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) ≥ 4m/s, aortic valve area (AVA) ≤ 1.0 cm\(^2\), and mean gradient (MG) ≥ 40 mmHg defines the diagnosis of classic severe AS.\(^3\) However, MG and AVA are discrepant (AVA ≤ 1.0 cm\(^2\), 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 ≥ 40 mmHg and AVA > 1.0 cm\(^2\) 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 LCAS. 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), 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
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 cm²/m² 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 cm²; thus, areas of 0.8–1.0 cm² 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 2 - Technical measurement aspects for AVA calculation.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Aortic sclerosis</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vmax, m/s</td>
<td>≤ 2.5</td>
<td>2.6-2.9</td>
<td>3-3.9</td>
<td>≥ 4</td>
</tr>
<tr>
<td>Mean gradient (mmHg)</td>
<td>&lt; 20</td>
<td>20-39</td>
<td>≥ 40</td>
<td></td>
</tr>
<tr>
<td>Valve area (cm²)</td>
<td>&gt; 1.5</td>
<td>1.5-1.5</td>
<td>≤ 1.0</td>
<td></td>
</tr>
<tr>
<td>AVA index (cm²/m²)</td>
<td>&gt; 0.85</td>
<td>0.61-0.85</td>
<td>≤ 0.6</td>
<td></td>
</tr>
<tr>
<td>DVI</td>
<td>&gt; 0.5</td>
<td>0.26-0.50</td>
<td>≤ 0.25</td>
<td></td>
</tr>
</tbody>
</table>

AVA, aortic valve area; Vmax, maximum aortic valve velocity on continuous Doppler; DVI, ratio between Doppler velocity index (obtained by pulsed Doppler of the left ventricular outflow tract) and continuous Doppler of the aortic valve.⁴

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.⁽⁵⁾ That is, a small flow reduction can lead to large gradient reductions. In this case, two situations are already well described:⁽⁶⁾⁽⁷⁾⁽⁸⁾classic low-flow LGAS (LFLGAS) due to a reduced LV ejection fraction (LVEF) < 50%;⁽⁹⁾ and paradoxical LFLGAS with a preserved LVEF (≥50%) but small and remodelled/hypertrophic LV and SVi ≤ 35 mL/m². 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/m². 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.⁽¹⁰⁾⁽¹¹⁾ Other studies reported that NFLGAS represents an “intermediate” stage between moderate and severe with faster progression and requiring vigilant observation.⁽¹²⁾ 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.⁽¹³⁾

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.⁽¹⁴⁾⁽¹⁵⁾ In LFLGAS, 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.⁽¹⁶⁾⁽¹⁷⁾ Some studies demonstrated that, under normal Q conditions, AVA measured at rest should be considered...
“true” and reflect AS severity rather than SVI or LVEF.\textsuperscript{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.\textsuperscript{15} Considering the complexity of “discrepant” AS, AVA, MG, and Vmax are insufficient. As seen above, an integrated approach is needed (Figure 1).

**Figure 1** – Adapted “discrepant” AS diagnostic algorithm.\textsuperscript{2}
Aortic Stenosis Assessment

My Approach To

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.

References


