

# Aortic Stenosis

## Introduction

Aortic stenosis is defined as the reduction of the orifice of the aortic valve caused by a failure of the leaflets to open fully during systole. This leads to progressive concentric left ventricular hypertrophy and eventual heart failure. Left ventricular outflow obstruction most commonly occurs at the aortic valve, however it can occur above the aortic valve (supravalvular) or below the aortic valve as in hypertrophic obstructive cardiomyopathy. Severe uncontrolled systemic hypertension (increased afterload) may have similar hemodynamic effects on the heart when compared to AS, since both disease states result in a significantly increased afterload. However cardiac reserve is severely limited in AS when compared to hypertension due to the reduced and fixed aortic valve area causing the symptoms of AS to be predominantly exertional.

## Etiologies

The most common cause of AS in a person over the age of 70 results from calcification of a normal trileaflet aortic valve. This process is sometimes referred to as “senile degeneration”. Known risk factors for developing degenerative calcific AS include hypercholesterolemia and diabetes. The exact cause of the degeneration is unknown, however it is speculated that high pressures and turbulence over long periods of time creates an inflammatory state resulting in infiltration of macrophages and T lymphocytes with resultant calcification.

The most common cause of AS in a person under the age of 70 results from a congenital bicuspid aortic valve. Approximately 2% of the population is born with a bicuspid aortic valve and about half of these individuals develop at least mild AS by the age of 50.

Rheumatic valvular disease is responsible for AS on occasion. There is almost always concurrent disease of the mitral valve present and frequently at least some AI accompanies AS in this situation. While the incidence of rheumatic AS is quite low in the US, the worldwide incidence is much higher.

Congenital AS results from fusion of the aortic valve leaflets at birth. Infants with congenital AS exhibit significantly more left ventricular hypertrophy than do adults, yet they rarely develop symptoms of heart failure. Sudden death without prior symptoms occurs in about 15% of cases.

Other rare causes of AS include inflammatory diseases (i.e. SLE or RA), severe familial hypercholesterolemia, ochronosis, Paget’s disease of the bone, and Fabry’s disease.

## Signs and Symptoms

The classic triad of symptoms of AS occur on exertion and include dyspnea, syncope, and angina. The development of AS takes many years and is initially asymptomatic. Dyspnea is the first symptom of AS in about 50% of the cases while syncope and angina account for 35% and 15% of initial symptoms respectively. The clinical significance of a patient with AS exhibiting symptoms cannot be underemphasized since the onset of symptoms is accompanied by a dramatic increase in mortality. If aortic valve replacement is not performed, patients presenting with dyspnea have a mean life expectancy of 2 years, those with syncope about 3 years, and those with angina an average of 5 years.

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Angina in AS occurs frequently in the absence of coronary artery disease. Instead, myocardial ischemia develops when the oxygen demand of the severely hypertrophied left ventricle exceeds oxygen supply. The Law of Laplace explains this phenomenon:

$$\text{LV wall stress} = \frac{\text{LV pressure} \times \text{LV radius}}{2 \times \text{LV wall thickness}}$$

Note: LV wall stress is directly proportional to myocardial O<sub>2</sub> demand, more specifically, O<sub>2</sub> demand = wall stress X HR

Using the above equation, we can understand the pathologic process that develops over many years in patients with AS. As LV pressure slowly increases over time due to worsening AS, a parallel increase in LV wall thickness occurs (concentric hypertrophy) in order to maintain the LV wall stress at a constant level (since LV wall stress is an important determinant of myocardial O<sub>2</sub> demand). Eventually, the LV is unable to hypertrophy any further, but the LV pressure continues to rise as the AS worsens. This leads to a rise in LV wall stress and thus a rise in LV myocardial oxygen demand. When the heart rate increases in response to exertion (heart rate is also a determinant of myocardial O<sub>2</sub> demand), a significant supply vs. demand mismatch occurs resulting in myocardial ischemia and the clinical symptoms of angina.

Effort syncope occurs in AS due to a sudden decrease in cerebral perfusion upon exertion. During exercise, the total peripheral resistance decreases significantly since blood is being shunted to working muscles. In the presence of significant AS, the cardiac output cannot increase enough to accommodate this decreased TPR and cerebral perfusion is compromised resulting in syncope. This idea can be further reinforced by recalling the following equation: MAP = CO X TPR (MAP = mean arterial pressure, CO = cardiac output, TPR = total peripheral resistance). So if the cardiac output cannot increase due to severe AS and the TPR decreases, the MAP will subsequently decrease leading to decreased cerebral perfusion and syncope. It is important to note that another important cause of syncope in patients with AS is arrhythmias, especially atrial fibrillation and AV nodal blocks, as will be described later.

