

LEFT VENTRICULAR OUTFLOW TRACT OBSTRUCTION

Definitions and Classification of LVOT Obstruction

Left ventricular outflow tract (LVOT) obstruction syndromes include subvalvar AS, valvular AS, aopravalvular AS. Congenital valvular aortic stenosis is usually bicuspid, but quadricuspid aortic valve associated with regurgitation and aortic dilatation may also rarely occur.¹ Aortic coarctation is also a form of LVOT obstruction.² Obstruction can occur singly or at multiple levels, as an isolated lesion, or in combination with septal defects or conotruncal anomalies. LVOT obstructions are congenital in the vast majority of individuals younger than 50 years although some variants of subaortic obstruction do exist.

Valvular Aortic Stenosis (Bicuspid Aortic Valve)

Epidemiology

Bicuspid aortic valve (BAV) is the most common congenital heart defect, with a prevalence estimated to 0.5-2%.^{3,4} There is a male predominance of approximately 3:1. In patients with symptomatic AS, younger than 65 years of age, a bicuspid valve is the most common pathological finding. Although BAV is more likely due to mutations in different genes with dissimilar patterns of inheritance,⁵ in about 20% to 30% of patients with a BAV, other family members also have a BAV and/or an aortopathy.⁶ Associated abnormalities (20% of patients with bicuspid valves) are coarctation and PDA. Aortic root and/or ascending aorta dilatation (bicuspid aortopathy) is present in 50% of patients.⁷ In addition BAV is found in several genetic syndromes involving left-sided obstructive lesions, such as Shone's syndrome (multiple left-sided lesions of inflow and outflow obstruction and parachute mitral valve), hypoplastic left heart syndrome, Williams syndrome with supra-aortic stenosis, and Turner syndrome with coarctation of the aorta.⁸ In patients with mutations known to affect normal aortic development, for example, FBN1 or TGF β pathway mutations, there is an increased prevalence of bicuspid aortic valve, suggesting an inherent link between bicuspid aortic valve formation and thoracic aortopathy in these groups.⁹ There is a shared genetic basis for left ventricular non-compaction and bicuspid aortic valve, with MIB1-NOTCH playing a crucial role.¹⁰ Relatives of patients with bicuspid aortic valve, thoracic aortic aneurysm, and thoracic aortic dissection also have a substantially higher aortic-specific mortality risk that follows a similar pattern.¹¹

Pathophysiology

The morphologic patterns of the bileaflet valve vary according to which commissures have fused, with the most common pattern involving fusion of the right and left cusps (Figure 1).

Approximately 13-30% of patients developed moderate or greater AR and 12-37% develop moderate or greater AS during follow up.¹² Aortopathy is present in approximately 20% to 40% of patients with a BAV and is associated with dilation of the aortic sinuses, the ascending aorta, and/or the arch.¹² Dilatation of the thoracic aorta is attributed to structural abnormalities of the medial layer of the aortic (and the pulmonary) wall such as decreased fibrillin, elastin fragmentation, and apoptosis, as well as valve-related haemodynamics and increased shear stress.¹³ The bicuspid valve is not stenotic at birth, but it is subjected to hemodynamic stress that leads to thickening and calcification of the leaflets.

Presentation and Natural History

The BAV condition exhibits a high lifetime morbidity burden where valvulo-aortopathy is close to unavoidable by age 90. The lifetime incidence of infective endocarditis is higher than that of aortic dissection.¹⁴ Symptoms usually develop in adulthood due to haemodynamically-induced calcification of the valve. By the age of 50 years 25-49% of patients will require surgery or suffer a major cardiac event.^{15,16} AS, AR, aortic aneurysm or dissection and endocarditis may occur.

Physical Examination

Ejection click followed by **murmur** of AS and possibly AR.

Investigations

Echocardiography The main task is to establish the diagnosis and exclude a tricuspid valve. The valve must be visualized in systole in the short-axis view since during diastole the raphe can make the valve appear trileaflet. In diastole, the orifice has a characteristic "fish mouthed" appearance. Evaluation of patients with a bicuspid valve, and LVOT obstruction in general, are presented in Figure 1, and Tables 1 and 2.

Transesophageal echocardiography or **cardiac magnetic resonance** may be needed in case of uncertainty.

Exercise stress testing is useful in patients with a mean Doppler gradient greater than 30 mm Hg or peak Doppler gradient greater than 50 mm Hg if the patient is interested in athletic participation or if clinical findings differ from noninvasive measurements.

Dobutamine stress testing may be used in the evaluation of a mild aortic valve gradient in the face of low LV ejection fraction and reduced cardiac output.

First-degree relatives of patients with a bicuspid aortic valve should be evaluated for the presence of a bicuspid aortic valve and asymptomatic thoracic aortic disease.

Therapy

Beta blockers in aortic root dilatation, and ACEI/ARB in hypertension are useful. Statins may also be used to slow the degenerative process. Patients with moderate AS (mean gradient at least 25 mmHg or peak at least 40 mm Hg) should be restricted from competitive sports.¹⁷

Valvuloplasty is the treatment of choice in children and perhaps young adults with BAV. Following successful valvuloplasty sudden death is extremely rare and exercise restriction is not recommended.¹⁸ Techniques for repairing a bicuspid valve might vary depending on the different valve phenotypes.¹⁹ In experienced centers, the Ross procedure may also be considered in the absence of AR or a dilated aorta.²⁰ The aortic root size should be taken into account. Aortic root size > 5.5 cm, or >4.5 cm when valve surgery is contemplated indicates AVR and root replacement,^{6,21} and changes in root size more than 0.5 cm/year is probably also an indication for root replacement.⁷ Recommendations are provided in Figure 2 and Tables 3-5.

