Does Presence of Discrete Subaortic Stenosis Alter Diagnosis and Management of Concomitant Valvular Aortic Stenosis?

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INTRODUCTION

Although aortic stenosis (AS) is a common valvular disease, discrete subaortic stenosis (DSS) or subaortic membrane (SM) is relatively uncommon. The combination of these two conditions is rarer still, and the hemodynamic consequences of these combined lesions have important considerations that may affect diagnosis and management. In this article, we present a series of three cases from our valve clinic diagnosed and managed using multimodality imaging and a brief literature review of this combined entity.

CASE PRESENTATIONS

Case 1

A 72-year-old, asymptomatic male veteran with moderate AS was referred for evaluation. Initial transthoracic echocardiography (TTE) revealed a calcified aortic valve with mild aortic insufficiency and a peak transaortic velocity of 3.7 m/sec and a mean gradient of 32 mm Hg. The peak velocity at the left ventricular outflow tract (LVOT) was elevated, raising suspicion for a fixed subaortic stenosis (Figure 1). Transesophageal echocardiography (TEE) confirmed the presence of SM (Figures 2 and 3, Video 1). Results of cardiac magnetic resonance imaging supported the diagnosis and revealed no other associated congenital lesions. Routine follow-up TTE 1 year later showed significantly elevated aortic gradients, with peak velocity and mean gradient of 4.7 m/sec and 53 mm Hg, respectively, with progression of aortic insufficiency to moderate. There was minimal change in the peak LVOT velocity (Figure 4). Because the patient was asymptomatic but with elevated gradients, stress echocardiography was performed that revealed dyspnea 7 min into exercise, with peak transaortic velocity of 5.8 m/sec and a mean gradient of 73 mm Hg (Figure 5). The patient underwent diagnostic catheterization, which revealed a 70% mid left anterior descending coronary artery stenosis and intracavitary assessment showing left ventricular

peak systolic pressure of 240 mm Hg, subaortic peak pressure of 210 mm Hg, and aortic systolic peak pressure of 180 mm Hg. The patient underwent successful bioprosthetic aortic valve replacement, resection of the SM, septal myomectomy, and single-vessel coronary artery bypass (left internal mammary artery to left anterior descending coronary artery). The resected SM was consistent with a partial (not circumferential) discrete fibrous membrane, extending from the left to the right fibrous trigone.

Case 2

A 66-year-old male veteran with known moderate AS and hypertension was referred for evaluation of exertional dyspnea and chest pain. Initial echocardiography (TTE followed by TEE) revealed evidence of a discrete SM (Figure 6A and 6B, Video 2). The aortic valve appeared to be bicuspid, with a peak velocity of 3.8 m/sec and a mean gradient of 32 mm Hg (Figure 7). Because of ongoing symptoms, he underwent cardiac catheterization that revealed right atrial pressure of 15 mm Hg, pulmonary capillary wedge pressure of 24 mm Hg, and an aortic mean gradient of 19 mm Hg with an aortic valve area of 1.2 cm^2 by the Gorlin equation. There was no obstructive coronary artery disease. Given these findings, a watchful waiting approach was recommended, and the patient's symptoms were attributed to hypertensive heart disease. He was seen 1 year later, with progression of his symptoms. TTE demonstrated transaortic peak and mean gradients of 88 and 50 mm Hg, respectively, and he underwent successful aortic valve replacement and resection of the SM, which was described intraoperatively as a fibrotic ring. Following this, he experienced dramatic reduction of his symptoms and is currently doing well.

Case 3

A 79-year-old male veteran with coronary artery disease and moderate AS was referred for progressive dyspnea. Repeat TTE suggested the presence of SM. The aortic valve was noted to be thickened with an immobile noncoronary cusp (Video 3). Peak velocity across the aortic valve was 3.9 m/sec, and peak and mean gradients were 60 and 34 mm Hg, respectively, with evidence of aliasing in the LVOT (Figure 8). TEE confirmed the diagnosis SM (Figure 9, Video 4). Over the next 6 months, the patient continued to have worsening dyspnea. Repeat TTE showed significantly elevated transaortic gradients with a peak velocity of 4.6 m/sec and peak and mean gradients of 84 and 49 mm Hg (Figure 10), respectively. LVOT gradients remained unchanged. The patient underwent aortic valve replacement and SM resection, with marked alleviation of his symptoms. The SM was a fibrous outgrowth that peeled off easily from the septum.

Figure 1 Continuous-wave Doppler on TTE in the apical five-chamber view showing two envelopes. The inner envelope (*thin arrow*) represents abnormally elevated LVOT velocity, and the outer envelope (*thick arrow*) represents elevated peak trans-aortic velocity.

Figure 2 TEE: midesophageal view showing a thin ridged SM (*arrow*). *LA*, Left atrium; *LV*, left ventricle.

