Look at the Valve— A Case of Aortic Stenosis That Isn't

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A 16-year-old woman presents complaining of chest discomfort, dyspnea, and palpitations that occur with exertion and 'eating fast.' Her symptoms resolve with rest or eating more slowly. She is a recent immigrant and has had no regular medical care. She is a high school sophomore with normal intelligence and was physically active until several years ago, when she began to notice a steady decline in her exercise capacity. On exam, her heart rate is 78bpm and regular, and her blood pressure is 123/70mmHg in the right arm and 110/70mmHg in the left arm. She has a III/VI systolic ejection murmur heard throughout the precordium, loudest at the right upper sternal border, that radiates to the carotids. The remainder of the cardiac exam is normal. Her lungs are clear and her extremities are warm. The only other abnormal finding on exam is yellowish raised skin lesions on the extensor surfaces of the arms and legs. Her mother recently established medical care and was found to have high cholesterol, which is being treated with a statin. There is no other significant family history, particularly of congenital or acquired heart disease.

Her electrocardiogram is normal. Laboratory data show normal renal and hepatic function, with normal complete blood count, brain natriuretic peptide (BNP) 11pg/ml, total cholesterol 628mg/dl, low-density lipoprotein (LDL) 601mg/dl, high-density lipoprotein (HDL) 20mg/dl, and triglycerides 85. Her echocardiogram shows normal left ventricular size and function. The aortic valve is trileaflet with mildly thickened leaflets and no abnormalities of other valves (see *Figure 1*). The peak aortic velocity was 3.8m/s (see *Figure 2*), giving a peak instantaneous gradient of 57mmHg and a mean gradient of 29mmHg. The left ventricular outflow tract (LVOT) velocity is 1.0m/s and the LVOT diameter is 1.8cm, yielding a calculated aortic valve area of 0.7cm^2.

A detailed evaluation of the echocardiogram noted several relevant findings. The first was the appearance of the aortic valve. On 2D imaging the valve opened well without regurgitation, but appeared to have a relatively small annulus. The second was the appearance of the ascending aorta, which was small by 2D echocardiography, and on color Doppler had a relative narrowing in the area of the sinotubular junction (see *Figure 3*). The findings of left ventricular outflow obstruction with an aortic valve that opened normally raised the possibility that while the aortic annulus was small, the outflow obstruction was largely at the subaortic or supra-valvular level. The appearance of the ascending aorta was most suggestive of supravalvular aortic stenosis. Careful efforts to determine the location of the maximal obstruction by transthoracic echocardiography (TTE) were unsuccessful, although there was evidence of atherosclerosis in the visualized portions of the aorta.

Her lipid panel, skin findings, and very premature atherosclerotic disease are consistent with a homozygous familial hyperlipidemia (FH). Although a transesophageal echocardiogram (TEE) would have allowed further assessment of the location of her LV obstruction, the concern for concomitant symptomatic coronary disease prompted a cardiac catheterization to evaluate for coronary artery stenosis and to further assess the left ventricular obstruction. Angiography demonstrated a significant stenosis of the left main coronary artery and supravalvular stenosis of the aorta (see *Figure 4*). The peak-to-peak gradient from the left ventricle to the ascending aorta was 30mmHg, with the majority of the obstruction occurring distal to the aortic valve. It was felt that the majority of her symptoms were related to her coronary disease and that her most life-threatening abnormality was the left main coronary stenosis. Therefore, she was

