Severe Aortic Stenosis with Low Gradient and Preserved Ejection Fraction

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Abstract

Some patients with aortic valve stenosis (AoS) have low gradients (mean transvalvar gradient < 40 mmHg), though with valve area compatible with severe AoS (AVA < 1.0 cm²) and preserved left ventricular ejection fraction (EF > 50%).Among these patients, it is possible to identify two groups: one with normal flow (indexed systolic volume, ISV > 35 mL/m²), which has a good evolution and prognosis comparable to patients with moderate AoS (AVA 1.0 to 1.5 cm²) and other with low flow (ISV ≤ 35 mL/m²). It is believed that patients from the first group occur as a result of short stature, small body size, or inadequate echocardiographic measurements, or inconsistencies of classification present in some of valvular heart disease management guidelines. In patients with low flow, there is a pattern of ventricular remodeling that evolves with increased afterload and significant concentric myocardial hypertrophy, as well as intrinsic systolic myocardial dysfunction (albeit with preserved EF), with a consequent decrease in left ventricular cavity and systolic volume. These changes are associated with worse prognosis, and these patients should be carefully evaluated so as not to have their symptoms underestimated and proper treatment postponed or neglected.

Introduction

Aortic stenosis (AoS) is aortic valve disease acquired more often, present in 4.5% of the population older than 75[1]. This valve disease will have an increasing importance in the coming decades according to a more pronounced aging of the population[2].

The most common etiologies are degenerative AoS, bicuspid aortic valve and rheumatic disease. In the evolution spectrum of these patients, the most common presentation is the one characterized by increased aortic transvalvular pressure gradients proportional to decreased valve area in patients with preserved left ventricular ejection fraction (EF) — AoS with normal flow and high gradient (NFHG AoS). As this condition evolves, the patients may present decreased ejection fraction secondary to ventricular remodeling and dysfunction and, therefore, may decrease transvalvular gradients, characterizing low-flow low gradient AoS (LFLG AoS) and reduced ejection fraction (< 50%).

A third group of patients has been recently described, in which there is a significant restriction on the valve opening, causing an aortic valve area (AVA) below 1.0 cm² (smaller or equal to 0.6 cm²/m², indexed by body surface area), but with an mean gradient between the left ventricle and the aortic root (G_{mean}) less than 40 mmHg, even with preserved ejection fraction (EF ≥ 50%)[3]. This condition is called AoS with low paradoxical gradient (LPG AoS). This is currently one of the most challenging situations both from the diagnostic and from the therapeutic point of view among valvular diseases. According to some authors, this would correspond to a more advanced stage of the disease among those with severe AoS[4].

Clinical case

Male patient, 81 years old, 69 kg, 1.70 m, body surface area: 1.8 m², with a history of valvular heart disease and hypertension. The patient recently reported fatigue on moderate exertion associated with occasional chest pain. Investigation for coronary artery disease, including coronary angiography and coronary angiography, was negative. The patient, until then, made regular use of hydrochlorothiazide, acetylsalicylic acid and enalapril. He was referred to our assessment due to increasing-decreasing aortic systolic murmur +++/6+. Two-dimensional transthoracic echocardiogram revealed the following left ventricular diameters: 45 x 31 mm; left ventricular septum: 14 mm; left ventricular posterior wall: 13 mm; left atrial dimensions: 40 mL/m² (VN < 29 mL/m²); left ventricular mass index: 131 g/m² (VN < 116 g/m²); LVEF (two-dimensional method, Simpson's rule: 56% (VN ≥ 55%); indexed systolic volume: 19 mL/m²; aortic valve presenting significant calcification, commissural distribution and along the cusps and restricted opening, area: 0.9 cm²; LV-AO gradient (maximum): 36 mmHg, LV-AO gradient (mean): 23 mmHg, moderate aortic insufficiency; maximum transvalvular aortic velocity: 3.04 m/s. Left ventricular diastolic filling demonstrating abnormal ventricular relaxation. E/e' ratio: 13 (when > 15, increased pulmonary capillary pressure is observed). Transthoracic echocardiographic analysis complemented with three-dimensional echocardiography demonstrated: LVEF: 49% (VN > 50%); aortic valve area: 0.75 cm². Two-dimensional global speckle tracking strain analysis revealed -17.8% (VN < -18%); apical four-chamber longitudinal strain (representation of septal and lateral

Keywords

Aortic Valve Stenosis; Systolic Volume; Echocardiography/methods; Left Ventricular Dysfunction.

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walls): -15.9% (VN < -18%). Blood pressure during echocardiography: 130 x 80 mmHg. Calculation of stroke work loss* (SWL) revealed: 15% (important when > 25%); valvuloarterial impedance calculation (Za)**: 8 mm Hg/mL/m² (important when > 5 mmHg/mL/m²) (Figures 1 to 4).

How to conduct this case?

Inconsistencies in the diagnosis of severe AoS

The anatomical severity of valvular heart diseases has been primarily assessed from clinical and echocardiographic data. On physical examination, AoS evolves with increasing/decreasing (or "diamond") systolic ejection murmur irradiating to the carotids. The greater the severity of AoS, the more intense is the murmur (and may even present a thrill) and the later will be its peak (mesotelesystolic). Increased aortic valve calcification will generate less mobility of its valves, with consequent hypophonesis of the second heart sound, and abnormal arterial pulse format (with slower rise and smaller amplitude — pulse parvus et tardus).

From the echocardiographic point of view, the most commonly used parameters to classify AoS as severe are[5,6]:

- transvalvar flow rate > 4m/s;
- G_{mean} > 40 mmHg;
- AVA < 1.0 cm².

Besides these, other parameters are used to better characterize the seriousness of this valve disease:

- ratio of flow rates between left ventricular outflow tract (LVOT) and aortic valve (a value < 0.25 characterizes severe AoS)[1];
- aortic valve calcium score as measured by computer tomography scan, most recently described (values above 2,000 Agatston arbitrary units (AU) for men and about 1,250 AU for women characterize severe AoS)[7] (Figure 5).

