered for intervention. RV outflow obstruction can be assessed by Doppler (transthoracic echocardiography usually gives superior angles of interrogation compared with transesophageal echocardiography), by MRI, or by diagnostic catheterization. In the catheterization laboratory, an end-hole catheter pulled back from the PA across the obstruction yields a typical tracing (Figure 1) that localizes the obstruction within the ventricle.

![Image](http://circ.ahajournals.org/)

**Figure 1.** A, Pullback from MPA to RV inflow in a patient with double-chamber RV. On pullback from MPA to RV (second to third beat), no systolic gradient is present, although the diastolic pressure falls, which indicates entrance into the ventricle. On further catheter withdrawal, a large gradient is present within the body of the ventricle (fourth to fifth beat). A pullback in a patient with subvalvar aortic obstruction would have a mirror-image tracing. B, Angiographic image of the subvalvar obstruction in the RV (arrows) in a patient with double-chamber RV. RVOT indicates RV outflow tract.

Surgical muscle resection with or without patching of the outflow tract remains the standard of care, although medical management can be useful in alleviating presenting symptoms. Patients respond both to increasing intravascular volume to dilate the outlet pathway and to a reduction in ventricular contractility with β-blockers or calcium channel blockers. Diuretics and afterload-reducing agents are contraindicated in this population. Although a number of pediatric case reports involve the use of angioplasty to palliate subvalvar pulmonary obstruction, no evidence exists that such an intervention is beneficial in the adult with severe muscular hypertrophy.

**Valvar Pulmonary Stenosis**

**Natural History and Physiology**

Isolated valvar pulmonary stenosis is present in 8% to 10% of patients with CHD. In the Second Natural History Study of congenital heart defects, patients with mild degrees of obstruction (<30 mm Hg peak-to-peak gradient at catheterization) who did not undergo surgery had a course that was indistinguishable from a control group with respect to survival, symptoms, and need for therapy. More severe obstructive gradients increase RV afterload and lead to chamber hypertrophy. As noted above, symptomatic patients tend to present with symptoms of exercise intolerance. The occurrence of symptoms and serious dysrhythmic events is generally related to the peak-to-peak gradient across the valve. Interestingly, we, and others, have observed that moderate valvar gradients, which may be very well tolerated in children, appear to...
ase them to develop later symptoms in adults with CHD. Extensive pulmonary hypertension and high LV end-diastolic pressures change simultaneously, which indicates obstruction at the valvar level. The peak-to-peak gradient is ~50 mm Hg. In aortic valve stenosis, the same pressure tracing morphologies are seen. B, Echocardiographic images of a patient with valvar pulmonary stenosis. Thickened doming valves are shown in both systole and diastole. Indications for Intervention

Patients with clinical symptoms, patients with RV systolic pressures approaching that of the aortic pressure, and those with global RV hypertrophy, especially with reduced systolic function, should be considered for intervention (Figure 2). Balloon valvuloplasty has supplanted surgical valvotomy as the treatment of choice for valvar pulmonary stenosis since the early 1980s. In the Second Natural History Study, 97% of 210 patients who underwent surgical valvotomy for pulmonary valve stenosis were in New York Heart Association class I at 25 years of follow-up, but 85% had some degree of pulmonary valve incompetence by echocardiography. The importance of pulmonary valve incompetence in adults has become increasingly clear, not just in isolated valvar stenosis but in all right-heart obstructive surgery. It is now accepted that significant, long-standing pulmonary regurgitation will lead to progressive RV dilatation and myocardial injury/dysfunction and is an important determinant in the development of later symptoms in adults with CHD. Extensive study is ongoing in this population with respect to timing of intervention for pulmonary regurgitation to avoid RV systolic failure and to the potential use of the new transcatheter valve-replacement therapies.

In adults with long-standing pulmonary stenosis and RV hypertrophy, secondary subvalvar obstruction may occur with acute removal of the RV afterload. The contractility of the suddenly unloaded RV outflow musculature may lead to near obliteration of the outflow tract immediately after intervention. As with double-chambered RV patients, fluid bolus administration and β-blockers can be very useful in this setting. Careful pullbacks, with end-hole catheters, will be able to distinguish a residual valvar obstruction from a new-onset reactive subvalvar obstruction (Figures 1 and 2). With elimination of the valvar obstruction, RV hypertrophy will regress during the first few weeks of follow-up. This results in a diminishing systolic gradient across the subvalvar RV outflow tract but may also result in increasing pulmonary insufficiency during follow-up as the RV chamber becomes more compliant. Surgical valvotomy or valve replacement is reserved for patients who do not respond to balloon interventions or who have already developed significant valvar insufficiency in addition to valve obstruction.