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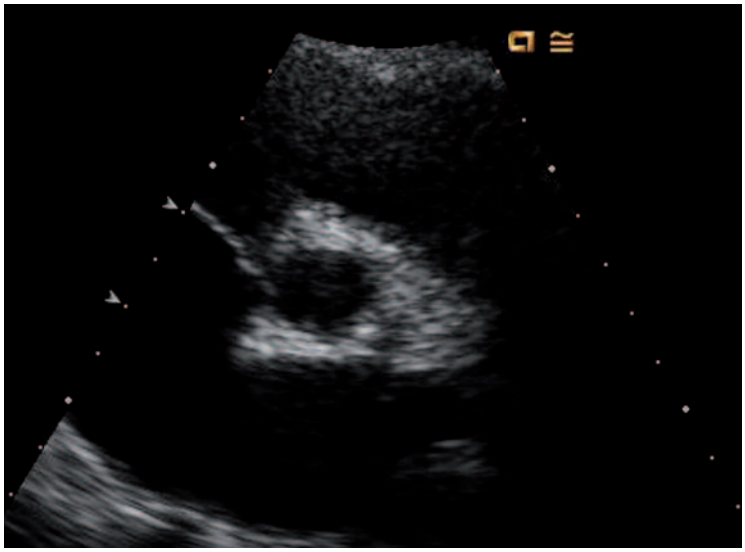
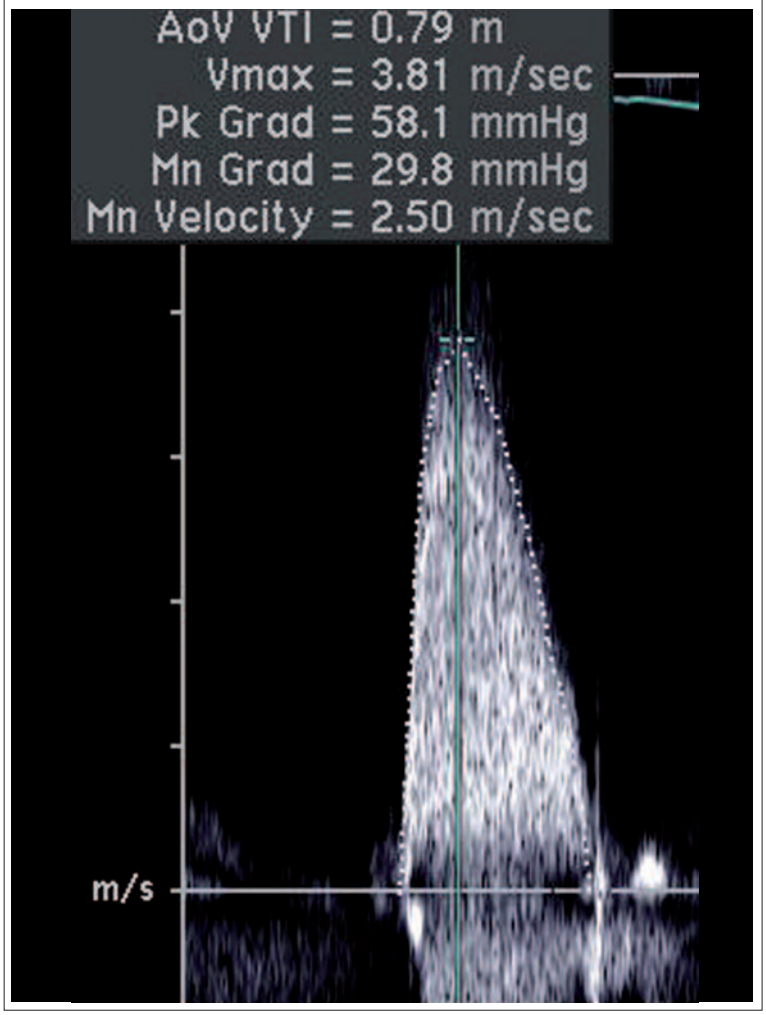
Figure 1: Parasternal Short-axis View of the Open Aortic Valve



Note the circular opening that appears similar in size to the aorta, suggesting the leaflets open normally

Figure 2: Doppler of the Aortic Gradient with a Peak Velocity of 3.8m/s



referred for minimally invasive off-pump bypass grafting with a left internal mammary artery (LIMA) to the left anterior descending (LAD), with significant improvement in her symptoms post-operatively. She will likely need aortic surgery at some point, but it was felt optimal to pursue this after six to 12 months of treatment for her hyperlipidemia, provided she remains asymptomatic.