Among the "classic" echocardiographic parameters, the one subject to greater variability and possibility of error in its measure, because it is a measure derived from the continuity equation, and not directly measured, is the AVA. It is calculated from the measurement of flow velocities in the LVOT and in the aortic valve and LVOT diameter. The AVA can vary significantly even with minor differences in the measurements conducted by the operator, mainly related to under- or overestimated LVOT, which is a major cause of error in the measurement of AVA[8]. We recommend indexing the measurement (AVAi), especially when there are threshold values and in patients with body surface measurements (especially very high or low) above average.

Besides this, as for the inconsistencies presented among the main parameters used in echocardiography to classify the severity of patients with AoS, some studies have shown in a large number of patients that the valve area that would correspond to an aortic transvalvular flow velocity > 4 m/s and G_{mean} > 40 mmHg would be around 0.8 cm[29,10]. Aiming to correct this distortion, the latest Brazilian Guidelines for Valvular Heart Diseases, published in 2011, began to present
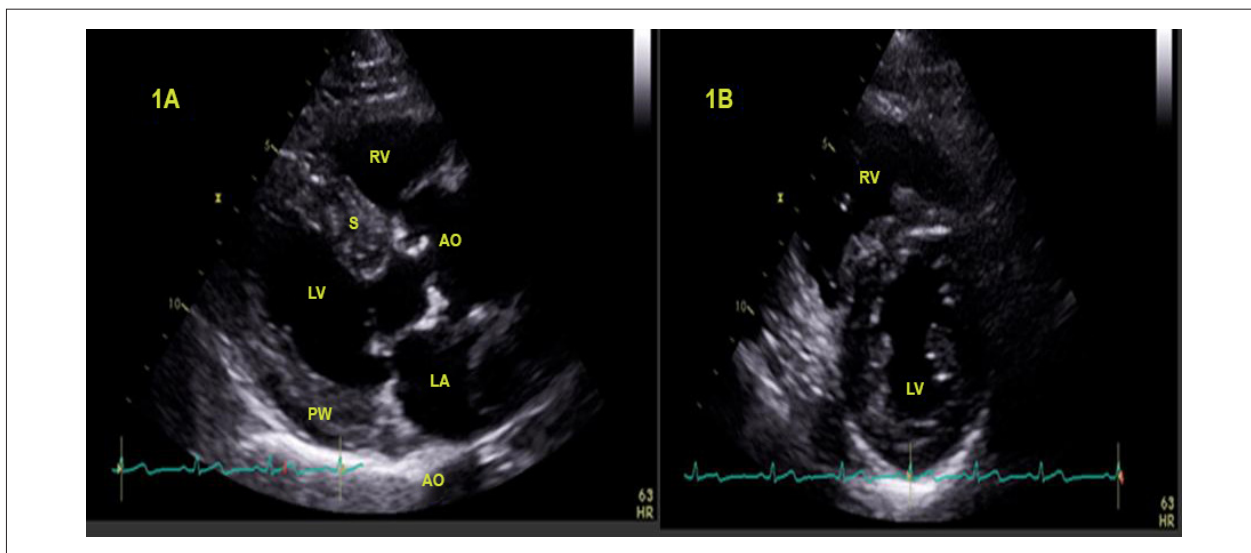

Figure 1 – *A:Two-dimensional transthoracic echocardiography (parasternal projection in the long longitudinal axis of the left ventricle).*
Demonstration of aortic valve opening and increased thickness of the ventricular septum and left ventricular posterior wall.
LV:left ventricle; RV: right ventricle; AO: aorta; LA: left atrium; S: ventricular septum; PW: left ventricular posterior (inferolateral) wall. B: Two-dimensional transthoracic echocardiography (left ventricular cross-sectional short axis parasternal projection).
Left ventricular hypertrophy.
LV: left ventricle; RV: right ventricle.