Dyspnea on exertion is due to heart failure. Both systolic and diastolic dysfunction typically contributes to heart failure in patients with AS. Other classic symptoms of heart failure are also common and include orthopnea, PND, and signs of right-sided heart failure (i.e. peripheral edema and right upper quadrant pain).

Other rare initial symptoms in patients with AS include embolic phenomenon from calcified AV plaques and massive gastrointestinal bleeding due to angiodysplasia (Heyde's syndrome). Heyde's syndrome is thought to be due to disruption of the pentamer structure of the von Willibrand factor as it traverses the severely stenotic aortic valve leading to an increase tendency to bleed from angiodysplasias.

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## Physical Examination

Auscultation of the heart in patients with AS can be very helpful in both diagnosis and determining the severity of disease. The typical murmur of AS is a high-pitched crescendo-decrescendo systolic ejection murmur heard best at the right upper sternal border radiating to the carotid arteries (see figure below). In mild AS the murmur peaks in early systole, however as disease progresses the peak moves later in systole. The intensity of the murmur typically increases as disease progresses however when heart failure develops and cardiac output declines, the murmur becomes softer. Thus the intensity of the murmur is NOT a good indicator of disease severity.

Auscultation at the cardiac apex may reveal a murmur that may sound holosystolic and mimic the murmur of mitral regurgitation. However this is commonly the result of radiation of the murmur of AS to the apex rather than coexistent mitral regurgitation. This finding is referred as Gallivardin's dissociation. To determine if the apical murmur is indeed due to MR or radiation of the murmur of AS, dynamic auscultation can be undertaken (see section on dynamic auscultation). The murmur of hypertrophic cardiomyopathy can also at times sound similar to that of AS. The Valsalva maneuver decreases the murmur of AS while it increase the murmur of hypertrophic cardiomyopathy.

The S<sub>2</sub> heart sound is often paradoxically split in patients with AS due to the significantly delayed closure of the aortic valve resulting from the increased time needed to complete LV systole. As disease progresses and the aortic valve leaflets lose their mobility, the intensity of S<sub>2</sub> decreases. When the S<sub>2</sub> sound is no longer audible, it can be concluded that the AS is relatively severe. A S<sub>4</sub> heart sound is also often present due to the severe concentric left ventricular hypertrophy that develops in AS. If a S<sub>3</sub> heart sound is present, then significant systolic dysfunction has developed which is common in end stage AS.

Perhaps the best bedside method to estimate the severity of AS is derived from evaluation of the carotid arteries. The phenomenon known as "pulses parvus et tardus" refers to a weak (parvus) and delayed (tardus) carotid upstroke. To assess for "parvus", it is often helpful to palpate your own carotid artery (assuming you do not have significant AS) while concurrently palpating the patient's carotid artery. It is important to note that in some elderly individuals the carotids may be stiff due to calcification, which may falsely normalize the carotid upstroke. To assess for "tardus", auscultate the patient's S<sub>2</sub> heart sound while palpating their carotid upstroke. The S<sub>2</sub> and carotid upstroke should occur almost simultaneously. If the carotid upstroke comes significantly after the S<sub>2</sub> heart sound, "tardus" is present indicating severe AS. Other physical exam findings in patients with AS include those of both right and left heart failure.

## Diagnosis

The EKG in patients with AS frequently shows LVH with strain and left atrial enlargement, however no findings are specific for AS. The chest radiograph may reveal a normal cardiac size since the hypertrophy in AS is concentric. Calcification of the aorta, pulmonary congestion, and post-stenotic dilation of the aorta are other non-specific findings.