This case emphasizes the importance of using all of the echocardiographic data available in making an accurate diagnosis. Doppler echocardiography is the mainstay of evaluation of aortic stenosis severity and there are ample data correlating Doppler data with outcomes in patients with valvular aortic stenosis. Specifically, in addition to allowing calculations of gradients and valve area, peak aortic velocity is an independent predictor of outcome in patients with valvular aortic stenosis.[1] Consequently, much attention is paid to the peak transvalvular Doppler velocity in assessing patients with valvular aortic stenosis. However, important information can be found in the 2D echo assessment as well. 2D echo imaging allows evaluation of the hemodynamic sequelae of aortic stenosis such as left ventricular hypertrophy, left ventricular systolic and diastolic function, and concomitant valve lesions. Importantly, 2D imaging also provides information about valve structure. While calcification of trileaflet aortic valves is common, it is important to identify bicuspid valves, with their attendant association with aortopathy. In some cases, the distinction may not make a significant difference in management; however, there are differences in the recommendations for surgical therapy of bicuspid aortic valves related to the ascending aortopathy found in some patients. The American College of Cardiology (ACC)/ American Heart Association (AHA) guidelines recommend surgical replacement of the aorta if it is over 4.5cm (when performing other valve surgery) or 5.0cm (with or without other valve surgery). Therefore, in order not to miss associated aortic pathology, an accurate assessment of the number of leaflets is important in decision-making and therapeutic interventions.

Additionally, noting the mobility of the leaflets may be the first clue that stenosis is occurring somewhere other than at the valve, as seen in this case. While valvular aortic stenosis is much more common, stenosis can develop either below or above the valve. While both are rare, subvalvular stenosis is more common than supravalvular stenosis.

Subvalvular Aortic Stenosis

Subvalvular aortic stenosis is most typically caused by a fibromuscular ring or ridge below the aortic valve. The ring may be immediately below the valve or up to 2cm

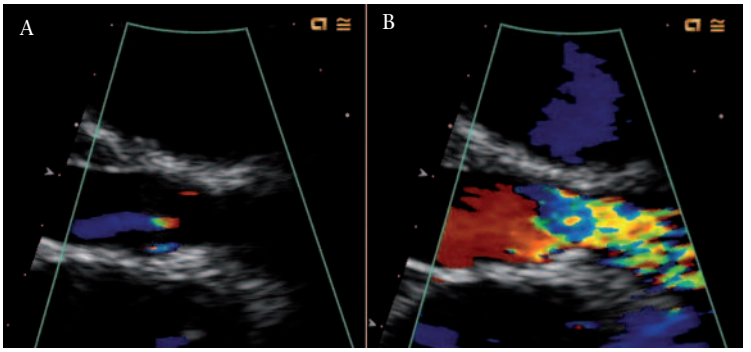
into the ventricle. They often extend onto the anterior mitral leaflet and may extend onto the ventricular surface of the aortic valve. Subaortic stenosis is a fixed obstruction and is different from the dynamic LVOT obstruction caused by hypertrophic cardiomyopathy. Subaortic stenosis is often isolated but may be associated with other congenital abnormalities such as ventricular septal defects, and may arise after surgery to repair a congenital defect, such as VSD closure. The tubular narrowing of the LVOT is particularly seen in patients with atrioventricular septal defects in whom part of the defect is a long narrow 'gooseneck' deformity of the LVOT.

Hemodynamically, the impact of a fixed subaortic obstruction due to a fibromuscular membrane is similar to that of valvular aortic stenosis and unlike the dynamic obstruction of hypertrophic cardiomyopathy, which is due to septal hypertrophy and systolic anterior motion of the mitral leaflets or chordae. Septal hypertrophy may occur in patients with fixed subaortic stenosis, however, and the relative contribution of each to LVOT obstruction may be difficult to discern. Even with trileaflet aortic valves that are otherwise normal, the turbulent flow under the aortic valve and the attachments to the aortic valve can result in leaflet thickening and concomitant aortic regurgitation.

Subaortic stenosis is most frequently diagnosed in childhood, although some cases may present in adulthood. Diagnosis of the abnormality is typically suspected when there is evidence of LVOT obstruction but 2D imaging shows pliable aortic valve leaflets. The fibromuscular ridge can be seen on 2D imaging (see *Figure 5*), although if it is posterior or close to the aortic valve, or image quality is poor, TEE may be necessary to better define the anatomy. While valve area *per se* is not a particularly germane calculation in this abnormality, severity is assessed by aortic velocity and evidence of hemodynamic consequence, such as LV hypertrophy (LVH) or LV dysfunction.