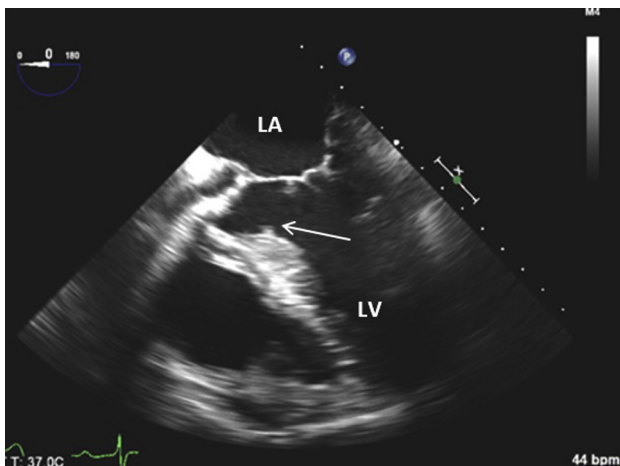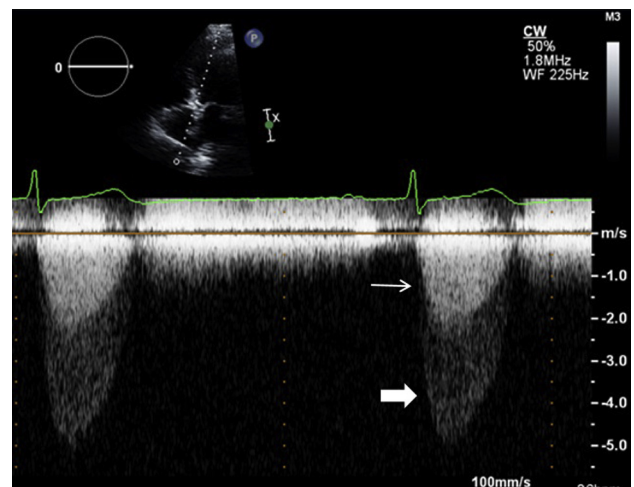Figure 3 Three-dimensional full-volume TEE showing crescent-shaped SM obliterating half of the LVOT (*arrow*).

Figure 4 Continuous-wave Doppler on TTE in the apical five-chamber view showing two envelopes. The inner envelope (*thin arrow*) represents the LVOT velocity that is overall unchanged but increased transaortic gradient (*thick arrow*) with peak systolic velocity of 4.7 m/sec.

DISCUSSION

Background

Etiology of DSS. There are four anatomic variants of DSS: thin fibrous membrane (the most common), thick funnel-shaped fibrotic ring, irregular fibromuscular tissue, and long tunnel-like obstruction[1] (Figure 11). DSS is considered an acquired condition given the near absence of the disease in newborns. Certain structural features have been identified to predispose to the development of DSS, such as increased mitral-aortic annular separation[2] as well as steepened aorto-septal angle.[3] These geometric changes give rise to turbulent flow across the LVOT, which has been hypothesized to give rise to endo-thelial proliferation in the LVOT and lead to the development of DSS.[4]

Epidemiology of DSS. The prevalence of DSS in the general population is difficult to estimate, because of the rarity of the condition. Prevalence has been estimated from 6.1 in 10,000 among all live births[5] to 6% to 6.5% among all patients.[6] DSS may be an isolated defect or associated with valvular AS and other congenital lesions,

such as ventricular septal defect, atrial septal defect, patent ductus arteriosus, coarctation of the aorta with or without being part of the Shone complex, and pulmonic stenosis.[1,7]

