Low-Flow Low-Gradient Aortic Stenosis: When is it Severe?

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Expert Analysis

A low flow state may occur with reduced left ventricular ejection fraction (LVEF) (i.e. Classical Low Flow) or with preserved LVEF (i.e. Paradoxical Low Flow) and it is often associated with a low transvalvular gradient given that the gradient is highly flow-dependent[1, 2]. In both types of low-flow, low-gradient (LF-LG), classical or paradoxical, it is difficult, from the resting echocardiographic exam, to differentiate a true-severe from a pseudo-severe stenosis. This distinction is nonetheless essential given that patients with true-severe AS generally benefit from aortic valve replacement (AVR), whereas those with pseudo-severe stenosis should be treated medically (Slide #1)[3]. Additional diagnostic tests such as dobutamine stress echocardiography (DSE) and aortic valve calcium scoring by multidetector computed tomography (MDCT) may be used to distinguish true- from pseudo- severe AS.

CLASSICAL LF-LG AS WITH REDUCED LVEF

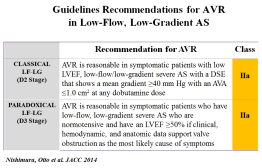
This entity is found in about 5-10% of the patients with severe AS[2] and it is characterized by a reduced LVEF (<50%) and a discordance between the aortic valve area (AVA<1 cm^2 and/or <0.6 cm^2/m^2, consistent with severe AS) and the mean gradient (MG<40 mmHg, consistent with non-severe AS) (Slide #2). In a low flow state, the gradient may be pseudo-normalized and thus underestimate the stenosis severity, whereas the AVA may be pseudo-severe and thus overestimate the severity.

Dobutamine stress echocardiography

A low dose (up to 20µg/kg/min) DSE is useful to differentiate true- versus pseudo- severe AS (Slide #2)[4]. Typically, true-severe AS shows little or no increase in AVA and substantial increase in gradient, which is congruent with the relative increase in flow, whereas pseudo-severe AS shows a marked increase in AVA and little or no increase in gradient in response to increasing flow. Accordingly, in the 2014 ACC/AHA guidelines[3], there is a class IIa indication for AVR in symptomatic patients with classical LF-LG AS if they show a mean gradient ≥ 40 mmHg and an AVA≤1.0 cm^2 at any dobutamine stage (Slide #1).

However, several patients have incomplete normalization of flow with DSE and may thus still have discordant AVA-gradient findings at the end of DSE: i.e. a peak stress gradient < 40 mmHg with a peak stress AVA< 1.0 cm^2. In such situation, one can calculate the projected AVA at normal flow rate (AVA_{Proj}), which provides an estimate of what would be the AVA at a normal transvalvular flow rate (i.e. 250ml/s)[5, 6]. This parameter is calculated as follows: $AVA_{Proj} = AVA_{Rest} + (\Delta AVA/ \Delta Q) \times (250 - Q_{Rest})$, where AVA_{Rest} and Q_{Rest} are the AVA and Q (stroke volume / LV ejection time) at rest and ΔAVA and ΔQ are the absolute increases in AVA and Q during DSE. The best cutoff value to identify true severe AS is an $AVA_{Proj} \leq 1.0$ cm^2. The AVA_{Proj} has been shown to be superior to the traditional parameters of AS severity proposed in the guidelines to assess the actual AS severity as well as to predict outcomes[5, 6]. The calculation of the AVA_{Proj} is thus helpful when the AVA-gradient discordance persists at the end of DSE. However, a minimum of 15% increase in flow is required to obtain a reliable estimate of this parameter. In

Slide 1: 2014 ACC/AHA Guidelines Recommendations for AVR in Patients with LF-LG AS


Guidelines Recommendations for AVR in Low-Flow, Low-Gradient AS

	Recommendation for AVR	Class
CLASSICAL LF LG (D2 Stage)	AVR is reasonable in symptomatic patients with low LVEF, low-flow/low-gradient severe AS with a DSE that shows a mean gradient ≥40 mm Hg with an AVA ≤1.0 cm² at any dobutamine dose	IIa
PARADOXICAL LF LG (D3 Stage)	AVR is reasonable in symptomatic patients who have low-flow, low-gradient severe AS who are normotensive and have an LVEF ≥50% if clinical, hemodynamic, and anatomic data support valve obstruction as the most likely cause of symptoms	IIa

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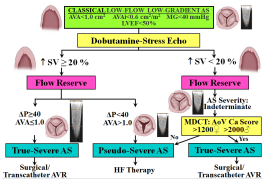
AVA: aortic valve area; DSE: dobutamine stress echocardiography; LVEF: LV ejection fraction.