Stroke-work loss (SWL): $\dfrac{100 \times (GM)}{AG + SBP}$

AG: LV-AO gradient (mean); SBP: systolic blood pressure
**Valvuloarterial impedance: Zva: SBP + AG/ISV,*
Where: SBP: systolic blood pressure; AG: LV-AO gradient (mean); ISV: indexed systolic volume.
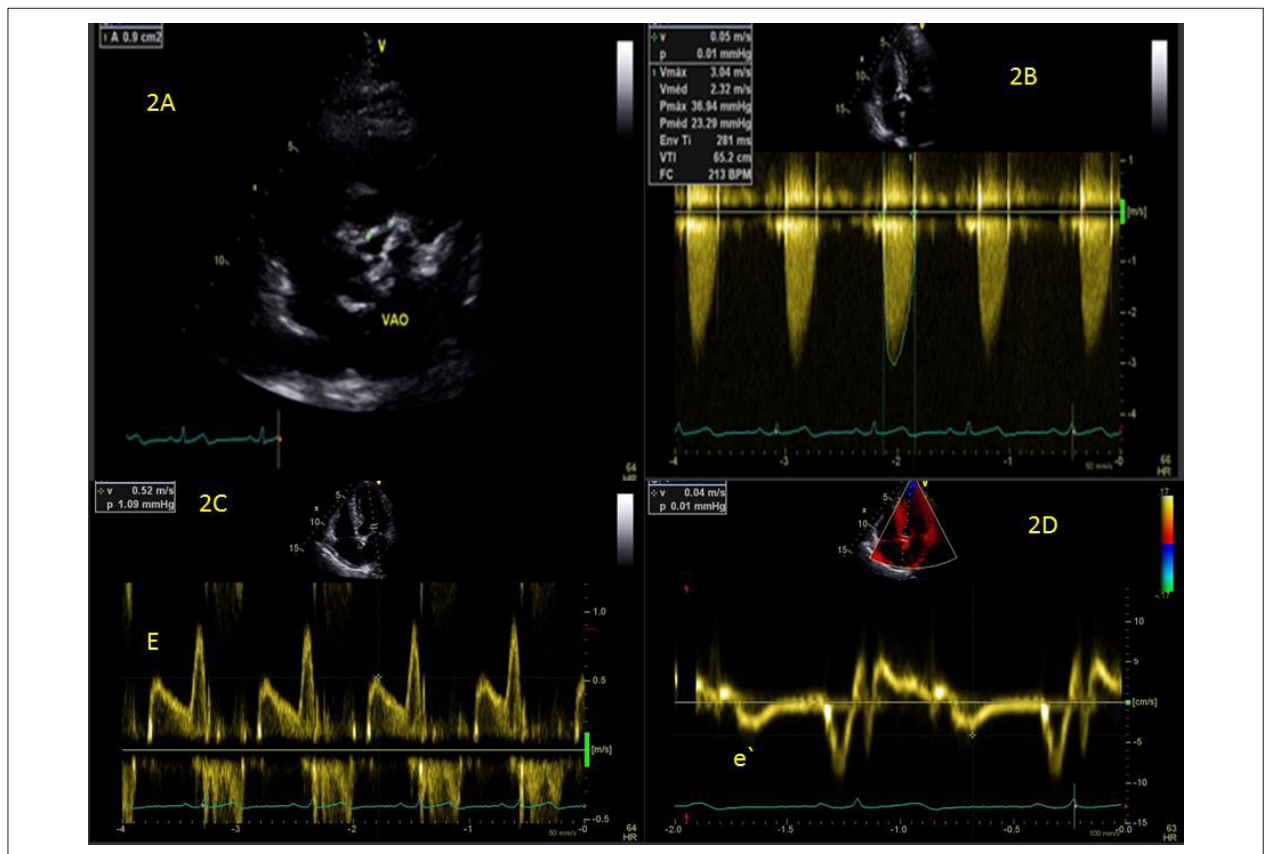
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Figure 2 – *A:Two-dimensional transthoracic echocardiography.*
Planimetric measurement of aortic valve area: 0.9 cm².
AO: aortic valve. B: Doppler echocardiography (continuous Doppler).
Measurement of maximum and mean gradients between the left ventricular outflow tract and the aortic root (LV-AO gradient). Maximum gradient: 36 mmHg; mean gradient: 23 mmHg.
Maximum speed measurement in the left ventricular outflow tract: 3.04 m/s. C: Doppler echocardiography (pulsed Doppler).
Measurement of speed during protodiastole (E wave): 0.52 m/s. D: Doppler echocardiography (Tissue Doppler).
Measurement of speed during protodiastole (e' wave): 0.04 m/s.

E/e' ratio: $\frac{0.52 \ m/s}{0.04 \ m/s}$: 13.

the value of 0.8 cm² as a new AVA cutoff point for severe AoS in its classification[1]. This change was suggested by Dumesnil et al.[11], among other authors[12]. On the other hand, despite the data of these studies, other recent international guidelines maintain the AVA cutoff point < 1.0 cm² for severe AoS.

Another factor that may be associated with the measurement of smaller valvular areas without the patient necessarily presenting a severe valvular heart disease is the presence of small ventricles in patients with short stature, particularly women[13]. In general, when correcting the AVA measured by echocardiography in the body surface, such differences in severity tend to be minimized. In this case, the cutoff value AVA < 0.6 cm²/m² for severe AoS is used[1,6]. Remember that, to assess the severity of AoS, the parameters should always be analyzed together.

Finally, it is important to remember that AVA measured by the continuity equation in echocardiography is the effective area, not the anatomical one, since it is about the measure of the flow rate that goes through the valve. This may account for the differences in the measurements between AVA measured by this method and that measured by planimetry or by Gorlin's hemodynamic equation[8,13].

Therefore, once a patient is characterized as having severe AoS by the valve area with no transvalvar flow velocity or G_{mean} compatible with the same classification, in addition to confirming the adequacy and reliability of the AVA measurement taken, it is essential to take into consideration the factors described so that the patient be provided with an appropriate therapeutic approach.

