



Paradoxical Low-Flow, Low-Gradient Aortic Stenosis—a Tough Nut to Crack in Echocardiographic Diagnosis

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In this issue, Abudiab et al.¹⁾ evaluated the characteristics of paradoxical low-flow low-gradient (PLF-LG) aortic stenosis (AS) among subjects who had been diagnosed with severe AS using conventional transthoracic echocardiography (TTE). The authors tried combining transesophageal echocardiography (TEE) with TTE to measure the left ventricular outflow tract (LVOT) diameter and calculate the aortic valve area (AVA). Such AVA calculation reclassified a significant proportion of patients previously diagnosed with PLF-LG severe AS by conventional TTE as moderate AS instead.

The present study is interesting for several reasons. First, the prevalence of PLF-LG AS was much lower than previously believed among severe AS, and meticulous examination using multiple modalities can increase diagnostic accuracy for complicated diseases. Second, TTE often overestimates AS severity, particularly in patients with a low volume status such as old age and small body mass index (BMI). Current diagnostic criteria for the low-flow state (stroke volume index <35 mL/m²) are likely to be insufficient in subjects with extremely small or large body builds. Third, TEE may play an additional role in the diagnosis of PLF-LG AS, and detailed

anatomic information regarding the aortic valve and perivalvular structure are complementary to conventional TTE.

Paradoxical low-flow, low-gradient aortic stenosis

Severe AS is defined as peak transvalvular flow velocity ≥ 4 m/s, mean gradient ≥ 40 mmHg, and/or AVA < 1.0 cm² or indexed AVA < 0.6 cm²/m².²⁾ However, up to 50% of patients with severe AS are known to have low-gradient AS, which is defined as AVA < 1.0 cm² or indexed AVA < 0.6 cm²/m² with a mean gradient < 40 mmHg. Low-gradient AS is further classified as either classical LF-LG AS, which is related to significant left ventricular (LV) dysfunction and low ejection fraction (EF), or paradoxical LF-LG AS, where LV EF is preserved.

PLF-LG severe AS is defined by AVA < 1.0 cm², indexed AVA < 0.6 cm²/m², mean gradient < 40 mmHg, LV EF $\geq 50\%$, and low transvalvular flow (indexed stroke volume < 35 mL/m²).²⁾ Reduced stroke volume and increased afterload are the major hemodynamic mechanisms of PLF-LG AS. The low-flow state can be related to small LV cavity (particularly in elderly females), significant diastolic dysfunction and restrictive LV filling, atrial fibrillation, and significant mitral or tricuspid valvular diseases. PLF-LG AS is known to account for approximately one third of patients with severe AS and preserved LV EF.³⁾ For patients with truly severe PLF-LG AS, surgical or transcatheter aortic valve replacement should be performed.

Pitfalls of echocardiography in low-flow aortic stenosis

Diagnosis of PLF-LG AS is challenging due to several reasons. First, the accuracy of echocardiographic AVA measurements is very important. In the presence of a low-flow state, the mean pressure gradient and peak flow velocity for continuous wave Doppler tracing were both low despite severe AS. AVA calculation using the continuity equation is also of critical importance. However, echocardiographic estimation of the LVOT area is prone to measurement errors; LVOT area estimates in conventional two-dimensional TTE are calculated using the LVOT diameter (i.e., the

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distance between the interventricular septum and anterior mitral leaflet at the insertion level of the aortic cups), given by $LVOT\ area = \pi(LVOT\ diameter/2)^2$. As the actual shape of LVOT in the cross-sectional plane is elliptical instead of circular,⁴⁾ the LVOT area obtained using two-dimensional TTE is well-correlated with (but tends to be smaller than) that obtained using three-dimensional TEE or multi-detector computed tomography (MDCT). Resultant AVA estimates from TTE are also smaller than those obtained from other imaging modalities.⁵⁾ Second, pseudo-severe AS should be differentiated. In the low-flow state, a non-severely stenotic aortic valve may not open completely, mimicking severe AS. Dobutamine-stress echocardiography is often useful for differential diagnosis between true- and pseudo-severe AS. Increases in stroke volume and a mean gradient ≥ 40 mmHg with AVA < 1.0 cm² during dobutamine infusion are a confirmed diagnosis of severe AS.²⁾ Third, the low-flow state defined by indexed stroke volume may be overstated in obese subjects. In these cases, stenosis severity and symptomatic status should be re-assessed. Exercise-stress echocardiography may also be useful.⁶⁾

The role of transesophageal echocardiography in low-flow aortic stenosis

Abudiab et al.¹⁾ used TTE and TEE together to diagnose PLF-LG AS. TEE was used to measure LVOT diameter and calculate AVA. Among 12 patients previously diagnosed with PLF-LG severe AS by TTE, only 5 were judged to have severe AS with TEE, i.e., 7 were reclassified to have moderate AS. The 7 patients re-classified as moderate AS tended to be older (81 ± 4 vs. 74 ± 10 years, $p=0.12$) and have lower BMI (27 ± 5 vs. 34 ± 7 , $p=0.07$) and lower mean transvalvular gradient (28 vs. 34 mmHg, $p=0.20$) compared to the 5 patients with true severe AS. As transvalvular flow can be physiologically low in elderly patients with small body builds, the diagnosis of severe AS should be made carefully. Detailed anatomical information from TEE may be complementary in defining severe AS. TEE provides more accurate values for AVA via planimetry, the degree of leaflet calcification, and LVOT geometry. Less severe leaflet calcification suggests a low probability of severe AS. Additional three-dimensional studies could maximize information regarding the LVOT geometry.

Given that the LVOT diameter measurement using two-dimensional TEE is essentially the same as for TTE, one may wonder why measurements with TEE may lead to such different results. However, considering the ellipsoidal shape of the LVOT geometry, the plane used to obtain the LVOT diameter with TEE may be different from that obtained with TTE.

Despite the authors' attempts to implement TEE as a complementary tool, the values obtained from the different modalities are not interchangeable. LVOT areas obtained via planimetry at cross-sectional planes with three-dimensional TEE or MDCT are systematically larger than LVOT areas obtained with TTE.⁴⁾⁵⁾ Different cut-off values have been suggested for different modalities, but there is no consensus regarding this issue.

In summary, PLF-LG AS is increasing in the elderly population, but is a challenging issue. Accurate diagnosis is subject to comprehensive interpretation of clinical data, meticulous echocardiographic study, and appropriate use of multiple diagnostic modalities. However, many issues related to PLF-LG AS remain to be understood: Is the low-flow state really harmful in subjects with small body builds? What does it mean for the aortic valve area to be 'small' and what constitutes a low transvalvular flow? What is the cut-off in defining pathologic entities in individuals corresponding to their metabolic needs? Future studies are expected to provide answers to the above questions.

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