Review Article

Integrating Echocardiographic Findings to Improve Diagnostic and Prognostic Assessments in Moderate Aortic Valve Stenosis: A Comprehensive Review

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Abstract

Aortic valve stenosis (AS) is the most common valvular heart disease in developed countries, with its prevalence on the rise due to aging populations. While severe AS has long been recognized as high-risk, recent studies have shed light on the significant association between moderate AS and cardiovascular morbidity and mortality. Yet, the data are still inconclusive. With noninvasive multi-modality imaging techniques advancing rapidly, we now have more insight into the underlying biology of AS. Echocardiography continues to serve as the primary noninvasive imaging modality for diagnosing and grading AS. This comprehensive review delves into the role of echocardiography in diagnosing moderate AS and how the findings can support clinicians in making well-informed decisions that impact patients' prognoses.

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Introduction

Aortic valve stenosis (AS) is a narrowing at the level of the aortic valve (AV) that obstructs the outflow from the left ventricle (LV). AS is the most prevalent primary valvular heart disease in developed nations. With the projected doubling of its incidence in elderly patients by 2050,[1] AS is poised to become an increasingly significant public health concern. Traditionally, severe AS has been viewed as the primary cause of adverse cardiovascular events, yet recent observational studies have highlighted that even moderate AS is associated with a significant risk of such events, including death.[2]

A recent large-scale study revealed that of the 1,961 patients with moderate AS, 57% were asymptomatic, 27% experienced mild symptoms, and 17% reported marked limitations in activity due to their symptoms. The study also uncovered that 53% of patients exhibited left ventricular ejection fraction (LVEF) ≥60%, 28% presented with LVEF =50–59%, and 20% had LVEF <50%. Tragically, during a median follow-up period of 50 months, 44% of the patients passed away.[3]

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A different study revealed that during a median follow-up period of 4.3 years, 45.3% of patients with moderate AS succumbed.[4]

The progressive nature of AS is yet another critical issue. A recent meta-analysis of 14 prospective studies revealed that the progression rates of aortic AS can be quantified in terms of aortic valve area (AVA) and mean pressure gradient (MPG), with respective rates of −0.08 cm^2/year and +4.10 mm Hg/year.[5] Patients with moderate AS are a heterogeneous group, with a wide range of disease progression rates and risks of cardiovascular events.[2] These findings emphasize the critical need to recognize the potential risks of moderate AS and to initiate appropriate management and intervention as early as possible.

With the burgeoning advances in multi-modality noninvasive imaging techniques, we now possess a more comprehensive understanding of the biological underpinnings of AS, enabling us to make more informed clinical decisions. Despite the growth of alternative imaging methods, echocardiography remains the primary noninvasive technique for diagnosing and assessing the severity and progression of AS.[6, 7]

This review will deliver a thorough analysis of echocardiography's contemporary role in diagnosing moderate AS, its impact on prognosis, and how it can support clinicians in making more informed clinical decisions to enhance the management of patients with moderate AS.

Prevalence

AS is a widespread condition, particularly among the elderly. A meta-analysis of 9,723 subjects revealed that AS has a prevalence rate of 12.4% among individuals aged 75 years and older, with severe AS accounting for 3.4% of cases.[8] This implies that approximately 1 in 8 adults in this age bracket are afflicted with AS. While commonly thought of as an older adult's disease, it is essential to note that AS can also occur in younger age groups, albeit with a lower prevalence.[9] The Tromsø study[10] revealed a significant increase in AS prevalence with age. Respectively, the percentages of AS prevalence in the age groups of 50–59, 60–69, 70–79, and 80–89 years were 0.2%, 1.3%, 3.9%, and 9.8%.

The prevalence of moderate AS remains elusive due to a few factors. Foremost, numerous studies have focused solely on severe cases, omitting patients with moderate AS. Furthermore, valvular heart disease, including AS, is frequently misdiagnosed in the general population, resulting in a paucity of precise information on its prevalence.[11] A recent large-scale study revealed that among approximately 37,000 echocardiographic studies performed for diverse reasons, with a mean patient age of 62.5 years, 952 cases (2.5%) demonstrated moderate AS.[12] In a separate large-scale registry study, researchers analyzed approximately 240,000 individuals aged 18 years and older who underwent echocardiography, revealing that 1.4% of the patients had moderate AS.[13]

Definition of moderate AS

The primary echocardiographic parameters used to assess the severity of AS are as follows:

1.Peak aortic valve jet velocity (AV Vmax): This parameter measures the highest velocity of blood flow through the AV during the systolic phase of the LV. AV Vmax is the preferred measure for determining AS severity.[14]

2.Mean aortic valve pressure gradient (AV MPG): Calculating the mean AV gradient for AS is complex and cannot be obtained from mean velocity. Nonetheless, imaging platforms have built-in measurement packages that can routinely perform this calculation.