Supravalvar Pulmonary Stenosis

Natural History

Native supravalvar pulmonary stenosis can occur as an isolated abnormality or in association with complex cardiac malformations such as tetralogy of Fallot, with fetal teratogenic exposure such as rubella or toxoplasmosis, or with genetic syndromes such as Williams or Noonan syndromes. Stenosis of the MPA, above the valve annulus, may also be the result of surgical scarring from operations such as a PA band or the arterial switch operation for transposition of the great arteries. The hemodynamic burden of this lesion is identical to that of valvar pulmonary stenosis. In some cases, it may be quite difficult for the echocardiographer to distinguish a doming, stenotic valve from a normal valve that cannot open fully owing to its abutment against a muscular supravalvar ridge. MRI and computed tomographic angiography can be very useful in this setting. In the catheterization laboratory, careful pressure measurements with an end-hole catheter can also help distinguish between valvar and supravalvar obstruction (Figure 3).

Indications for Intervention and Management

As in patients with valvar pulmonary stenosis, patients with exercise intolerance and those with significant resting gradients should be considered for intervention. Few data exist on catheter intervention for this patient population. Congenital supravalvar obstructions occur typically at the sinotubular junction of the MPA. Because of the elasticity of the MPA, which makes it resistant to balloon dilation, and the proximity to the pulmonary valve, which makes stent implantation undesirable, these patients are most often referred for surgery when obstruction is severe and they are symptomatic. Significant potential exists in this population for the use of experimental transcatheter, stent-based valve implants, as mentioned above.

Postoperative Conduit Obstruction

Surgical repairs for congenital atresia or hypoplasia of the RV outflow tract (pulmonary atresia and tetralogy of Fallot) or...
some cases, intraconduit balloon or stent angioplasty may be considered for intervention. Most often, adult patients have outgrown the conduit placed previously in childhood, and surgical conduit replacement is required. In patients who are symptomatic or who have significant resting gradients that result in RV hypertrophy with or without systolic dysfunction should be considered for intervention. Most often, adult patients have outgrown the conduit placed previously in childhood, and surgical conduit replacement is required. In some cases, intraconduit balloon or stent angioplasty may be useful in treating discreet stenoses within an RV-to-PA conduit.

Although stent angioplasty may be successful in reducing obstruction in adult patients in the short term, particularly with noncalcified conduits, it does not address the issue of the insufficient conduit valve, a nearly universal finding late after implantation. As such, stent angioplasty alone is not an ideal long-term solution, even in patients with otherwise acceptable conduits. As a surgical alternative, this group of patients is currently the main focus of investigators working on stent-based transcatheter pulmonary valve implantation. This patient population is particularly attractive for this stent-based technology, because the size of the pathway receiving the implantable valve is known and fixed, in contrast to the many patients with marked dilatation (often dynamic in nature) of the native RV outflow tract related to prior obstruction and surgical intervention.

Branch PA Stenosis

Natural History

Branch PA obstructions may be isolated or multiple in number, or they may occur diffusely throughout the pulmonary tree. Postmortem studies in children have revealed these lesions to consist of primarily fibrous intimal proliferation, with medial hypoplasia and loss of elastic fibers in affected vascular segments. Isolated congenital obstruction of the proximal PA is rare, but when it occurs is more often the result of prior surgical interventions (ie, Blalock-Taussig shunt or PA banding). Multiple or diffuse narrowings of the branch PAs, especially in conjunction with other cardiac or systemic malformations, is a marker for congenitally acquired genetic or infectious diseases. Williams syndrome, Noonan syndrome, congenital rubella, and Alagille syndrome all commonly present with branch PA stenosis, hypoplasia, or both. It is rare that these systemic diseases remain undiagnosed into adulthood.

Pathophysiology and Natural History

Because of the innumerable parallel pathways available in the pulmonary tree, an isolated branch PA stenosis may not impose a significant afterload on the ventricle. Rather, the higher resistance of that pathway will result in blood being redistributed among the unobstructed (or less affected) segments in a proportion that is inversely related to the resistance of each branch pathway. Patients may be remarkably symptom free, even with severe maldistribution of flow, unless pulmonary parenchymal disease (ie, pneumonia) affects the well-perfused segments. In that setting, with the majority of ventilation occurring in the poorly perfused lung, the V/Q mismatch is maximized, and patients may become seriously compromised.