Epidemiology

The LPG AoS is an underdiagnosed condition, since the low gradient presented by patients may make them be interpreted as having moderate rather than severe valve disease. Consequently, these patients may have their symptoms underestimated and proper treatment, when indicated, may occur late.
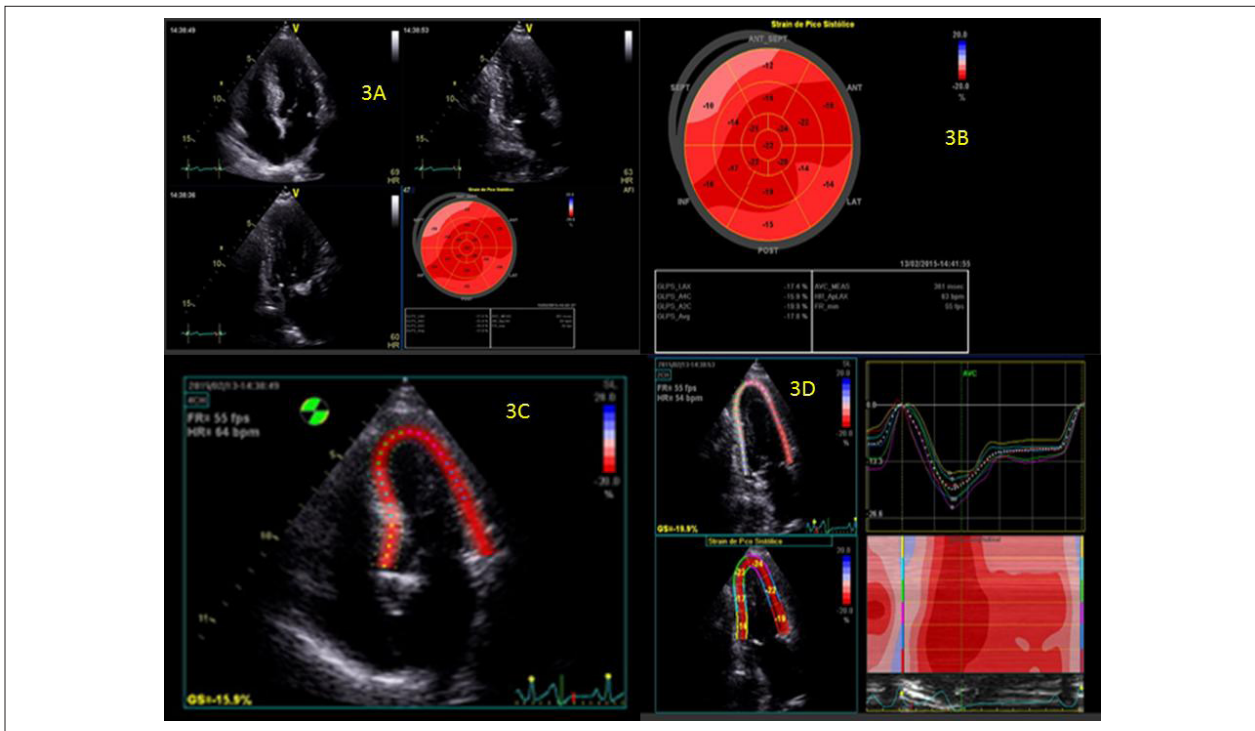
Figure 3 – A, B, C, D: Echocardiography for measurement of left ventricular longitudinal strain. Average global longitudinal peak strain (GLPS avg): -17.8% (VN < -18%).
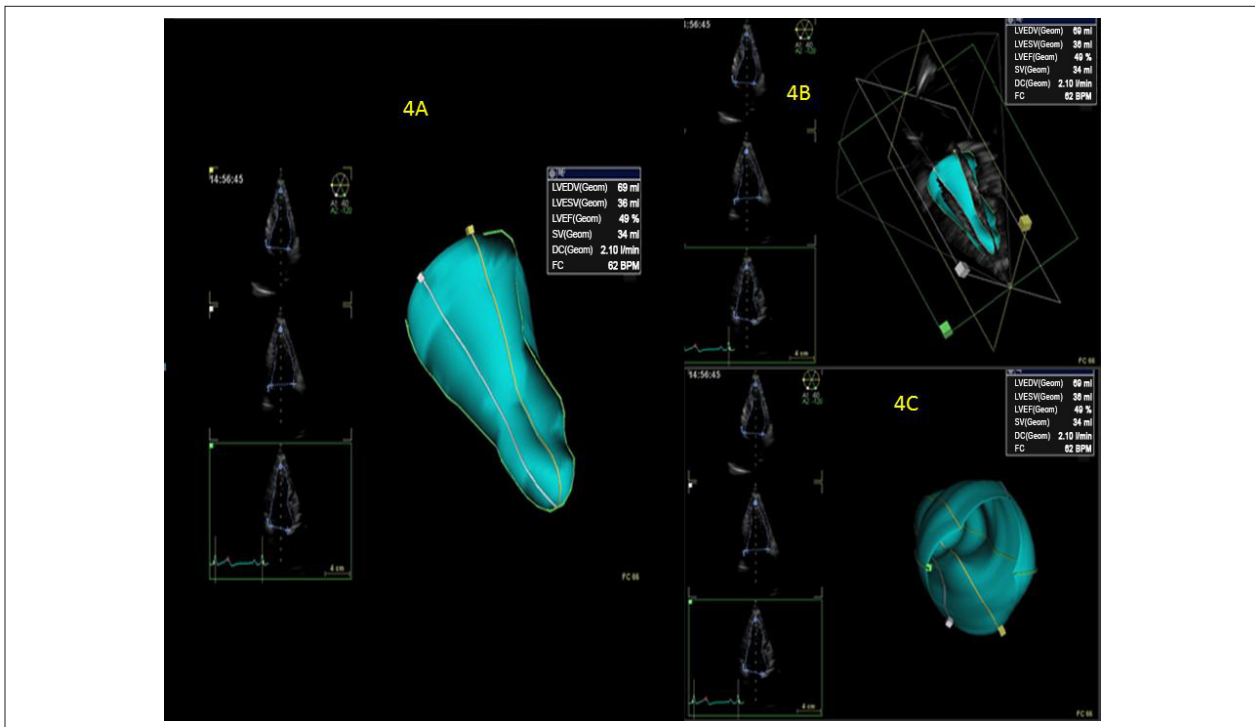