Differences in the Adult and Childhood Forms of DSS. Although concurrent aortic regurgitation has been well described in pediatric patients with DSS, valvular AS is not as common.[8] The turbulent flow from the DSS is also thought to result in
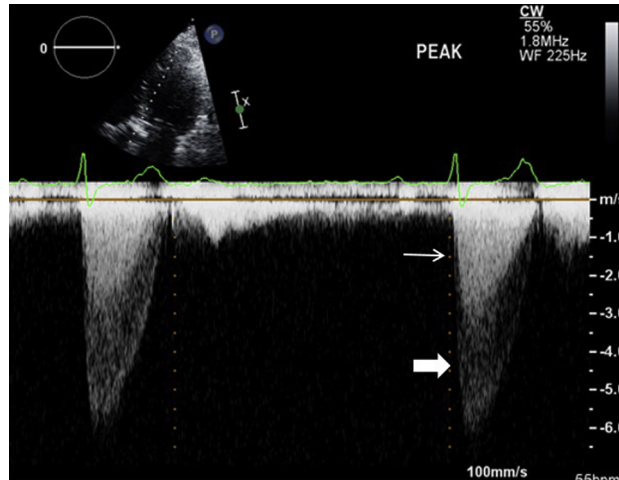
Figure 5 Continuous-wave Doppler on stress echocardiography in the apical five-chamber view during peak exercise. Note both the LVOT (*thin arrow*) and transaortic (*thick arrow*) velocities increased proportionally with exercise. Peak transaortic velocity is 5.8 m/sec, with mean gradient of 73 mm Hg.
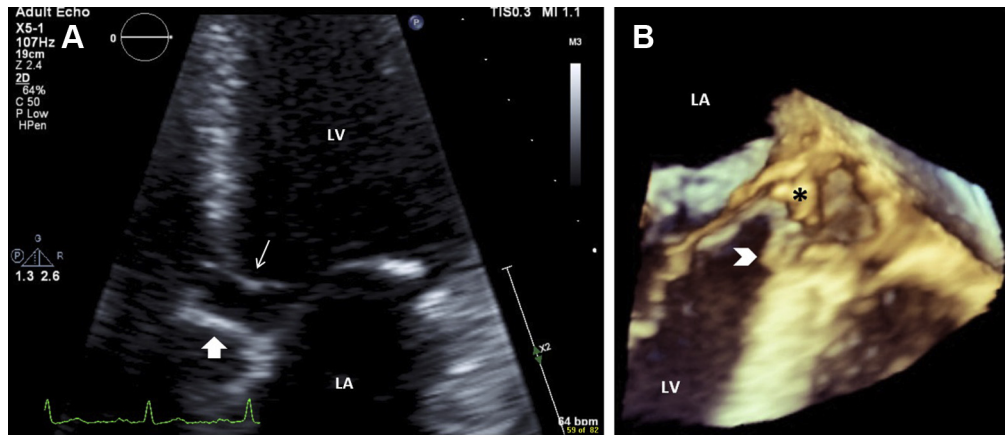

Figure 6 (A) Two-dimensional TTE from the apical five-chamber view showing SM (*thin arrow*) and thickened aortic valve leaflets (*thick arrow*). **(B)** Three-dimensional TEE showing the subaortic fibrotic ring (*arrow*) and thickened aortic valve leaflets (*asterisk*). *LA*, Left atrium; *LV*, left ventricle.
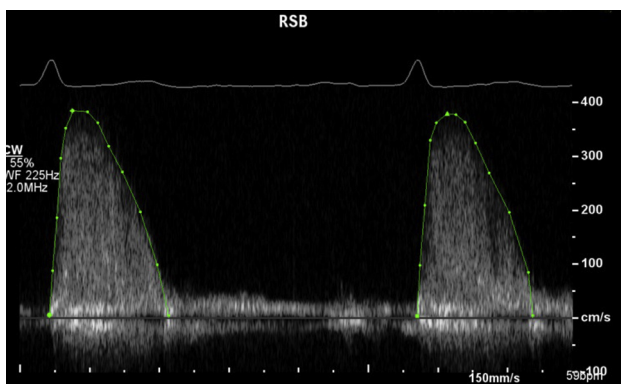

Figure 7 TTE continuous-wave Doppler from right sternal border (RSB) with peak transaortic velocity of 3.8 m/sec and mean gradient of 32 mm Hg.

progression of aortic regurgitation. thereby justifying the need for early life excision of these membranes.[8] Aggressive surveillance and early membrane resection have been recommended to avoid need for valve replacement.[9]