With more diffuse branch PA disease, affecting segments of both lungs, RV afterload and systolic pressure may be increased significantly. In this setting, as with other obstructive lesions, the PA pressure past the most distal obstruction will be normal (Figure 3); however, unaffected lung segments in such a patient will be exposed to both high pressure and high flow (distributed from obstructed areas). These pa-
Patients are uniquely at risk of developing segmental pulmonary vascular disease.

Although uncommon, the diagnosis of branch PA stenosis should always be considered in patients with a history of CHD who present with symptoms of pulmonary embolism: dyspnea, fatigue, and segmental lung ventilation-perfusion mismatches. In patients with symptoms or severe maldistribution of flow, intervention is indicated both to redistribute flow more appropriately and to reduce RV afterload.

Echocardiography cannot readily identify the level of obstruction in the PAs past the first branch point in children or past the bifurcation of the MPA in most adults. MRI increasingly has become used to assess PA anatomy and flow, particularly because it allows simultaneous assessment of RV ejection fraction and regurgitant volumes of the right-sided valves, when needed. Angiography, however, remains the “gold standard” for defining PA anatomy, whereas quantitative lung perfusion scans (technetium-99m) have been invaluable in identifying discrepancies in segmental or lobar pulmonary flow. Of course, without invasive hemodynamic data, neither a lung scan nor an MRI can distinguish a significant segmental obstructive lesion from an unobstructed lung segment with pulmonary vascular disease and high resistance.

**Indications for Intervention**

Indications for catheter intervention include symptoms, a significant decrease in pulmonary blood flow to the left or right lung (or a specific lobe), or elevated RV afterload as determined by the ratio of RV systolic to systemic systolic pressures. Although most proximal stenoses of the prehilar area can be repaired surgically, more distal branch PA obstructions are difficult for the surgeon to reach without the potential for extensive pulmonary parenchymal injury. As a result, the management of branch PA stenosis has been predominantly the domain of the interventionalist since 1983. Current techniques have been best applied to isolated lesions and involve balloon angioplasty, stent angioplasty, and the use of cutting balloons when standard balloons have failed.

Outcomes in patients with diffuse pulmonary obstructions (Williams, Noonan, and Alagille syndromes and rubella) have been generally poor. This can be attributed to 2 factors. First, given the large number of vessels typically involved, successful dilation of even a few significant lesions will not result in an immediate decrease in RV afterload. Second, when angioplasty is successful, the newly unobstructed lung segment will suddenly face high flow, as blood is redirected from unobstructed segments, as well as high pressure. This may result acutely in a “reperfusion injury” with significant segmental pulmonary edema that may require ventilatory support. This does not occur when the proximal PA pressures are normal after intervention, such as in valvar pulmonary stenosis.

**Conditions With Increased LV Afterload**

Similar to congenital obstructions on the right side of the heart, left-sided congenital obstructive disease may occur at the subvalvar, valvar, or supravalvar levels and peripherally in the aorta (coarctation of the aorta). Although LV obstructive lesions may occur in isolation, they may also be a part of a number of genetic syndromes. For example, hypertrophic cardiomyopathy (subaortic stenosis) is associated with Noonan’s syndrome, supravalvar aortic stenosis is virtually always associated with William’s syndrome, and coarctation of the aorta is part of Turner’s syndrome. Left-sided obstructive lesions may not occur in isolation. Shone’s complex presents with multiple left-sided obstructive lesions and may include a supravalvar mitral ring, parachute mitral valve deformity, subaortic stenosis, valvar obstruction (typically bicuspid or unicommissural valves), and distal aortic arch obstructions.

As on the right side, with significant obstruction of the LV outflow, chamber hypertrophy leads to reduced compliance and higher atrial filling pressures. On the left side, higher venous pressure and congestion may result in pulmonary edema, particularly in higher-output states. Thus, dyspnea on exertion is the most frequent presenting sign of clinically important left-heart obstructive disease. Ventricular arrhythmia and sudden cardiac death may also occur. Rarely, patients may present with angina/coronary insufficiency, when LV myocardial oxygen requirements are increased (with increased wall thickness), and when elevated ventricular diastolic pressures or early atherosclerotic changes may limit coronary flow.