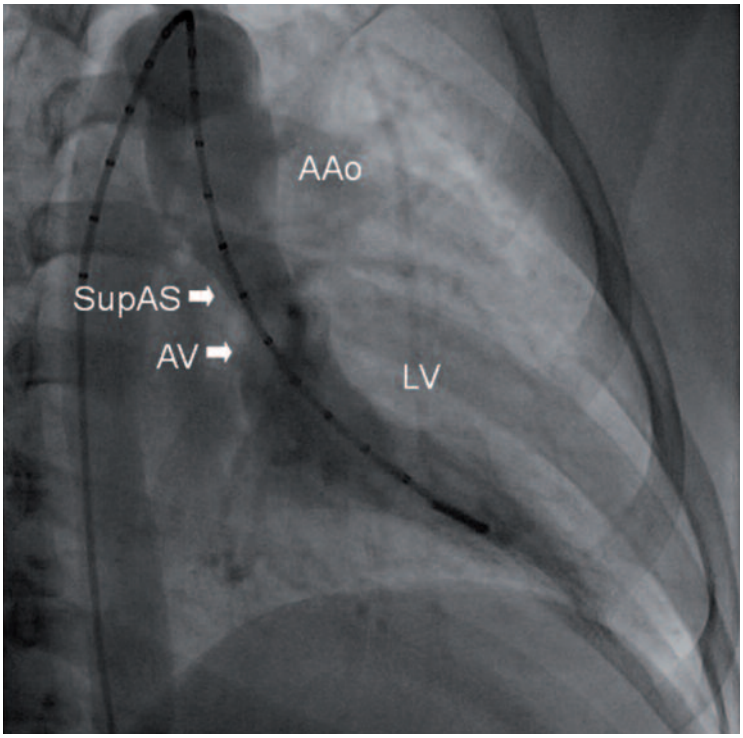
The indications for repair are similar to those for valvular aortic stenosis. Subaortic membranes must be excised surgically as balloon angioplasty is not useful in alleviating the stenosis and is associated with rapid recurrence of obstruction. Based on the ACC/AHA Guidelines for the Care of Adults with Congenital Heart Disease, surgical repair is recommended if the mean gradient is >30mmHg and/or peak gradient is >50mmHg as assessed by Doppler echocardiography. Surgery is also recommended for lesser gradients if there is progressive aortic regurgitation and an LV end systolic dimension >50mm or LV ejection fraction (LVEF) <55%. Surgery could be considered at lesser gradients if pregnancy is planned, if there is LVH, or if the patient plans to participate in competitive sports.[2]

Figure 3: Parasternal Long-axis View of the Ascending Aorta with Color Doppler



A: Trace aortic insufficiency with narrowing distal to the aortic valve. B: Color Doppler demonstrating turbulent flow in the area of narrowing seen on the other view.

