My Approach to Aortic Stenosis Assessment with Discrepant Quantification

Como eu Faço: Avaliação da Estenose Aórtica com Discordância em sua Quantificação

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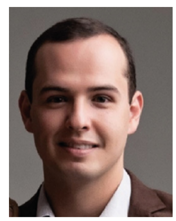

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Introduction

Aortic stenosis (AS) is the most common primary valve disease and an important cause of morbidity and mortality worldwide.[1] Echocardiography is the first-line method for its diagnosis, quantification of severity, prognosis, and determination of intervention timing.[2]

The association of maximum velocity (Vmax) $\geq$ 4m/s, aortic valve area (AVA) $\leq$ 1.0 cm², and mean gradient (MG) $\geq$ 40 mmHg defines the diagnosis of classic severe AS.[3] However, MG and AVA are discrepant (AVA $\leq$ 1.0 cm², MG < 40 mmHg) in 30–40% of the population with severe AS, leading to low-gradient AS (LGAS),[4] the focus of this article. Less frequently, high-gradient AS can also occur in cases of MG $\geq$ 40 mmHg and AVA > 1.0 cm² due to high flow situations.[5]

Understanding the factors that lead to this discrepancy is essential to avoiding misdiagnosis and classifying different severe AS phenotypes.

Understanding the discrepancy phenomenon and classifying aortic stenosis

AS with a discrepant valve area and gradient may be due to measurement errors, physiological reasons (small body surface, flow states, and arterial hypertension), and guideline inconsistencies in AVA/MG criteria. Thus, it is important to first correct physiological factors and confirm measurements. If the discrepancy persists, the phenotype must be classified according to the flow state; if the severity remains uncertain, it must be confirmed by other methods.[5] Classically, the flow is evaluated by the ejection fraction and stroke volume index (SVi). All of these aspects are discussed below.

Aortic valve area, stroke volume, or mean aortic transvalvular gradient calculation errors

Measuring errors are usually the main cause of discordant aortic stenosis. The most common error is related to underestimation in left ventricular outflow tract diameter (LVOTd), either due to imaging difficulties, especially if severe calcification is present, or because it is not clear where to measure LVOTd, or a circular LVOT geometry is assumed, whereas it is mostly elliptical. Errors involving just a few millimeters of LVOTd lead to exponential errors in stroke volume (SV) and aortic valve area (AVA) calculation using the continuity equation, leading to misdiagnosis of severe LGAS. To minimize these limitations, AOS grading recommendations (Table 1) also include calculating the ratio between the velocity time integral (VTI) on pulsed Doppler (PW) of the left ventricular outflow tract (LVOT) and on continuous Doppler (CW) of the aortic valve (AOV), which is a dimensionless index. Also, if the patient has a small body surface and is not obese, it is recommended to index AVA to body surface (AVAi)[1], although this indexation method is controversial.[6]

Errors can also occur when obtaining Doppler velocities. According to the Doppler equation, angles greater than 20 degrees between the ultrasound beam and the analyzed jet underestimate the velocity and, consequently, the

Keywords

Aortic Stenosis; Echocardiography; Diagnosis.

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gradient. Doppler alignment can be challenging and require multiple windows.

Strict attention to the measurement technique is the first step to reducing errors and avoiding discrepancies (Table 2). Testing measurement reliability involves calculating the predicted LVOT and comparing it with the measured diameter. If the measured LVOT is 2 mm greater or less than the predicted value, measurement error or elliptical geometry is possible. Another measurement that shows an error is an AVAi ≤ 0.6 cm^2/m^2 with a VTI ratio > 0.25. In such cases, complementary measurements and other imaging methods are required to confirm measurement accuracy.

Inconsistent guidelines in the definition of severity by AVA/gradient

Some studies suggested that a gradient ≥ 40 mmHg is related to an area < 0.8 cm^2; thus, areas of 0.8–1.0 cm^2 may be in a gray zone, with intermediate gradients of 30–40 mmHg, which would justify the discrepancy between valve area and gradient.[3]

Table 1 - Aortic stenosis grading recommendations.