**Subvalvular Aortic Stenosis**

**Pathophysiology and Natural History**

Subvalvar aortic stenosis comprises a spectrum of obstructive processes in the LV outflow tract that range from a discrete subaortic membranous obstruction to a fibromuscular tunnel-type obstruction to the more familiar hypertrophic cardiomyopathy. Regardless of the presenting anatomic features, each of these lesions tends to be progressive during childhood.

In patients with discrete subaortic stenosis, a thin fibrous membrane stretches across the LV outflow tract from the septal surface to the anterior leaflet of the mitral valve. The membrane may be of variable thickness and of variable distance below the aortic valve annulus. The membrane typically has a central lumen that narrows the LV outflow pathway proximal to the aortic valve. In children, the progression of obstruction may be rapid. They may develop progressive aortic insufficiency, a result of the distortion of the valve anatomy as the membrane extends onto the valve leaflets. In adults, obstruction progression is much slower, with less change in the degree of aortic regurgitation over time.

With the tunnel-type obstructive lesion, a thick fibromuscular tubular narrowing diffusely reduces the diameter of the outflow tract. At any given time, the degree of obstruction in both discrete and tunnel LV outflow obstruction is fixed, with the gradient across the outflow increasing proportionately to the increase in cardiac output. These lesions will present with heart murmurs long before hypertrophy and reduced LV compliance lead to symptoms of pulmonary venous congestion.

In contrast to membranous and fibromuscular obstructions, hypertrophic cardiomyopathy features a dynamic muscular obstruction of the outflow tract. In this population, the
gradient may increase dramatically with decreased afterload or with an increase in contractility (inotropic state). The dynamic nature of this obstruction is easily demonstrated in the catheterization laboratory by the Brockenbrough-Braunwald-Morrow sign (Figure 4), which occurs with the cardiac cycle immediately after a premature ventricular contraction.

Under normal circumstances, after a premature ventricular beat, the physiological pause before the next ventricular contraction allows for increases in both ventricular filling and intracellular calcium transport. With the next ventricular contraction, stroke volume is increased, the result of increased preload and contractility. In the normal heart, both LV and aortic systolic pressure will have a corresponding increase. In patients with discrete membranous or fibromuscular subaortic obstruction, the ventricular contraction after the premature beat will increase the outflow gradient slightly, due to the increased stroke volume of the subsequent beat, even as aortic pressure increases or stays the same; however, in the patient with hypertrophic cardiomyopathy, the increased inotropy after the pause causes a marked increase in muscular contraction and a sharp rise in outflow obstruction associated with a fall in aortic pressure. Unlike the other 2 subaortic obstructions, hypertrophic cardiomyopathy may present with sudden arrhythmic death in an otherwise healthy and undiagnosed patient and may be unrelated to the degree of outflow obstruction at rest.

**Indications for Intervention**

The principal effect of subaortic obstruction is increased ventricular afterload, with the same potential hypertrophy, arrhythmia, chamber compliance, and pulmonary venous congestion issues seen in other left-sided obstructive lesions. For fixed subaortic obstructive lesions, for patients who become symptomatic, or when significant LV hypertrophy is present, especially in the presence of systolic dysfunction, intervention is indicated. Surgery remains the definitive therapy for these lesions, although a number of authors have published small series using balloon angioplasty in children and in the veterinary literature. Balloon angioplasty may be effective in transiently reducing the level of obstruction in patients with thin membranes but appears to be palliative only because the obstruction invariably returns.

In patients with hypertrophic cardiomyopathy, the risk of sudden arrhythmic death appears to be independent of the degree of outflow obstruction. Underlying myocardial disorganization in the affected tissues may be the primary arrhythmogenic source. Thus, all patients with this diagnosis should be treated medically. β-Blockers or calcium channel blockers remain first-line therapy in this population. Implantable defibrillators are being used in the population at risk. When obstruction becomes significant, surgical myomectomy improves symptoms and transcatheter alcohol ablation of the septal tissue (by infusion into the feeding coronary branch) has developed as a promising alternative.

**Congenital Valvar Aortic Stenosis**

**Pathophysiology and Natural History**

Congenital aortic valve abnormalities are common in the population. A nonobstructive bicuspid aortic valve occurs in ≈1% of the population, with aortic valve stenosis presenting clinically in 3% to 8% of all CHD patients. Young adults with unobstructed bicuspid aortic valves are most often asymptomatic and undiagnosed. Most patients are discovered on the basis of a cardiac murmur, in the absence of other symptoms. With significant obstruction, LV afterload increases, the myocardium hypertrophies, and chamber compliance is reduced, which results in higher left atrial filling pressures. Blood pressure distal to the obstruction is normal. Rarely, patients may present with pulmonary venous congestion or coronary insufficiency with the increased output and workload associated with exertion. Children are almost never symptomatic, even with the most significant obstructions; however, aortic stenosis tends to progress and becomes more clinically significant as patients age.