Figure 4 – A:Two-dimensional transthoracic echocardiography
Oblique apical projection. Measurement of volumes, three-dimensional ejection fraction and left ventricular ejection volume.
LVEDV: left ventricular end-diastolic volume: 69 mL; LVESV: left ventricular end-systolic volume: 36 mL; LVEF: three-dimensional left ventricular ejection fraction: 49% (VN > 50%); SV: stroke volume, left ventricular stroke volume: 34 mL. B: Three-dimensional transthoracic echocardiography. Apical oblique projection with the demonstration of multiple spatial rotation plans for obtaining the three-dimensional image of the left ventricle. C: Three-dimensional transthoracic echocardiography. Oblique apical projection from the mitral valve plane to view the inside of the left ventricle.
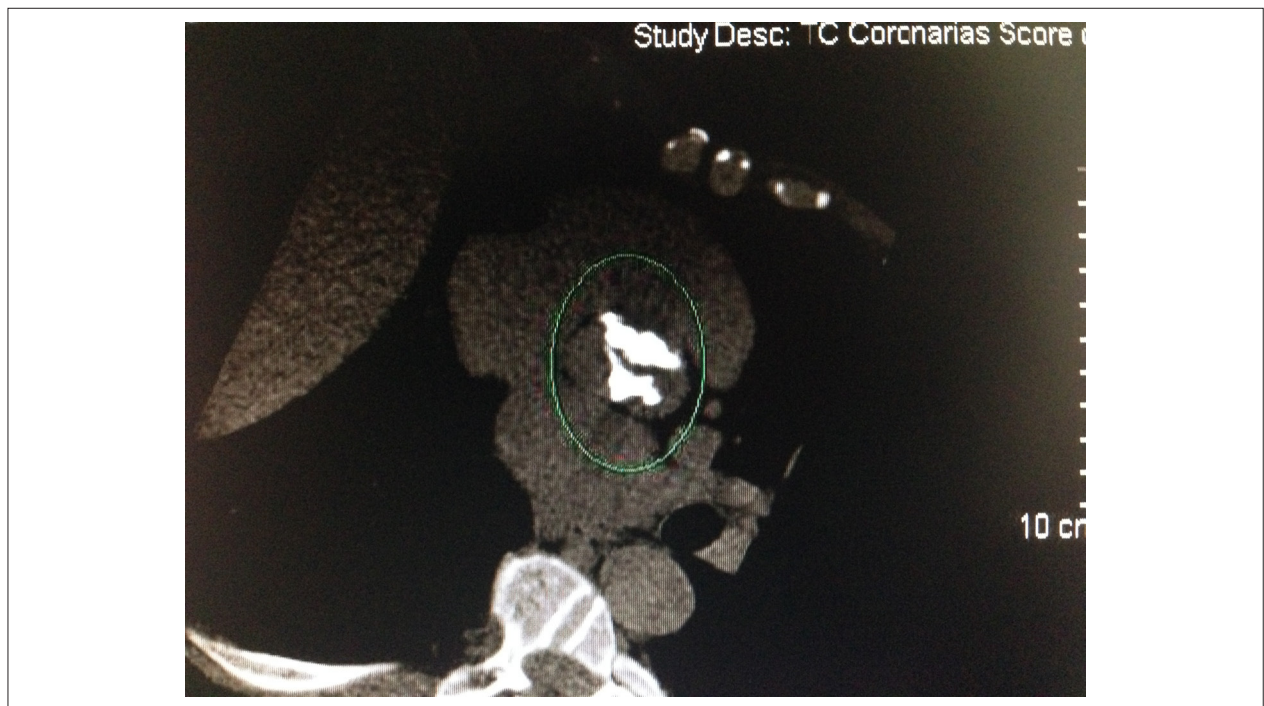
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Figure 5 – *Computed tomography of the chest with measurement of aortic valve calcium score in patients with severe AoS with G_{mean} 33 mmHg. In this case, the measured calcium score was 4001 Agatston's arbitrary units*[7].

Some studies have shown a prevalence of up to 30% of patients with LPG AoS and low flow, among those with severe AoS[3,11,14]. These patients are more often elderly, women and patients with high blood pressure (hypertension)[3,14,15]. Furthermore, in the study of Clavel et al.[16], they also had a higher incidence of coronary artery disease and diabetes mellitus than patients with NFHG AoS ("classic" AoS). In the national clinical practice, however, there is a lower incidence of LPG AoS, perhaps reflecting different populations or underdiagnosis.

Pathophysiology

Patients with LPG AoS have a more pronounced concentric remodeling, with greater hypertrophy and more fibrosis. The greater afterload to which the myocardium of AoS patients is chronically exposed is responsible for a larger ventricular wall stress and subendocardial hypoperfusion. Thus, there is deposition of predominantly subendocardial fibrosis, with direct interference on systolic myocardial strain, that is, the standard with which the heart muscle contracts during systole. The longitudinal function would be the first to change, since it is the component that depends on proper functioning of subendocardial fibers. The assessment of such strain is able to demonstrate a more subtle change in myocardial function even with normal ejection fraction. It can be assessed, when necessary, by the displacement of the mitral annulus, the LV strain measured by tissue Doppler or two-dimensional speckle tracking[4,15].

Increased fibrosis was documented by Herrmann et al.[4] by both delayed enhancement evaluation in magnetic resonance imaging and by pathological anatomy analysis. A higher amount of fibrosis was observed in patients with LPG AoS than in those with NFHG AoS (3.9% vs. 1.8%). An inverse relationship between the amount of myocardial fibrosis and displacement of the mitral annulus was found, demonstrating that despite EF > 50%, it is possible to quantify changes in myocardial function using another method. Such changes, associated with low systolic volume, would then lead to the existence of low transvalvular gradients. In Figure 6, it is possible to identify myocardial fibrosis assessed by delayed enhancement.

Electrocardiography

With respect to echocardiographic parameters, patients with LPG AoS and low flow presented lower AVA and speed ratios than patients with high gradients[11]. In addition to that, they present lower systolic volume (indexed systolic volume < 35 mL/m²). Such changes would be consistent with the hypothesis that these patients have a more advanced disease in which the greater restriction to ventricular outflow caused by valve disease entails greater pressure overload to the left ventricle. This, in turn, is responsible for causing a stronger degree of concentric myocardial hypertrophy, decreasing ventricle size with consequently lower stroke volume and lower gradients. Some studies evaluating echocardiographic data showed that patients with LPG AoS were those with higher relative wall thickness and smaller LV cavity compared to patients with moderate AoS or NFHG AoS[3,4].