Figure 4: Aortography Demonstrating a Stenosis Above the Aortic Valve



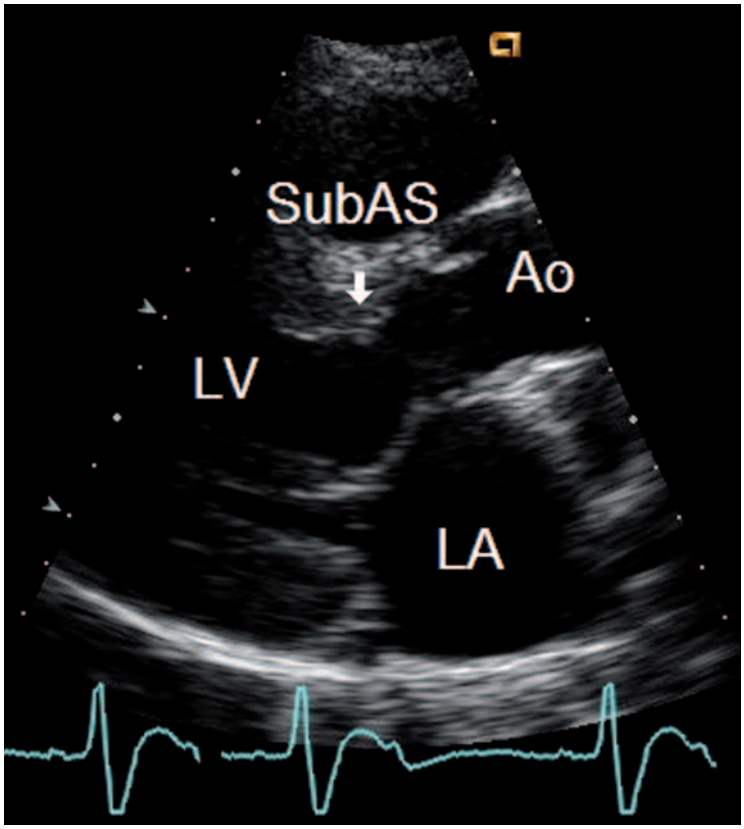
AAo = aorta; AV = aortic valve; LV = left ventricle; SupAS = supra-aortic stenosis.

Patients require lifelong follow-up after repair as the fibrous rings may recur.[3] Aortic regurgitation may be progressive, even after surgical treatment of the subaortic stenosis. Risks for recurrence of subaortic stenosis include proximity of the fibrous ring to the aortic valve, severe obstruction, and the need to peel the ring from the valve leaflets during repair.[4]

Supravalvular Aortic Stenosis

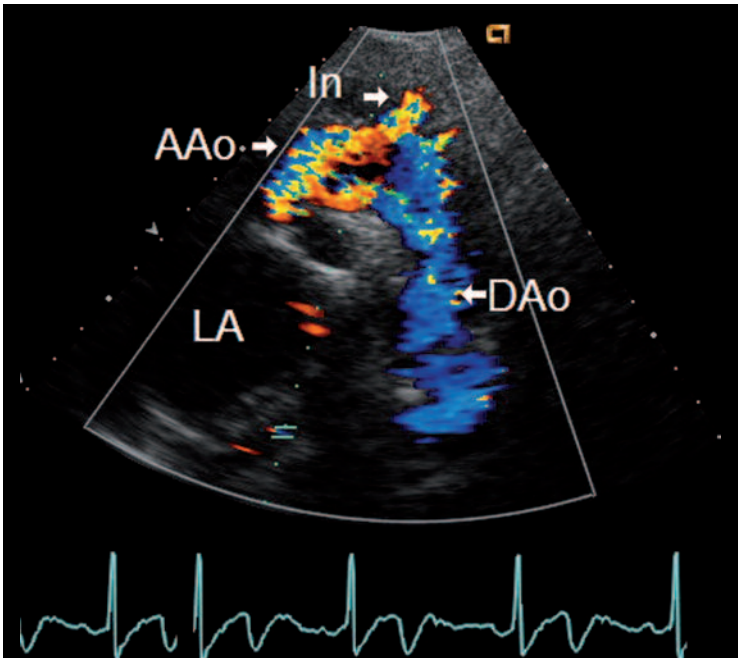
Supravalvular aortic stenosis occurs in the ascending aorta, typically distal to the coronary ostia in the area of

Figure 5: Parasternal Long-axis View of a Subaortic Membrane



Ao = aorta; LA = left atrium; LV = left ventricle; SubAS = subaortic stenosis.

Figure 6: Suprasternal Notch Views of Supravalvular Aortic Stenosis with Color Doppler Showing the Coanda Effect



Note the turbulent flow directed to the innominate artery.
AAo = ascending aorta; Dao = descending aorta; In = innominate artery; LA = left atrium.

the sinotubular junction. Unlike subaortic stenosis, the obstruction tends to be due not to a discrete ring, but rather to an 'hourglass' deformity of the proximal aorta, with maximal narrowing distal to the coronary ostia near the sinotubular junction. It may also be due to a hypoplastic segment of the ascending aorta and, very rarely, to a discrete ridge. The difference in pathology is emphasized by the frequent occurrence of obstruction throughout the proximal aorta, including the coronary ostia, even in patients with a seemingly discrete hourglass-shaped focal stenosis.[5] The flow alteration in supravalvular aortic stenosis is distinctive, resulting in a higher blood pressure in the right arm due to a Coanda effect entraining flow to the right subclavian artery (see *Figure 6*).[6]