In contrast, adults with DSS typically have slower rate of hemodynamic progression and longer event-free survival compared with their pediatric counterparts.[10] This finding was reported in an international cohort by Van der Linde *et al.*,[6] who followed 149 adult patients without repair and found a rate of increase in peak LVOT gradient of approximately 1 mm Hg per year. This is consistent with our observation (Figure 12A and 12B). Predictors of progression in adult series included a higher LVOT gradient at baseline and presence of associated congenital heart disease. Van der Linde *et al.* also found no significant change in aortic regurgitation grade over a mean follow-up period of 6.3 years. In fact, a retrospective analysis showed an increased incidence of AS. These adult patients with DSS had a higher rate of surgery for AS than aortic
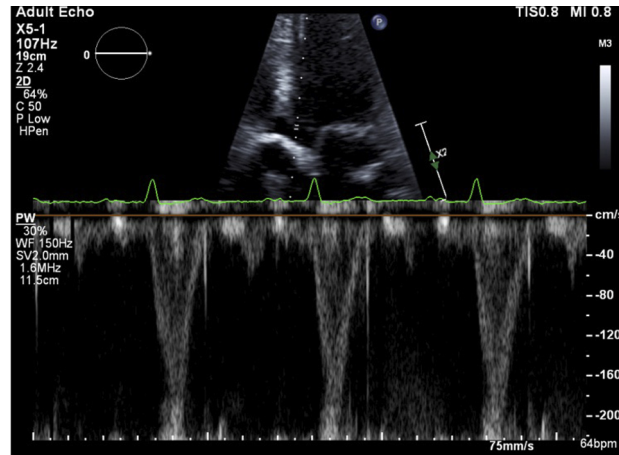
Figure 8 Pulsed-wave Doppler on TTE at the LVOT in the apical five-chamber view showing increased velocity and aliasing.
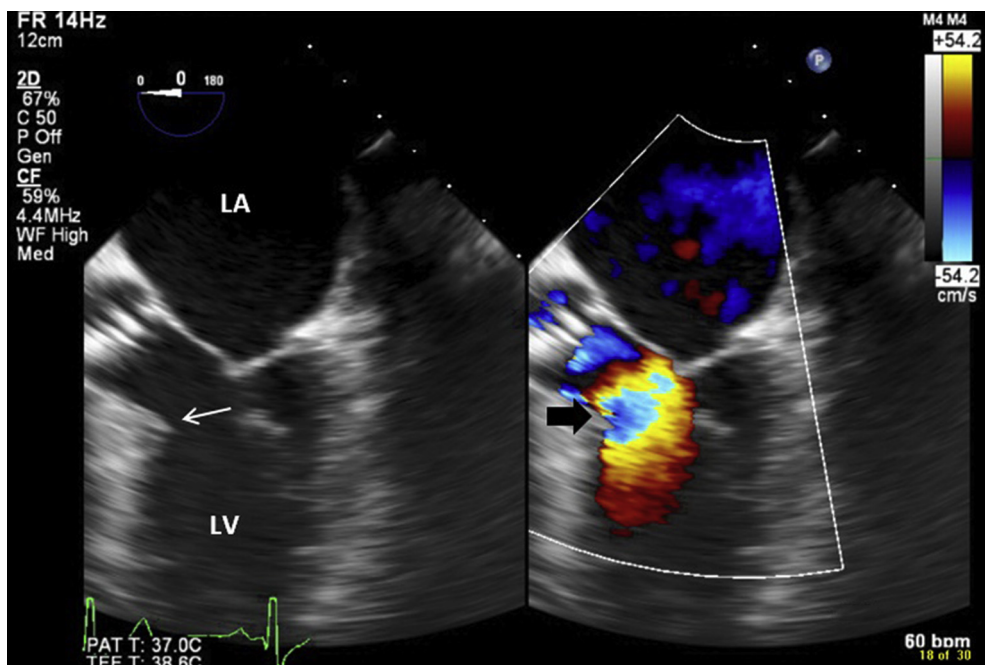

Figure 9 TEE: midesophageal view showing SM (*white arrow*) with flow acceleration (*black arrow*) at the LVOT by color Doppler and aortic regurgitation. *LA*, Left atrium; *LV*, left ventricle.

regurgitation, and the majority of these patients did not have bicuspid aortic valve.[11] The reason for this disparity in the natural history is not clear. Plausible explanations may include an intact, more pliable aortic valve in pediatric patients that is susceptible to endothelial damage from the turbulent flow, with resultant aortic regurgitation. In contrast, adults with traditional risk factors for AS, including hypertension, diabetes mellitus, and hyperlipidemia,[12] may be susceptible to accelerated calcification of the aortic valve due to altered hemodynamic shear stress. This was observed in all our patients, who demonstrated more rapid AS progression in the presence of SM compared with those with isolated valvular AS (Figure 13A and 13B).