Hachicha et al.[3] were among the first authors to describe this form of AoS. They evaluated parameters related to
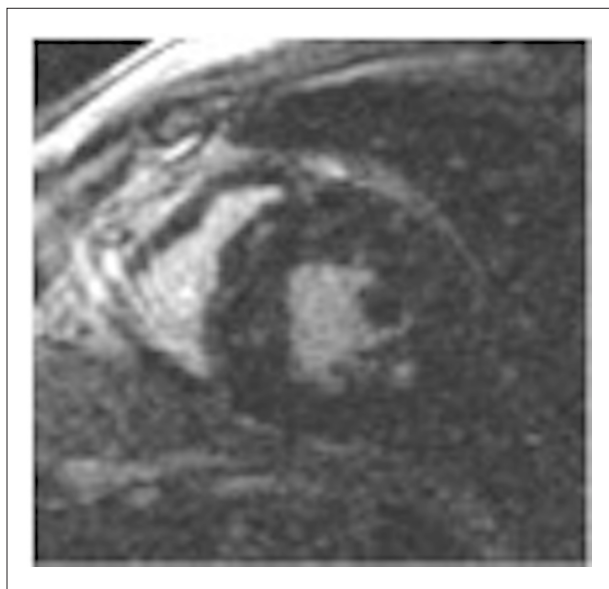
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Figure 6 – *Myocardial fibrosis assessed by delayed enhancement in cardiovascular magnetic resonance imaging. In this case, 7.6% of the myocardium correspond to fibrosis.*

afterload, showing increased systemic vascular resistance and valvuloarterial impedance and decreased systemic arterial compliance. Some discreet degree of LV diastolic dysfunction was noticed. However, systolic function parameters were significantly reduced compared to patients with NFHG AoS: stroke work, indexed systolic volume, mean transvalvular flow, cardiac output and rate and, finally, ejection fraction (although > 50%)[3]. Analyzing only patients with LPG AoS, those with ISV < 35 mL/m^{2} (therefore with low flow) had significantly more abnormal afterload assessment parameters than patients with ISV > 35 mL/m^{2} (without low flow)[17].

Lancellotti et al.[15] studied the three myocardial strain components (longitudinal, radial and circumferential) and observed an increase in global afterload imposed on the left ventricle (measured by valvuloarterial impedance) in patients with low-flow LPG AoS as well as a smaller myocardial strain, especially circumferential, as analyzed by two-dimensional speckle tracking.   They found increased levels of brain natriuretic peptide (BNP) (with cutoff point at 61 pg/mL)[15].

Adda et al.[18] compared 82 patients with LPG AoS and low flow versus normal flow.   In the population studied, patients with low-flow LPG AoS presented smaller valve area (0.7 vs. 0.86 cm[2]), greater valvuloarterial impedance (5.5 vs. 4 mmHg/mL/m^{2}) and worsening of longitudinal LV function (basal longitudinal strain -11 vs. -14%)[18]. Thus, it is possible to define two groups of patients with LPG AoS: one group with low flow, with more intense morphological and functional changes and worse prognosis, and another with normal flow despite the low gradient, with fewer structural abnormalities and consequently better outcomes.

Three-dimensional echocardiography may be useful in assessing patients with AoS in which there is disagreement between the valve area and the aortic valve gradient,

as well as for measuring LVEF more accurately. The two largest international echocardiography societies (American Society of Echocardiography and the European Association of Cardiovascular Imaging)[5,7,10,12] recommend that LVEF be measured using three-dimensional echocardiography in centers where such method is available. Three-dimensional echocardiography provides a better anatomical analysis of the aortic valve, thus avoiding the limitations of geometric inferences found with the two-dimensional analysis. The measurement of longitudinal strain also allows discriminating patients who have preserved LVEF, but who have decreased cardiac mechanics analysis. The calculation of valvuloarterial impedance (Za) enables to analyze the relative importance of valvular afterload and arterial afterload, being especially relevant in patients with aortic stenosis and hypertension. Cardiac work loss calculation also adds information to the analysis in this group of patients.

Coronary tomography

Clavel et al.[7] evaluated the presence of aortic valve calcification by aortic valve calcium score in patients with AoS and defined values of 2,065 UA for men and 1,275 UA for women, when severe. However, in patients with AVA < 0.6 cm[2]/m^{2} G_{mean} < 40 mmHg, which amounted to 27% of patients, only 50% had aortic valvular calcification above these values. On the one hand, these data confirm severe AoS in about half of patients. In the other patients, we would find severe AoS, with a lower degree of valvular calcification. Interestingly, many patients had average ISV of 43 mL/m^{2}, therefore not characterizing low flow. As demonstrated by Mehrotra et al.[19], patients with LPG AoS and ISV > 35 mL/m^{2} may have lower myocardial structural abnormalities and prognosis similar to patients with moderate AoS[19]. It would be possible that patients with higher calcium scores were those with lower ISV.

Treatment and prognosis

Proper classification of patients with LPG AoS requires utmost caution, since it leads to potential indication of interventional treatment on the aortic valve, either by surgical valve replacement or percutaneous implantation of aortic valve depending on the patient's risk profile. On the one hand, no indication of surgical intervention results in natural risks related to severe valvular heart disease (with mortality rate of about 1% per year). On the other hand, indication of intervention on the valve exposes patients to the risks related to it (including operative mortality around 3%)[1]. Indication of surgery for patients with LPG AoS is 40% to 50% smaller than those with NFHG AoS, probably because the severity of these patients is underestimated given the low gradient[20,21].

Table 1 summarizes echocardiographic data for differentiation among the subgroups of severe AoS.