Parameter	Aortic sclerosis	Mild	Moderate	Severe
Vmax, m/s	≤ 2.5	2.6-2.9	3-3.9	≥ 4
Mean gradient (mmHg)		< 20	20-39	≥ 40
Valve area (cm^2)		> 1.5	1.0-1.5	≤ 1.0
AVA index (cm^2/m^2)		> 0.85	0.61-0.85	≤ 0.6
DVI		> 0.5	0.26-0.50	≤ 0.25

AVA, aortic valve area; Vmax, maximum aortic valve velocity on continuous Doppler; DVI, ratio between Doppler velocity index integralobtained by pulsed Doppler of the left ventricular outflow tract and continuous Doppler of the aortic valve.[1]

Flow state

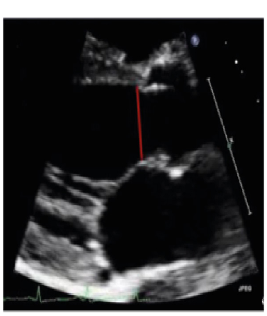
Low-flow states can also justify AVA-MG discrepancies for underestimating the gradient even in the presence of severe stenosis. The fluid dynamics principle states that the pressure gradient is directly proportional to the square of the flow and inversely proportional to the square of the valve area.[7] That is, a small flow reduction can lead to large gradient reductions. In this case, two situations are already well described:[1,3,5,8] classic low-flow LGAS (LFLGAS) due to a reduced LV ejection fraction (LVEF) < 50%;[2] and paradoxical LFLGAS with a preserved LVEF (≥50%) but small and remodeled/hypertrophic LV and SVi ≤ 35 mL/m^2.

Another situation representing almost half the cases of "discrepant" AS but still generating much debate is low-gradient stenosis with normal flow LGAS (NFLGAS), where LVEF is also preserved and SVi is > 35 mL/m^2. As it does not seem plausible from a fluid dynamics perspective, it is usually attributed to measurement errors, a small BSA, or inconsistent guidelines. However, some studies showed that when these factors are excluded, up to 50% of such patients have true severe AS, suggesting that it is a real entity.[9,10] Other studies reported that NFLGAS represents an "intermediate" stage between moderate and severe with faster progression and requiring vigilant observation.[11] Assessing transvalvular flow rate (Q) (in addition to SVi) and systemic arterial compliance (SAC) may help explain this entity and refine the LGAS diagnosis and prognosis.[12]

The transvalvular flow rate (Q) is the volume ejected per unit time through the aortic valve during the ejection period and it is measured as SV/ejection time (ET). Q expresses the true energy required to open the valve, making it a more accurate flow parameter.[12,13] In NFLGAS, Q may be low despite a normal SV due to an increased ET. This increased ET is due to increased valve resistance or reduced SAC. On the other hand, a reduced SAC can also reduce the MG under normal flow conditions.[9,14]

Some studies demonstrated that, under normal Q conditions, AVA measured at rest should be considered

Table 2 - Technical measurement aspects for AVA calculation.