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The echocardiogram can both confirm the diagnosis of AS and quantify the severity. Two-dimensional echocardiography can demonstrate a thickened aortic valve, reduced leaflet mobility and concentric LVH. Doppler is used to quantify the severity of AS by measuring the pressure gradient across the aortic valve and by calculating the aortic valve area (AVA). The velocity of blood flow across the aortic valve, as determined by m-mode Doppler, is used to calculate the transaortic pressure gradient using the modified Bernoulli equation: pressure gradient =  $4v^2$  where  $v$  = velocity. The AVA is calculated using the continuity equation:

$$A_1 \times V_1 = A_2 \times V_2$$

$$A_2 = (A_1 \times V_1) / V_2$$

Where  $A_1$  is the area of the left ventricular outflow tract,  $V_1$  is the velocity of flow at the left ventricular outflow tract,  $A_2$  is the area of the aortic valve, and  $V_2$  is the velocity of flow at the aortic valve. All of the above except  $A_2$  can be directly measured using either m-mode or Doppler echocardiography. The AVA is the calculated as shown above.

Cardiac catheterization is indicated when the angina of AS may be due to coexistent coronary disease or when aortic valve replacement is indicated. Rarely catheterization may be needed if echocardiography is unable to determine if severe AS is present. During cardiac catheterization, the cardiac output and pressure gradient are measured and used to calculate the AVA using the Gorlin equation below:

$$AVA = CO/SEP \times HR / (44.3(G))^{1/2}$$

The pressure gradient is found simply by using the catheter to measure the pressure in the aorta, then advancing the catheter into the LV and taking another pressure reading. The difference between these two pressures is the pressure gradient. The mean transaortic valve pressure gradient is used in the Gorlin equation to calculate the AVA. The cardiac output is calculated using either the Fick principle or the indicator-dilution principle. It is important to note that the Gorlin formula was originally derived using patients with mitral stenosis, not aortic stenosis. The Gorlin equation is also flow dependant, so if the patient has a significantly decreased ejection fraction, the AVA may be underestimated. Another useful indicator of severity of AS, the valvular resistance (VR), can be calculated during cardiac catheterization. The equation to do so is below:

$$VR = (\text{pressure gradient} \times HR \times SEP \times 1.33) / CO$$

	AV gradient (mmHg)	AVA (cm <sup>2</sup> )
Mild	< 25	> 1.5
Moderate	25-50	1 – 1.5
Severe	51-80	0.7 – 1
Critical	> 80	< 0.7

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### Treatment

The only effective treatment for aortic stenosis is removal of the mechanical obstruction. To this end, only aortic valve replacement has been shown to achieve this while reducing mortality. Aortic valve debridement via surgery or ultrasound debridement is a poor alternative to AVR. High rates of aortic regurgitation occur with these procedures and the AS may recur in a large percentage of patients. Pharmacological therapy is in general not effective in AS. In fact, in severe AS, many of the standard cardiovascular medications such as ACE inhibitors and B-blockers are considered contraindicated.

Aortic balloon valvuloplasty is very beneficial in congenital AS where no calcification of the AV has occurred, however, every other type of AS is accompanied by significant calcification and this modality is generally not effective. In adults with AS, valvuloplasty does not result in regression of LVH. In fact, at 6 months after valvuloplasty about 50% of patients have completely restenosed their AV to the same extent as before the procedure. The procedural mortality rate is 2-5%, similar to that of aortic valve replacement (AVR). In addition, long term studies have shown that the overall mortality of patients undergoing AV valvuloplasty for AS are the same as if they did not have the procedure at all. Therefore, the role of valvuloplasty is limited to palliative treatment of severe AS or as a bridge to AVR in patients with severe AS.

Surgical AVR is the definitive treatment for all types of AS excluding congenital AS. Any patient who is symptomatic from AS should undergo AVR as soon as possible. AVR is generally not indicated for asymptomatic patients unless echocardiographic surveillance reveals rapidly progressing AS with LV dysfunction or severe calcification of the AV. Even in patients with critical AS, AVR is still beneficial. The ejection fraction may double or return to normal and the LVH usually regresses. It is rarely ever considered too late to replace the aortic valve in patients with critical AS unless coexisting conditions increase the risk of surgery.

A good approach to AS is to order regular echocardiograms and if the pressure gradient is  $> 30$  mmHg, repeat the history and physical every 6 months and instruct the patient to notify their physician if any signs of AS develop.

In general, patients with a low transaortic valve gradient of less than 30 mmHg and advanced heart failure do not improve after AVR. It is thought that in this subgroup irreversible myocardial remodeling has occurred. However, a minority of these patients to improve significantly after AVR, so the risks of no improvement must be discussed with these patients before AVR is undertaken.