When obstructed, the mechanism of aortic stenosis in young adults is generally fibrotic rather than calcification. But, these valves do tend to calcify and become obstructed or insufficient at an earlier age than the typical senescent tricommissural aortic valve. In addition, patients with bicuspoid valves have been found to have abnormalities of the connective tissues of the aorta and are prone to marked dilation of the ascending aorta even in the absence of significant obstruction or insufficiency. These patients should be followed up noninvasively to rule out rapid aortic growth, because root replacement may be required to prevent...
dissection. Currently, no clear consensus exists for this population as to the size at which prophylactic aortic root replacement should be performed.

**Indications for Intervention**

Currently accepted indications for intervention include symptoms of exercise intolerance with LV hypertrophy, with or without systolic dysfunction, a persistent decrease in myocardial systolic performance due to excessive afterload, or progressive dilation of the aortic root and ascending aorta (despite medical therapy) in association with an obstructed or regurgitant valve. Surgical valve replacement remains the treatment of choice for adult patients. A group from the Toronto General Hospital has recommended concurrent ascending aorta and/or root replacement for ascending aorta dimensions in excess of 4.5 cm. Balloon valvuloplasty may also be used as a bridge to surgical valve replacement, to assess the LV myocardial response to afterload reduction. In children, clinically important obstructions may present without symptoms and without calcification. Balloon valvuloplasty has been shown to have excellent short- and medium-term outcomes in this population. In general, peak-to-peak gradients of >50 mm Hg at rest (with normal cardiac output) are accepted as the threshold for intervention in children. The patient age at which balloon therapy is not indicated is not well defined.

A number of percutaneous valve implants have been developed recently and are undergoing initial clinical trials. This holds particular promise for the patient with combined calcific aortic stenosis and regurgitation. Current trials are limited to patients who have been refused surgery owing to age, cardiomyopathy, or other comorbid conditions.

**Supravalvar Aortic Stenosis**

**Pathophysiology and Natural History**

Supravalvar aortic stenosis is an unusual cardiovascular finding and is usually a marker for the Williams-Beuren syndrome, an easily recognizable neurodevelopmental disorder characterized by connective tissue and central nervous system abnormalities. Isolated supravalvar aortic stenosis occurs at the level of the sinotubular junction in ~70% of patients with cardiovascular manifestations. Diffuse hypoplasia and stenosis of the branch PAs is the most frequent associated finding, occurring in 41% to 57% of patients with supravalvar aortic stenosis. Other less frequent associations include coarctation of the aorta, valvar pulmonary stenosis, septal defects, and atrioventricular valve prolapse.

Physiologically, the supravalvar obstruction creates an increased afterload for the LV, depending on the severity of the narrowing, similar to valvar aortic stenosis; however, unlike valvar stenosis, the supravalvar lesion also imposes high pressure on the coronary arteries. A pathology series reported dilatation and tortuosity, as well as premature atherosclerotic disease, in this population, similar to patients with uncontrolled systemic hypertension, although the incidence of clinically severe coronary disease appears to be very small in the population with Williams-Beuren syndrome. Congenital stenosis of the coronary, renal, subclavian, splanchic, and carotid arteries has also been observed.

With a defined elastin-gene heterozygosity identified as the cause of the arteriopathy associated with this syndrome, it is interesting to note the unusual clinical course associated with these arterial obstructions. Mild supravalvar aortic obstructions (<20 mm Hg gradient) tend to regress or remain stable, as with aortic valve stenosis; however, some patients with more severe supravalvar obstructions have had regression in the degree of obstruction during long-term follow-up. On the pulmonary side, the tendency toward regression is the rule rather than the exception.

**Indications for Intervention**

Because a documented chance of regression exists, isolated supravalvar aortic stenosis without clinical or echocardiographic findings of LV dysfunction should be monitored noninvasively. In the setting of excessive LV afterload or with clinical symptoms, surgery is the treatment of choice. Interventional procedures are likely to fail. The thickened elastic tissue of the aortic root will be resistant to balloon angioplasty, like that of the supravalvar pulmonary stenosis, and stenting has no role so close to the aortic valve leaflets and the coronaries. In this type of systemic syndrome, the patient’s overall condition, including neurodevelopmental and endocrine status (not just the cardiovascular component), must be considered in making a recommendation to intervene.