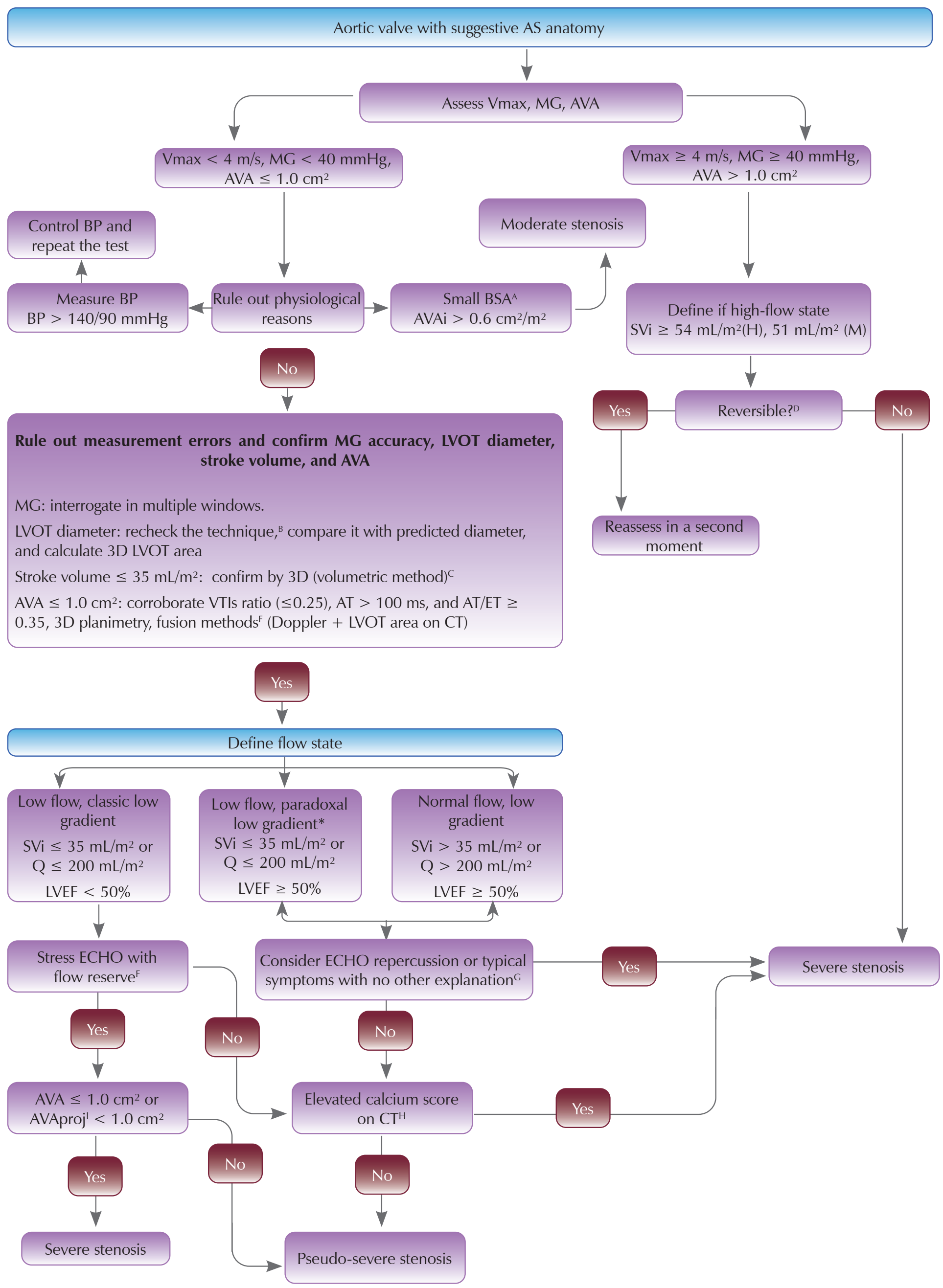


Pay strict attention to the LVOT measurement technique
Longitudinal paraesternal Zoom the image Inner edge to inner edge Measure at mid-systole, parallel and preferably adjacent to the aortic valve
LVOT measurements at ring level or less than 2 mm from the ring are more most accurate for SV and AVA calculations
Use the same LVOT for all tests.
If the measurement is not feasible or the LVOT differs from the predicted diameter[A] (by > or <2 mm), do not use the continuity equation[B]; rather, use the dimension index and other methods
Pay attention when obtaining velocities
Position the PW sample volume in the same place where the LVOT was measured and ensure the best envelope. Obtain unforced expiratory apnea velocities to avoid changing the sample volume location. Interrogate aortic transvalvular velocity with CW using multiple windows. Report the incidence where the highest velocity and gradient was obtained for serial comparison and prognostic assessment. If LVOT PW velocity is >1.5 m/s (fixed subvalvular acceleration[C]), MG, SV, and AVA are not reliable.
Always average three measurements in cases of sinus rhythm and five measurements in cases of arrhythmia