Pregnancy

Patients with bicuspid aortic valves may have an associated aortopathy making them prone to dilation and potentially dissection of the aortic root or ascending aorta. In women with bicuspid aortic valves, the aortic root and ascending aorta should be evaluated before pregnancy. Although data are limited, it is usually recommended that patients with aortic root dilatation associated with congenital bicuspid aortic valves should be advised to avoid pregnancy if their aortic root dimensions are ≥ 4.5 cm.²² Results from the ROPAC registry suggest that even patients with severe AS tolerate pregnancy well, unless if they are symptomatic.²³

Subvalvular Aortic Stenosis

Subvalvular 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 hypertrophic cardiomyopathy.²⁴ In patients with ***membranous obstruction***, a thin fibrous membrane of variable thickness and with a central lumen stretches across the LV outflow tract from the septal surface to the anterior leaflet of the mitral valve. In adults, as opposed to children, progression of the obstruction and development of AR is slow over time. With the ***tunnel-type obstruction***, a thick fibromuscular tubular narrowing diffusely reduces the diameter of the outflow tract. This condition has to be differentiated from hypertrophic cardiomyopathy. Aortic regurgitation is present in 30–80% of patients and thought to develop secondary to aortic valve damage caused by the high-velocity subvalvular jet.²⁵ Surgery is offered when symptoms in the context of a peak gradient > 50 mmHg or LV hypertrophy with reduced systolic function develop. Survival is excellent after surgery for discrete subaortic stenosis, but over time the LVOT gradient slowly increases, mild AR is common, and reoperation for recurrent discrete subaortic stenosis may be needed.²⁶ Myectomy does not show additional advantages, and because it is associated with an increased risk of complete heart block, it should not be performed routinely.²⁶ Stress testing

to determine exercise capability, symptoms, ECG changes or arrhythmias, or increase in LVOT gradient is reasonable in the presence of otherwise equivocal indications for intervention. Lifelong cardiology follow-up is recommended in all patients with subaortic stenosis. Patients without operation should be subjected to yearly echocardiograms. Discrete subaortic stenosis progresses very slowly in adulthood, but patients with associated congenital lesions, particularly a VSD, are at risk for faster disease progression and should be monitored cautiously.²⁵ In patients with isolated thin discrete subaortic stenosis, transluminal balloon tearing of the membrane is another option with good long-term results.²⁷ Women with serial left heart obstructive lesions have higher maternal cardiovascular event rates.²⁸ **Pregnancy** is contraindicated in symptomatic patients with significant LV outflow obstruction or coronary artery abnormalities.²² General recommendations are provided in Figure 2 and Tables 6 and 7.

Supravalvular Aortic Stenosis

Rare condition usually associated with the Williams-Beuren syndrome (neurodevelopmental disorder characterized by connective tissue and central nervous system abnormalities).^{24,29} Isolated supravalvar aortic stenosis occurs at the level of the sinotubular junction in 70% of patients with cardiovascular manifestations. The supravalvar lesion may involve the entire aortic root, the coronary arteries, and/or the aortic valve, and in children it is felt to be a progressive disease, perhaps related to an inadequate growth of the supravalvar aortic root and the sinotubular junction. However, progression of subvalvular AS in adulthood is rare.³⁰ Diffuse hypoplasia and PA stenosis, coarctation of the aorta, and septal defects, are other associated conditions. TTE and/or TEE and either MRI or CT should be performed to assess the anatomy of the LVOT, aortic and mitral valve, the ascending aorta, and main and branch pulmonary artery anatomy. Adults with a history or presence of supravalvar AS should be screened periodically for myocardial ischemia. Due to the potential of regression, surgery is recommended in the case of symptoms in the context of a peak gradient > 70 mmHg or LV dysfunction (Figure 2 and Tables 8 and 9).

Supravalvar AS, whether associated with Williams syndrome or nonsyndromic, has a strong likelihood of being an inherited disorder. Undetected family members may be at risk for hypertension, coronary disease, or stroke; therefore, all available relatives should be screened. Patients with significant obstruction, coronary involvement, or aortic disease should be counseled against **pregnancy**. Women with serial left heart obstructive lesions have higher maternal cardiovascular event rates,²⁸ and pregnancy is contraindicated in symptomatic patients with significant LV outflow obstruction or coronary artery abnormalities.²²

Cor triatriatum

Cor triatriatum occurs when a membrane divides either the left atrium (sinister), or right atrium (dexter).³¹ Cor triatriatum sinister is usually associated with other congenital malformations, specifically ASD, VSD, or anomalous pulmonary venous connection (partial or total). The left atrial appendage is invariably in the same chamber as the mitral valve, separated from the pulmonary veins by the membrane. Supravalvular mitral stenosis is typically caused by a fibrous ring on the atrial side of the mitral valve, separating the mitral valve from both the left atrial appendage and the pulmonary veins. The finding will have similar physiology to cor triatriatum and similar indications for intervention. It can be associated with an abnormal mitral valve that may also require intervention (Table 10).

Congenital mitral stenosis

Parachute mitral valve is most commonly found in the presence of other congenital abnormalities, such as the components of Shone complex.⁸ Indications for intervention in mitral stenosis are the same with those in patients with non-congenital mitral disease. Follow-up is presented in Table 11.

Turner syndrome

Women with Turner syndrome are at substantial risk of bicuspid aortic valve, coarctation, and aortic enlargement. Dissection may occur at smaller aortic diameters than in non-Turner aortopathy, and prophylactic surgery is reasonable, particularly if rapid dilation is present (Tables 12 and 13, and Figures 3 and 4).³²

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