**Coarctation of the Aorta**

Coarctation of the aorta is a congenital narrowing of the aorta that accounts for 5% to 8% of all CHD. The obstructive lesion occurs just distal to the origin of the left subclavian artery where the fetal ductus arteriosus had previously inserted into the aorta. The obstruction is usually a discrete, tubular narrowing, but common anatomic variations include long-segment stenosis and transverse aortic arch hypoplasia proximal to the coarctation. Histological abnormalities of the medial layer can be seen in the affected area. Between 50% and 85% of patients with coarctation also have a bicuspid aortic valve.

Obstruction of the aorta distal to the takeoff of the subclavian and carotid arteries creates not only an afterload for the LV but also a maldistribution of flow, similar to the branch PA obstructions. Although the proximal/upper segment of the aorta receives blood flow normally from the LV, there will be a diminished pressure head reaching the lower portions of the body distal to the obstruction (Figure 5). The juxtaglomerular apparatus in the kidneys, perceiving a low-flow condition, modulates vascular tone and intravascular volume through the secretion of vasoconstrictive substances to attempt to restore perfusion pressure in the distal aorta. With the fixed obstruction at the coarctation and maintenance of flow (cardiac output), the result is a significant blood pressure elevation proximal to the coarctation. Over time, the body will develop alternate pathways from the ascending to the descending aorta in the form of collateral arterial vessels.
Common clinical manifestations include angina, exertional fatigue, and leg weakness/claudication with exertion. They also complain of headaches, nosebleeds, cool extremities, and heart failure from chronically increased LV afterload. For the adult with unrepaired, isolated coarctation, the average survival is ≈35 years of age, with a 25% survival rate beyond 50 years of age.71

Patients may have undergone prior surgical or interventional procedures for coarctation. Surgical scarring or poor growth of the repaired segment after a childhood repair may result in restenosis. Older surgical repairs, in which Dacron conduits were used to bypass the obstructed segment, may become obstructed themselves. This may occur when a child outgrows the conduit placed, when neoendothelialization of the prosthesis narrows the lumen significantly, or as the result of “kinking” of the conduit from scarring or patient growth. In some patients, congenital hypoplasia of the proximal aortic arch may be unmasked as obstructive when the discrete coarctation site is opened successfully. In any of these recurrent coarctation situations, the clinical presentation and the underlying physiology are the same.

**Indications for Intervention**

Current indications for intervention in an adult patient include clinical symptoms, hypertension at rest, or severe hypertension with exertion. Because the hypertension associated with coarctation is due to a mechanical obstruction in the circulation, patients cannot be treated with any pharmacological therapy that reduces vascular tone, diminishes intravascular volume, or lessens cardiac output. The blood pressure, as measured in the arms, may be “corrected” with such medical therapy, but the result will be substantial reduction in the perfusion pressure of the lower part of the body. Coarctation of the aorta requires a mechanical solution to eliminate the pressure difference between upper and lower segments.

Surgical reconstruction of the aorta was the treatment from 194573 until the 1980s, when balloon angioplasty became a competitive option.74,75 More recently, endovascular stents for both native and recurrent coarctation of the aorta have gained acceptance as the procedure of choice in teenagers and young adults who have achieved full growth.76–84 Although early and mid-term follow-up data appear to favor stent angioplasty over balloon dilation in adults, stenting the aorta may still be associated with serious adverse events.85–88 Long-term outcomes remain unknown.

Covered stents89 may become the primary therapy in the future in an effort to avoid the potential complications of arterial dissection, tear, or rupture, but they are not yet available in the United States in sizes large enough for a typical aorta. No comparative studies have yet appeared that compare covered stents with other options.

**Conclusions**

Obstructive disease is relatively common in the adult population with CHD and may affect ventricular function significantly. Although most adult cardiologists are experienced and comfortable with the pathophysiology of isolated valvar and subvalvar aortic valve stenosis, right-sided outflow and arterial obstructions are less common. More distal obstructions in either the right or left sides of the circulation produce redistribution of blood flow to lower-resistance pathways, which creates more complicated physiologies. Comfort with
the physiology of the simple obstructions is critical in understanding the more complex congenital malformations that will be presented in the next article in this series.

Disclosures

None.

References


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