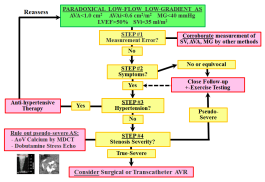
patients with no or minimal increase in stroke volume and flow rate (i.e. patients with no flow reserve), DSE generally remains non-conclusive and other imaging modalities, such as MDCT, are required to differentiate true- versus pseudo- severe stenosis (Slide #2).

Slide 2: Algorithm for the Assessment of Stenosis Severity and the Management of Classical (low LVEF) LF-LG AS



AS: aortic stenosis; AVA: aortic valve area; AVAi: indexed AVA; MG: mean gradient; LVEF: LV ejection fraction; SV: stroke volume; MDCT: multidetector computed tomography; AVR: aortic valve replacement.

Slide 3: Algorithm for the Assessment of Stenosis Severity and the Management of Paradoxical (preserved LVEF) LF-LG AS



AS: aortic stenosis; AVA: aortic valve area; AVAi: indexed AVA; MG: mean gradient; LVEF: LV ejection fraction; SV: stroke volume; MDCT: multidetector computed tomography; AVR: aortic valve replacement; AoV: aortic valve.

Multidetector computed tomography

Aortic valve calcium scoring by MDCT is useful to corroborate stenosis severity when DSE is not feasible or not conclusive[7, 8]. MDCT has the advantage of being independent of hemodynamics/flow and is applicable to all patients. Moreover, calcium scoring does not require the injection of contrast agents. Recent studies showed that lower cutoff values of aortic valve calcium score should be used in women (≥1200 AU) than in men (≥2000 AU) to identify true severe AS and predict mortality (Slide #2)[8, 9].

PARADOXICAL LF-LG AS WITH REDUCED LVEF

Paradoxical LF-LG AS occurs in 5-15% of patients with AS[2] and it is defined as a preserved LVEF (≥50%), a low LV outflow (i.e. stroke volume index <35 mL/m^2), a small AVA (≤1 cm^2 and ≤0.6 cm^2/m^2), and a low gradient (<40 mmHg) (Slide #3)[2, 3]. In these patients, the low flow state is generally related to a pronounced LV concentric remodeling with impaired LV filling, and reduced systolic global longitudinal strain (despite normal LVEF)[1, 2, 10, 11]. Other factors may also contribute to the reduced stroke volume in the context of a preserved LVEF including: atrial fibrillation, concomitant mitral regurgitation, tricuspid regurgitation, or mitral stenosis etc. In the ACC/AHA guidelines[3], a new class IIa indication of AVR was included for patients with paradoxical LF-LG AS if they are symptomatic, normotensive and the clinical, anatomical, and hemodynamic factors support the presence of a severe stenosis as the most likely cause of symptoms (Slide #1). This recommendation further emphasizes the importance of confirming the stenosis severity in these patients.

In patients with paradoxical LF-LG AS who are hypertensive, it is first recommended to initiate or optimize anti-hypertensive therapy and reassess symptoms and echocardiographic parameters of flow and stenosis severity, once blood pressure is normalized (Slide #3)[3]. As in patients with classical LF-LG AS, a low dose DSE or exercise stress echocardiography (in presence of mild or ambiguous symptoms) may also be used in patients with paradoxical LF-LG to differentiate true- versus pseudo- severe stenosis and the same parameters and criteria of AVA, MG, and AVA_{Proj} can be applied to these patients[12]. However, DSE is often not feasible or not conclusive in patients with paradoxical LF-LG AS, and particularly in those with severe restrictive physiology and/or concomitant mitral regurgitation. Hence, aortic valve calcium scoring by MDCT has become the modality of choice to confirm stenosis severity in these patients and one can used the same cut-point values of aortic valve calcium score (≥1200 AU in women and ≥2000 AU in men) as those described above for classical LF-LG AS (Slide #3)[8,9].

CONCLUSION

LF-LG AS poses some important challenges with regard to confirmation of stenosis severity and therapeutic management. A low dose DSE is generally used to differentiate true- versus pseudo- severe AS and support the indication of AVR in patients with classical LF-LG who have significant flow reserve. The calculation of the AVA_{Proj} is helpful in situations where the AVA-gradient discordance and thus the uncertainty about stenosis severity persist at the end of DSE.

Aortic valve calcium quantification by MDCT may be helpful to distinguish true- from pseudo- severe stenosis in patients with classical LF-LG AS in whom there is no or minimal increase in flow during DSE

and/or in whom the results of DSE are inconclusive. MDCT is also the modality of choice to confirm stenosis severity in patients with paradoxical LF-LG AS.

References

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