Lancellotti et al.[22] studied the prognosis of 150 patients with severe AoS with EF > 55% and normal exercise test (no symptoms or arrhythmias and normal blood pressure curve) — thus "truly asymptomatic". Patients were divided into four groups according to G_{mean} and ISV. The primary composite endpoint included cardiovascular death or indication of aortic valve replacement for

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Table 1 – Echocardiographic differential diagnosis between different types of severe AoS

	NFHG AoS	Reduced EF LFLG AoS	Low-flow LPG AoS	Normal flow LPG AoS
AVA (cm²)	< 1.0	< 1.0	< 1.0	< 1.0
Indexed AVA (cm²/m²)	≤ 0.6	≤ 0.6	≤ 0.6	≤ 0.6
Transvalvar aortic flow rate (m/s)	> 4.0	< 4.0	< 4.0	< 4.0
Mean transvalvar gradient (mmHg)	> 40	< 40	< 40	< 40
Ejection fraction	≥ 50%	< 50%	≥ 50%	≥ 50%
Ratio of flow rates	< 0.25	≥ 0.25	≥ 0.25	≥ 0.25
Indexed systolic volume (mL/m²)	-	-	< 35	>35
Valvuloarterial impedance	-	-	> 5.5	< 5.5
LV strain	-	-	Abnormal	Abnormal
Speckle tracking	-	-	Abnormal	Abnormal

AoS: Aortic stenosis; AVA: aortic valve area; AVAi: indexed aortic valve area; NFHG: normal flow, high gradient; EF: ejection fraction; LFLG: low-flow, low-gradient; LPG: low paradoxical gradient.

symptoms or ventricular dysfunction (EF < 50%). Both G_{mean} < 40 mmHg and ISV < 35 mL/m² were predictors of poor outcome (damage ratios of 2.3 and 1.7 — p = 0.004, respectively). Patients with LPG AoS and ISV > 35 mL/m² ("normal flow") had a better outcome. In this subgroup, 83% of patients remained free of events after two years of follow-up compared to only 27% of patients with LPG AoS with ISV < 35 mL/m² (low flow). Patients with LPG AoS with normal flow had longitudinal myocardial function preserved and lower levels of BNP (34 ± 5). On the other hand, those with LPG AoS with low flow had greater concentric remodeling, greater global LV afterload, higher levels of BNP (95 ± 18) and intrinsic myocardial dysfunction associated with a lower left ventricular cavity.

It is worth noting that the patients evaluated had no body surface differences among the groups, which could interfere with the evaluation of systolic volume (patients with lower body surface may have lower stroke volume and lower gradient and this may not necessarily constitute an abnormality). Furthermore, stroke volume measurements performed by the volumetric method or derived from LV outflow velocity-time integral (VTI) measurement obtained similar results.

On the other hand, Jander et al.[8] and Dumesnil and Pibarot[23] compared the evolution of 435 patients with AoS with AVA < 1.0 cm² and G_{mean} < 40 mmHg with other 184 patients with moderate AoS (AVA 1.0 to 1.5 cm² and G_{mean} 25 to 40 mmHg) and found similar outcomes in both groups (cardiovascular death, aortic valve replacement and heart failure secondary to valvular heart disease). Among patients with AVA < 1.0 cm² and low gradient, 51% had ISV < 35 mL/m² and the comparison of these patients with those with ISV > 35 mL/m² did not reveal differences in the outcomes assessed. The studies, however, were heavily criticized for their selection bias[23]. Patients with severe AoS and low gradient evaluated by Jander et al.[8] did not present the classic structural characteristics of patients with BGP AoS

and low flow: increased global LV afterload, more significant ventricular remodeling, lower left ventricular cavity and intrinsic myocardial dysfunction. It was assumed that patients classified as "serious" by Jander et al.[8] could actually represent less severe patients, which were misclassified due to small body size, echocardiography measurement errors or, since unindexed AVA was used, due to classification inconsistencies found in the current guidelines[25].

In another evaluation by Herrmann et al.[4], patients with BGP AoS with greater amounts of fibrosis had less favorable postoperative response with higher mortality and worse global LV function and functional class[4].

There is a clear benefit of aortic valve replacement surgery in patients with LPG AoS[3,16,17,24,25]. Hachicha et al.[3] evaluated 512 patients with severe AoS (defined by indexed AVA < 0.6 cm²/m²), of which 35% had ISV < 35 mL/m². In this group, the average G_{mean} was 32 mmHg with more than 55% of patients presenting G_{mean} < 30 mmHg. Despite having preserved EF (> 50%), patients with low flow had lower ejection fraction (62% vs. 68%) and survival decreased by three years (76% vs. 86%, p = 0.006) and non-surgical treatment (patient maintained under clinical treatment) was associated with a three-times higher mortality risk. Valvuloarterial impedance > 5.5 mmHg/mL/m² (damage ratio 2.6, 95% CI 1.2 to 5.7)[3] was also associated with higher mortality.

Mohty et al.[17] analyzed 768 patients with severe AoS (AVA < 1 cm²) with EF > 50%. Of these, 99 patients had low-flow BGP AoS, while 172 patients had BGP AoS with ISV > 35 mL/m². The presence of low-flow BGP AoS was a predictor of mortality (damage ratio 1.84, p = 0.014) and surgical treatment improved the survival of these patients (mortality of 63% in five years in operated patients compared to 38% for those maintained under clinical treatment, p = 0.007). Note that even patients undergoing only valve replacement (without any coronary artery bypass grafting associated) presented benefits from the

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intervention. Patients with low-flow BGP AoS had survival rates of 32% in ten years against 55% among those with ISV > 35 mL/m². Similar results were found by Tarantini et al.[26], in which aortic valve replacement was associated with a decrease of 76% in the risk of death of patients with BGP AoS, and Pai et al.[24], with a survival rate of 90% in operated individuals against 20% in those maintained under clinical treatment in five-years' follow-up.