Echocardiographic Assessment of DSS with Valvular AS

Two-Dimensional and Three-Dimensional Echocardiography. Presence of DSS should be suspected when flow acceleration is noted below the aortic valve on pulsed-wave and/color Doppler imaging, revealing aliasing at the LVOT. The membrane may appear as a thin band (Figure 6A and 6B) or a ridge within the LVOT. This could be either partial or circumferential. Multiple echocardiographic views should be obtained for optimal visualization. Two-dimensional and three-dimensional TEE can provide additional anatomic assessment and details of the SM (Figure 3) not otherwise appreciated on two-dimensional TTE.
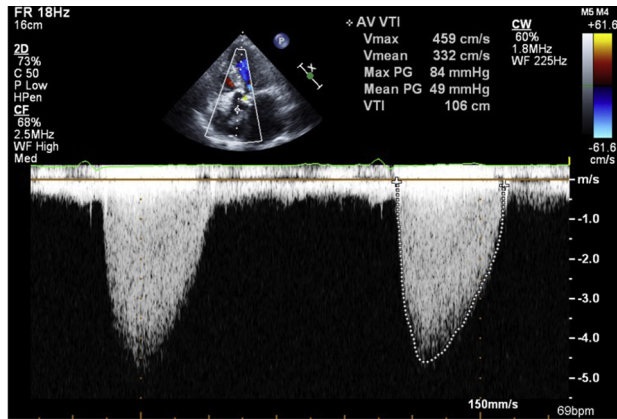
Figure 10 Continuous-wave Doppler on TTE in the apical five-chamber view showing peak transaortic velocity of 4.6 m/sec and mean gradient of 49 mm Hg.
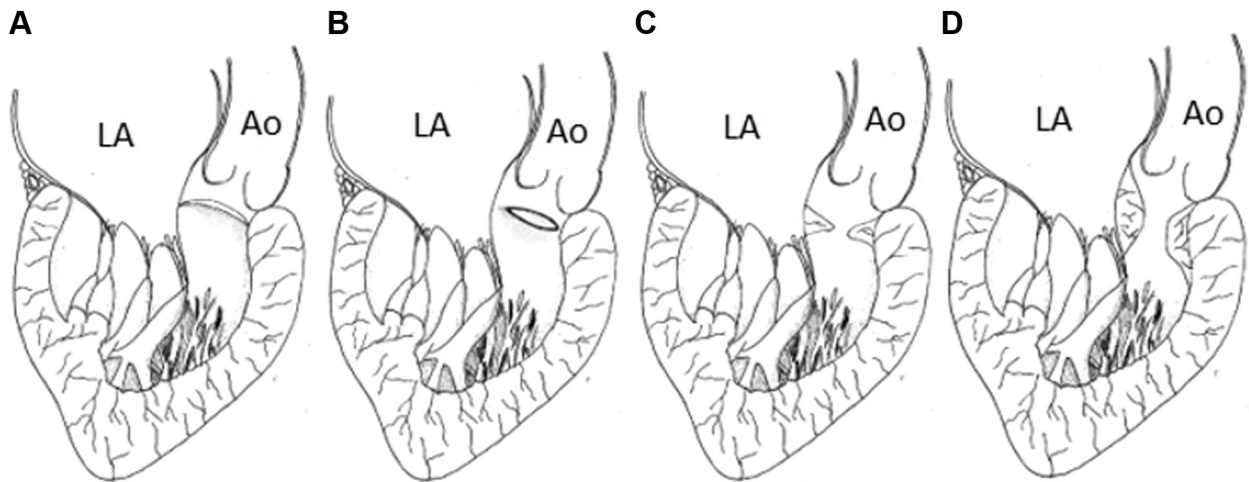
Figure 11 Schematic of four different DSS types: **(A)** thin fibrous membrane (most common), **(B)** thick funnel-shaped fibrotic ring, **(C)** irregular fibromuscular tissue, and **(D)** long tunnel type. *Ao*, Aorta; *LA*, left atrium.
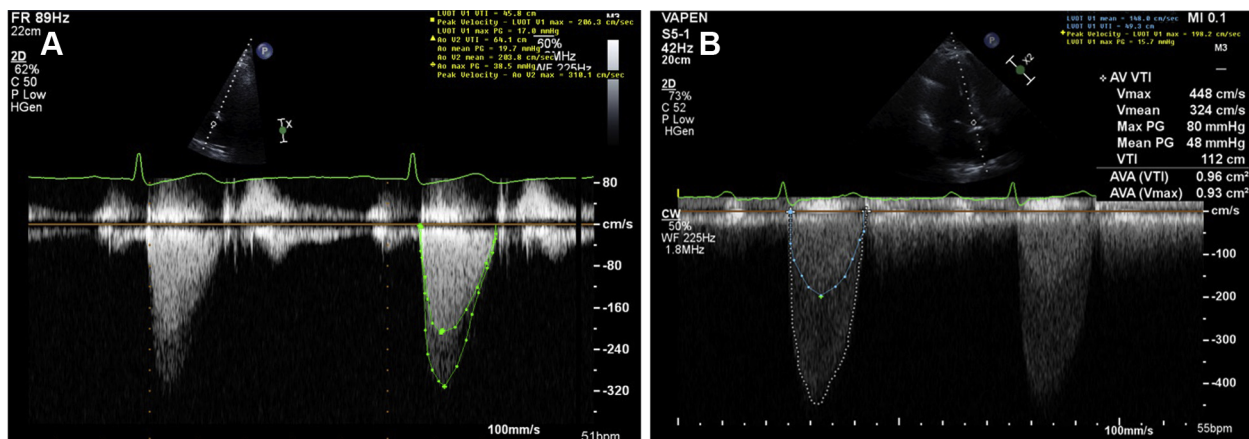
Figure 12 **(A)** Continuous-wave Doppler on TTE in the apical five-chamber view showing two envelopes from case 1. The inner envelope represents the LVOT velocity, and the outer envelope represents the transaortic velocity. Peak systolic LVOT velocity is 2.1 m/sec, with transaortic velocity of 3.2 m/sec. **(B)** Six months later, the LVOT velocity remained relatively unchanged at 2 m/sec, but the transaortic peak systolic velocity is now 4.5 m/sec.