The physiology of supravalvular stenosis is also similar to valvular aortic stenosis, except that in supravalvular aortic stenosis the coronary ostia are proximal to the obstruction, unlike subaortic and valvular aortic stenosis. Any of the disease processes that cause supravalvular stenosis may also result in ostial narrowing of the coronary arteries. In some patients, the coronaries may be dilated, possibly in response to high pressures, while others have ostial stenosis resulting in impaired perfusion. Readily inducible myocardial ischemia may occur due to the combination of LVH and altered coronary perfusion, including impaired diastolic filling.

Although supravalvular aortic stenosis is rare, it is seen frequently in two conditions: Williams syndrome and homozygous familial hyperlipidemia (FH). The genetic abnormalities of Williams syndrome include an elastin abnormality that results in supravalvular aortic stenosis. Williams syndrome includes other non-cardiac features such as developmental delay, 'elfin' faces, and a very friendly demeanor ('cocktail personality'). Supravalvular stenosis is usually identified in infancy or childhood in Williams syndrome patients, but may be progressive such that it does not become significant until patients are older.

Homozygous FH results from a lack of LDL receptors that leads to profoundly elevated LDL levels beginning in childhood, and causes very premature atherosclerosis. Homozygous FH is very rare, while not surprisingly, heterozygous FH is more common. Premature atherosclerosis in the form of coronary artery disease, aortic stenosis, and supravalvular aortic stenosis due to atherosclerosis is common in adolescents and young adults with homozygous FH. Supravalvular aortic stenosis has been reported in as many as 44% of patients with homozygous FH.[7,8] There remains uncertainty as to whether the stenosis is purely due to atherosclerosis or if there are structural abnormalities as well.

Symptoms of supravalvular aortic stenosis are similar to those of aortic stenosis. However, as seen in our patient, coronary artery disease in patients with homozygous FH or coronary obstruction in Williams syndrome must raise suspicion that exertional symptoms may not be solely due to supravalvular obstruction. The threshold for surgical repair of supravalvular aortic stenosis is greater than that for subvalvular aortic stenosis. Surgery is recommended for those patients with symptoms and/or a mean Doppler gradient of >50mmHg or a peak Doppler gradient of >70mmHg. Patients with lesser degrees of obstruction can be considered for surgical repair if there are symptoms, planned increase in exercise, planned pregnancy, LVH, or LV dysfunction.[2] Coronary obstructions may require intervention but, like surgical procedures to alleviate supravalvular aortic stenosis, this should be undertaken only in centers with experience of supravalvular stenosis. Repair of supravalvular aortic stenosis requires surgery in the majority of cases. The tenuous hemodynamic situation of patients with significant supravalvular aortic stenosis has been highlighted by the increased risk of induction during surgical procedures. Sudden afterload and preload reduction can result in hemodynamic collapse.[9]

Patients with supravalvular aortic stenosis also require lifelong care, with follow-up with congenital heart disease centers recommended annually. In those patients with homozygous FH, the primary goal is treatment of the lipid abnormality with apheresis and aggressive medical and dietary treatments, including statins, cholesterol binders, and a low-fat diet. In some patients, there may be regression of plaque with aggressive treatment; however, progressive atherosclerosis is the norm.[10]

Conclusion

Valvular aortic stenosis is common, and echocardiography is the standard diagnostic technique for assessment of disease severity. Doppler echocardiography is invaluable in evaluating LVOT obstruction, but failure to 'look at the valve' may result in an incorrect diagnoses. When encountering the patient with LVOT obstruction but pliable valve leaflets, obstruction due to subvalvular or supravalvular stenosis should be sought. While rare, subvalvular and supravalvular aortic stenosis are not treated in the same manner as valvular stenosis, and the expected disease course is not the same. Therefore, an accurate diagnosis is important. ■

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