Conclusion

Among patients with AoS BGP, we can point out two distinct subgroups[11,14,19]. In the first subgroup, there is no low flow (ISV > 35 mL/m²) and the structural changes are not significant compared to patients with moderate AoS, and there are controversial data on whether they should be maintained under clinical follow-up until they present the "classic" criteria recommended by the current guidelines for intervention[17]. In the second group, there is low flow (ISV < 35 mL/m²), and the combination of increased afterload and decreased cardiac output indicates lower myocardial reserve. Chronic left ventricle exposure to high systemic vascular resistance levels, as well as obstruction of blood outflow caused by the decrease in valve opening exceeds the limit of the compensatory myocardial mechanisms and leads to an intrinsic compromise of their function (even with maintenance of normal ejection fraction values), with a consequent decrease in cardiac output.

They present a worse prognosis and greater benefit from interventional treatment, where feasible. Note that the surgical indication of AoS still fundamentally depends on the presence of symptoms. However, identification of high-risk patients may reduce the likelihood of sudden death in asymptomatic patients[1,5].

The elderly symptomatic patient in the example given had AoS with low LV-AO gradients (maximum: 36 mmHg and mean: 23 mmHg) and low indexed left ventricular systolic volume (19 mL/m²) with preserved LVEF (56%) measured by two-dimensional echocardiography. However, the valve area measured using three-dimensional echocardiography was 0.75 cm², total two-dimensional longitudinal strain was slightly decreased (-17.8%), although the strain that represents the septal and lateral walls presented a more consistent decrease (-15.9%, greater ventricular septal mass). Other parameters, such as increased left ventricular mass index (136 g/m²), valvuloarterial impedance (Za): 8 mmHg/mL/m² and stroke work loss of 15% confirmed the presence of low-flow low-gradient AoS and normal LVEF. The patient was referred for surgical treatment, which confirmed the diagnosis of severe aortic stenosis, presenting a significant clinical improvement.

When well indicated and performed with proper technique, various complementary methods currently available allow differentiating these subgroups with good accuracy (algorithm). It is possible to deliver a more accurate diagnosis of these patients, preventing their symptoms
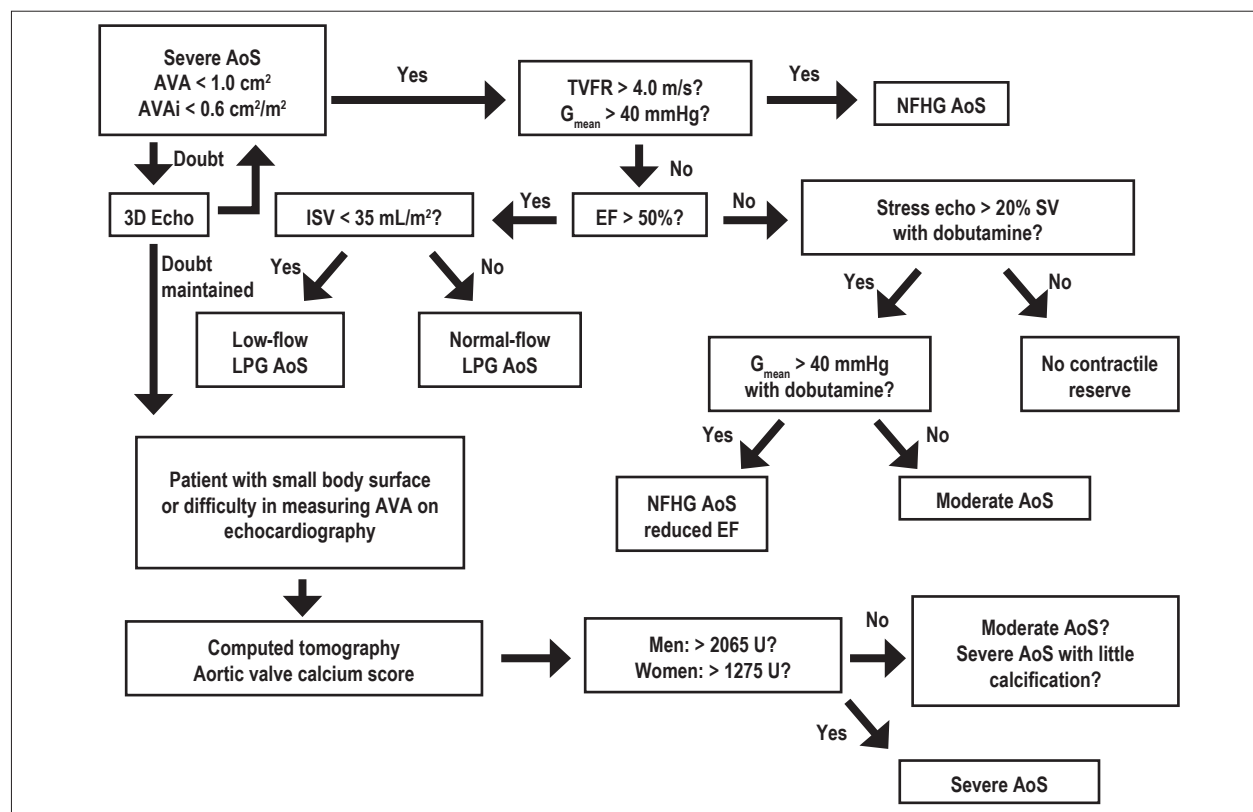
Algorithm – *Severe AoS diagnosis.*
AoS: Aortic stenosis; AVA: aortic valve area; AVAi: indexed aortic valve area; TVFR: transvalvular flow rate; NFHG: normal flow, high gradient; ISV: indexed systolic volume; EF: ejection fraction; SV: systolic volume; LPG: low paradoxical gradient; G$_{mean}$: mean gradient; Echo: echocardiography.

from being neglected, and leading to the outbreak of interventional treatment in due course.

Authors' contributions

Research creation and design: Sampaio RO, Vieira MLC; Data acquisition: Sampaio RO, Pires LJT; Data analysis and interpretation: Tarasoutchi F; Manuscript drafting: Sampaio RO, Pires LJT; Critical revision of the manuscript for important intellectual content: Sampaio RO, Pires LJT, Vieira MLC, Tarasoutchi F.

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