A

B
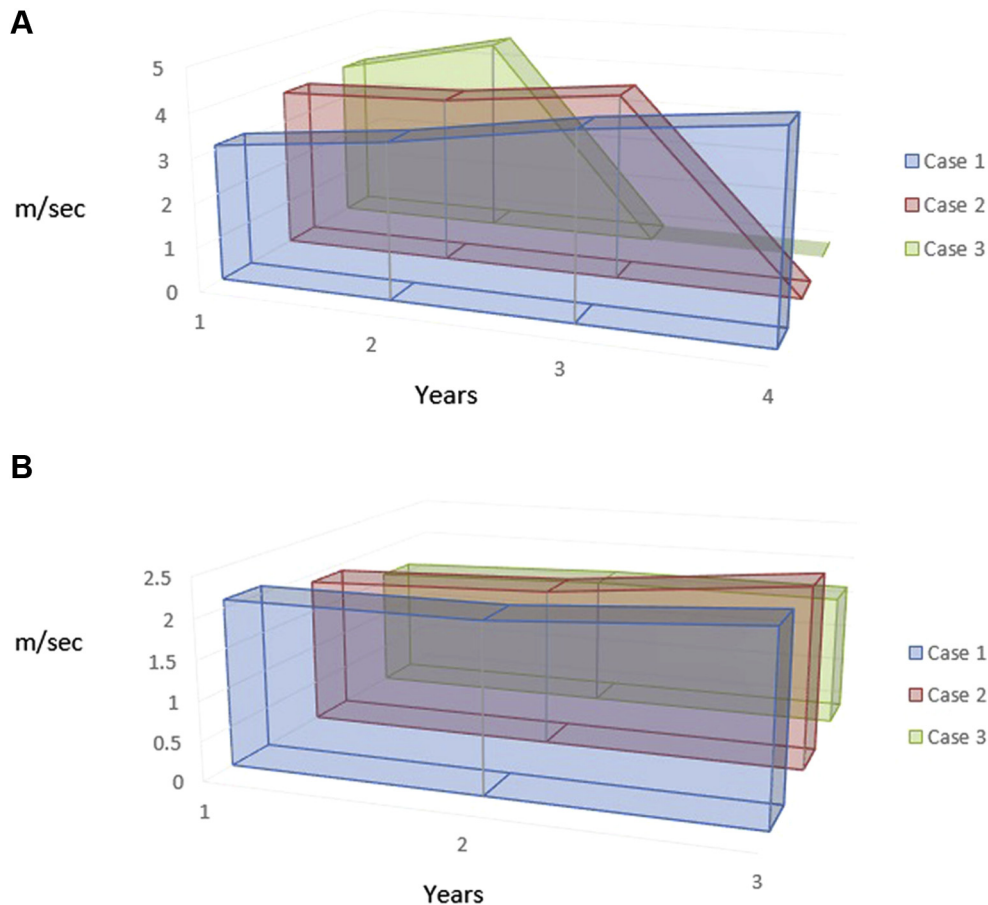
Figure 13 **(A)** Notice the rapid increase in aortic valve peak velocities from our cases. **(B)** LVOT peak velocities remain overall unchanged over time for our patients.
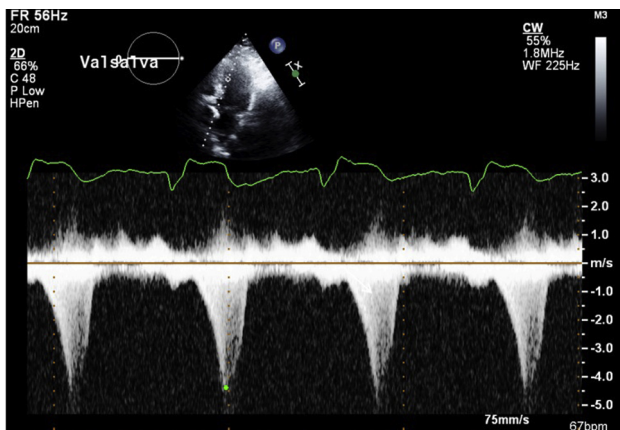
Figure 14 Continuous-wave Doppler with Valsalva maneuver on TTE in the apical five-chamber view showing late peaking, dagger-shaped profile signifying dynamic LVOT obstruction.

When evaluating severity of AS in the presence of DSS, the degree of aortic cusp calcification and excursion can be important clues, along with estimation of anatomic orifice area of aortic valve by planimetry on two-dimensional and three-dimensional TEE.[13]

Associated bicuspid valve disease may be present and portend accelerated AS.[11]

It is important to differentiate DSS from hypertrophic obstructive cardiomyopathy. DSS is a fixed LVOT obstruction compared with dynamic LVOT obstruction from hypertrophic obstructive cardiomyopathy, which can manifest as either concentric or asymmetric left ventricular hypertrophy. Systolic anterior motion of the mitral leaflet and the associated posteriorly directed eccentric mitral regurgitation is important to note.

Doppler Assessment. A high subaortic velocity (generally >1.5 m/sec) is often initially recognized in the form of turbulence by color Doppler (Figure 9, Video 4) and should prompt a careful interrogation using pulsed-wave Doppler along the LVOT. A parabolic subaortic spectral Doppler pattern is most consistent with a fixed LVOT obstruction (Figures 1 and 4) compared with the mid- to late-peaking, dagger-like pattern in dynamic outflow tract obstruction (Figure 14) seen in hypertrophic obstructive cardiomyopathy.