AVA, aortic valve area; CW, continuous wave Doppler; LVOT, left ventricular outflow tract; MG, mean gradient; PW, pulsed wave Doppler; SV, stroke volume; V, velocity. [A]Predicted LVOT = (5.7 × BSA) + 12.1 (do not use in obese patients). [B]VTI: velocity time integral. The continuity equation is calculated as: SV/VTI CW, where SV = (0.785 × LVOT²/2). [C]Sigmoid septum, subvalvular membrane, or obstructive hypertrophic cardiomyopathy can lead to subvalvular acceleration and MG and SV overestimation, with AVA underestimation of AVA even in the absence of significant stenosis (correlate with valve anatomy).

"true" and reflect AS severity rather than SVi or LVEF.[10,13] So, in classic LGAS, differently from what is recommended, flow normalization with echo under stress would only be necessary at a value of Q < 200 mL/s.[15]

Considering the complexity of "discrepant" AS, AVA, MG, and Vmax are insufficient. As seen above, an integrated approach is needed (Figure 1).



Source: adapted from Vahanian et al.[3]. LVEF: left ventricular ejection fraction; AVAproj = projected aortic valve area; MG: mean gradient; BS: body surface; AVAi: aortic valve area index; SVi: stroke volume index; LVOT: left ventricular outflow tract; VTI: velocity time integral; AT: acceleration time: ET: Ejection time; CT: computed tomography; Vmax: maximum speed; VTI: velocity time integral; Q: flow rate. 3D: three-dimensional; A - Do not index in obese individuals (BMI ≥30 kg/m²) B - Predicted diameter = (5.7 x Body surface) +12.1; C — 3D SV cannot be measured if mitral regurgitation is greater than mild. D - High flow situations may be reversible in patients with anemia, fever, hyperthyroidism or arteriovenous fistula and irreversible in significant aortic regurgitation. E - Use higher limits to define severe AOS: Svi ≥42 ml/m² and AVA <1.2 cm². F - Flow reserve = >20% increase in SV or Q in response to low-dose dobutamine. Pseudosevere aortic stenosis = AVA >1.0 cm2 with increased flow. G - LV hypertrophy (in the absence of coexisting hypertension), LV longitudinal global strain < 16% (no other cause) (if apical sparing pattern, consider associated amyloidosis), Zva (or arterial impedance = MG + systolic blood pressure/SVi) > 4.5 mmHg/ml/m², arterial vascular compliance (SVi/systolic blood pressure - diastolic blood pressure) <0.6 ml/m²/mmHg). H - Thresholds for severe aortic stenosis assessed by aortic valve calcification on CT (Agatston units): men >3,000, women >1,600 = highly likely; men >2000, women >1200 = likely; men < 1600, women < 800 = unlikely. I - Maximum AVA obtained when Q = 250 ml/s calculated as resting AVA +(ΔAVA/ΔQ) x (250-Qrest). SA: aortic stenosis.

Figure 1 – *Adapted "discrepant" AS diagnostic algorithm[3].*

Conclusion

Discrepant AS is a challenging entity that can present as multiple phenotypes and requires an echocardiographic approach integrated with other imaging modalities. The most appropriate combination of methods should be used for each patient with consideration of the clinical context.

Authors' contributions

Research conception and design: Beck ALS, Ribeiro LCM; Manuscript writing: Beck ALS, Ribeiro LCM; Critical review of the manuscript for important intellectual content: Beck ALS; Bibliographic research: Beck ALS, Ribeiro LCM; Table and reference formatting: Ribeiro LCM

Conflict of interest

The authors have declared that they have no conflict of interest.

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