In patients with AS and DSS, interrogation with continuous-wave Doppler may reveal a double-envelope pattern (Figures 1 and 4), with the inner envelope representing the gradient at the SM and the outer envelope representing the peak velocity across the aortic valve. The next step would be to quantitate the severity at each level. While doing so, one needs to consider the hemodynamic principals of serial stenoses.
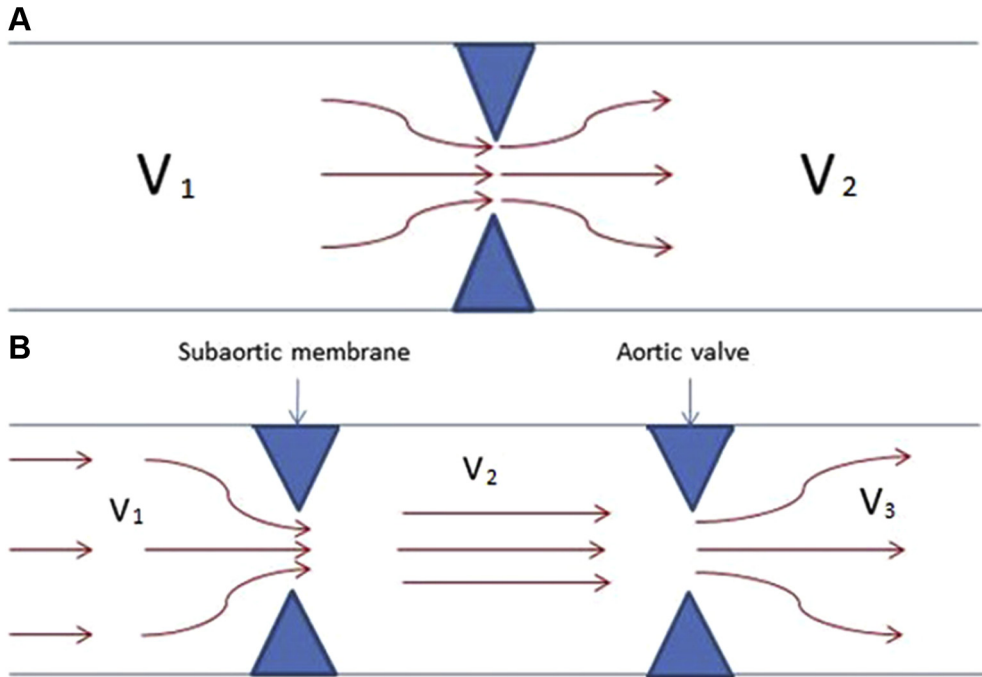
Figure 15 **(A)** Schematic representation of flow acceleration at a stenosis. V_1 represents velocity proximal to stenosis. V_2 is the velocity distal to stenosis. **(B)** V_1 is velocity in the proximal LVOT just before SM. V_2 is velocity between the two stenoses, SM and aortic valve. V_3 is velocity in the proximal ascending aorta. As an example from case 1 at the patient's initial presentation, V_1 was 1.2 m/sec, V_2 was 2.1 m/sec, and V_3 was 3.6 m/sec. Using these values, the peak transaortic gradient can be derived by the full Bernoulli equation: $4 \times (3.6^2 - 2.1^2) = 34$ mm Hg. Transaortic mean gradient cannot be calculated when proximal velocity is >1.5 m/sec.
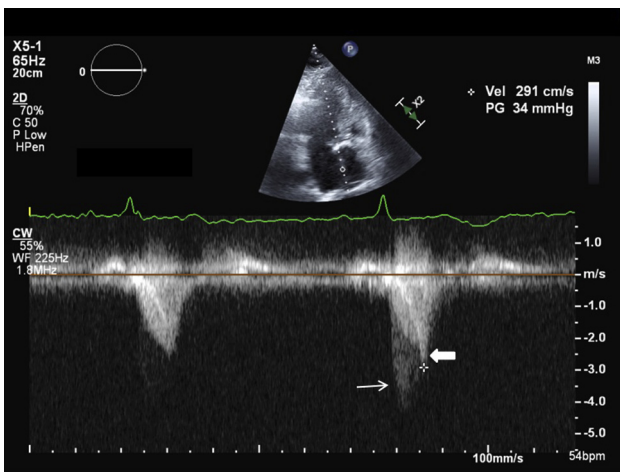
Figure 16 Continuous-wave Doppler on TTE in the apical three-chamber view in a patient with concomitant AS and dynamic LVOT obstruction showing the early-peaking transaortic velocity (*thin arrow*) and the late-peaking LVOT velocity (*thick arrow*).

Hemodynamic Principles of Serial LVOT Stenoses

The difficulty of hemodynamic evaluation of serial stenoses is in the challenges of determining hemodynamic significance at each level of obstruction and the effect of the sum of its parts. The echocardiographic assessment of such serial fixed stenoses invalidates the assumptions of the simplified Bernoulli equation. At the same time, one must keep in mind the different types of DSS and its impact on pressure recovery.[14]

Severity of AS is measured by estimating transaortic peak and mean pressure gradients as well as aortic valve area, calculated by using the continuity equation.[15] Peak instantaneous gradient is calculated by measuring the jet velocity across the stenosis and using the simplified Bernoulli equation ($P = 4V^2$, where P is the instantaneous pressure gradient and V is the velocity across the stenosis). Mean gradient is calculated by averaging the instantaneous pressure gradients over the ejection period. The simplified Bernoulli equation assumes that the proximal velocity (V_1) is < 1.0 m/sec and, therefore, negligible. Above this threshold, additional considerations including viscosity and friction become important and can lead to overestimation of pressure gradients.[16] When the proximal velocity is > 1.5 m/sec, using the full Bernoulli equation ($P = 4V_2^2 - V_1^2$, where P is the instantaneous pressure gradient, V_1 is the velocity proximal to the stenosis, and V_2 is the velocity distal to the stenosis) as depicted in Figure 15A is recommended.[15] Although peak gradient can be calculated in this manner, mean gradient which is a better measure of severity of stenosis cannot be calculated when proximal velocity is > 1.5 m/sec.[15]

In serial stenoses (Figure 15B), the velocity distal to the SM but proximal to the aortic valve (V_2) is usually >1.5 m/sec, and the pressure gradient across the aortic valve should be measured as $P = 4(V_3^2 - V_2^2)$.[16] It is difficult to accurately measure V_2, as it is often overestimated because of the phenomenon of pressure recovery. According to this phenomenon, the pressure distal to the stenosis is higher than at the vena contracta (the narrowest point of the jet) because of deceleration of flow with conversion of kinetic energy to pressure. Doppler echocardiography, however, uses the highest localized velocity at the vena contracta to calculate an instantaneous pressure gradient leading to an overestimation of the true gradient across the SM. Pressure recovery may be more problematic in tunnel-like

subaortic stenosis than in discrete membranes.[14] Therefore, when one encounters serial stenoses as in our three cases, although we can measure the overall gradient across the aortic valve, it is difficult to estimate the accurate pressure gradient at each level of stenosis, especially given the parallel timing of the aortic valve and SM flow profiles, which is unlike the flow profiles seen with dynamic LVOT obstruction that occurs in late systole (Figure 16). For the same practical reasons, the continuity equation cannot be used to measure the aortic valve area.

In adult patients with DSS, it is known that the progression of LVOT gradient over time is minimal.[6] Given this, when patients with concomitant AS and SM are followed over a period of time, as in our three cases, if there is no dramatic change in V_2 (velocity across the SM; Figure 15B), the increase in pressure gradient across the aortic valve on serial studies can be attributed to worsening valvular AS rather than SM.

Other Imaging Modalities. Invasive catheterization is of value when diagnostic uncertainty remains despite thorough noninvasive assessment. Careful measurement of pressure at each level of obstruction using an end-hole or micromanometer catheter is recommended.[16] The role of cardiac magnetic resonance imaging is limited to evaluation for the presence of other congenital abnormalities.[6]

Management

There are currently no adult guideline statements addressing management issues for those with concomitant DSS and AS. The guidelines have only outlined management options for each condition separately. According to the American College of Cardiology and American Heart Association 2008 adult congenital heart disease guidelines, surgery is recommended in those with DSS and peak instantaneous gradient of 50 mm Hg or mean gradient of 30 mm Hg on echocardiography regardless of symptoms.[8] As for severe valvular AS, surgery should be considered at the onset of symptoms and/or presence of left ventricular dysfunction.[17] In adults with DSS and severe AS, our experience has shown the predominant obstruction is at the valve; because of this, one could follow guidelines similar to isolated valvular AS. Exercise testing is useful in asymptomatic patients to elicit symptoms and determine optimal timing for surgical intervention.[8,18]

CONCLUSION

Serial stenoses with DSS and AS are rare and can pose diagnostic challenges when assessing hemodynamic significance at each level of obstruction. An important observation consistent throughout all our cases is that LVOT gradients do not change significantly over time, while increases in transaortic gradients have a more accelerated course in those with DSS than those without, similar to what has been previously observed in congenital AS with DSS.[19] This altered natural history of AS in the presence of DSS would call for closer monitoring. Understanding there are limited data, on the basis of our institutional experience we recommend clinical monitoring every 6 months with repeat echocardiography once a year or earlier if there is a change in symptoms. Surgery is recommended when AS is severe and symptoms develop, and a watchful waiting approach may be appropriate in asymptomatic patients.

SUPPLEMENTARY DATA

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