3.AVA: The cross-sectional area of the AV orifice can be calculated based on the continuity equation formula using Doppler echocardiography findings. AVA is less flow-dependent and can be used in low-flow states. Direct planimetry in 2D or 3D is another method to measure AVA directly.[6]

4.Doppler velocity index (DVI): DVI, also known as the dimensionless index (DI), is an additional measure for assessing AS severity. It is calculated by dividing the Doppler-derived velocity or velocity time integral measurement in the left ventricular outflow tract (LVOT) by the Doppler measurement at the AV.[7, 14, 15]

According to recent guidelines, moderate AS is characterized by an AVA ranging from 1.0 to 1.5 cm², a peak aortic jet velocity between 3 m/s and 4 m/s, or a mean transvalvular pressure gradient of 20 to 40 mm Hg.[15, 16]

Indexing AVA for body surface area (BSA) may not be suitable for all patients, particularly those who are morbidly obese. Nevertheless, it can be useful for grading AS severity in patients with small body sizes, children, and adolescents.[2]

Various conditions have been proposed as indicators of moderate AS by some experts, as summarized in Table 1.[17]

When all echocardiographic findings are consistent, diagnosing moderate AS is relatively straightforward. However, a recent study involving 1,974 patients (mean age: 73 years) with moderate AS revealed discordant grading in 788 cases, constituting 40% of the total.[18]

Discordant grading due to potential measurement errors

In instances of conflicting criteria in patients with moderate AS, discordant grading is common due to potential measurement errors. Thus, the initial step in evaluating these patients is to guarantee the precision of Doppler echocardiographic measurements and accurate assessment of the LVOT. Notwithstanding the circular

Table 1. Conditions proposed as indicators of moderate AS

Conditions	Peak Aortic Velocity		AV Mean Gradient		AVA		AVA Index		BMI
1	3.0-4.0 m/s	or	20 to <40 mm Hg	and	1.0 – 1.5 cm^2				
2	3.0-4.0 m/s	or	20 to <40 mm Hg	and	<1.0 cm^2	with	>0.6 cm^2 /m^2	in	<30 kg/m^2
3	3.0-4.0 m/s	or	20 to <40 mm Hg	and	<1.0 cm^2	with	>0.5 cm^2 /m^2	in	≥30 kg/m^2
4	3.0-4.0 m/s	or	20 to <40 mm Hg	and	>1.5 cm^2	with	<0.9 cm^2 /m^2	in	<30 kg/m^2
5	3.0-4.0 m/s	or	20 to <40 mm Hg	and	>1.5 cm^2	with	<0.8 cm^2 /m^2	in	≥30 kg/m^2

AV, Aortic valve; AVA, Aortic valve area; AVA index, AVA (cm^2) /body surface area (m^2); BMI, Body mass index

assumption in the continuity equation formula, the LVOT is often elliptical. The minor diameter of the elliptical LVOT typically corresponds to the anteroposterior diameter of the LVOT as measured in the parasternal long-axis view. As such, measuring LVOT in the long axis may result in an underestimation of the cross-sectional LVOT area, leading to inaccurate grading of AS severity. Magnetic resonance imaging measurements of the elliptical LVOT area, when used as input in the continuity equation, increased indexed AVA by 29% in a previous study.[19]

To achieve accurate measurements and enhance reproducibility when measuring LVOT diameter in a parasternal long-axis view, the following guidelines should be observed:

Precise measurement: The LVOT diameter should be accurately measured from the inner edge to the inner edge of the septal endocardium and the anterior mitral leaflet in mid-systole. However, if image quality is suboptimal in mid-systole, the LVOT should be measured at the largest diameter systolic frame, which is typically seen in end-diastole.[6]

Zoom mode and transducer angulation: Optimal image quality can be achieved by utilizing the zoom mode and adjusting the transducer's angulation with care.

Gain and processing adjustment: The quality of the images can be significantly improved by adjusting the gain and processing settings appropriately.

There is a degree of variation among experts regarding the preferred LVOT measurement location. While some advocate for measuring within a 3 mm to 1.0 mm range from the valve orifice, recent guidelines and the majority of experts recommend measuring at the level of the leaflet insertion, commonly known as the virtual annulus.[2, 14]

Three-dimensional echocardiography and transesophageal echocardiography have been shown to enhance the accuracy of LVOT measurements, which can ultimately lead to more precise AVA calculations using the continuity equation. A study involving 66 patients undergoing AV replacement and coronary artery bypass graft surgery revealed that the 2D diameter (the radius method) underestimated the LVOT area by 21% compared with 3D planimetry (the plane method), and by 18% compared with 3D biplane measurement (the ellipse method). Based on these findings, the study suggested that 3D echocardiography could prove useful in decision-making for surgical intervention in patients with moderate to severe AS.[20] The diameter of the LVOT is directly proportional to BSA regardless of sex, and it can be estimated using the following formula[21]: LVOT diameter (mm)= 5.7 × BSA (m^2) + 12.1. The standard deviation for the formula-derived LVOT diameter was 1 mm, indicating that in 50% of the patients, the LVOT diameter would be within 1 mm of the value derived from the formula, while 95% of the cases would be within a range of 2 mm. Thus, this equation can be employed as a reliable alternative when measuring LVOT diameter with transthoracic echocardiography is difficult or impossible.[21]

Precise measurement of the LVOT velocity time integral is essential for accurate AVA calculation, and care must be taken to avoid measuring too close to the valve or in the region of flow acceleration as this can result in overestimation. Furthermore, it is critical to trace the velocity time integral envelope correctly, focusing on the inner envelope rather than the outer one. To cross-check LVOT stroke volume, other methods such as the biplane Simpson's method can also be utilized.

Incorrect measurement of Doppler-derived echocardiographic findings is also a potential source of error. Accurate measurement of peak aortic jet velocity requires proper alignment between the jet and the ultrasound beam. For optimal alignment, it is advisable to assess the jet from multiple acoustic windows. Adopting non-apical echocardiography windows, particularly the right parasternal view, can significantly alter the grading of AS severity.[22, 23] A recent study found that the incorporation of the right parasternal view method and the apical method resulted in a reclassification of AS severity in approximately 10% of cases.[24]

The British Society of Echocardiography (BSE) advises that the assessment of AS in all patients should be conducted using the PEDOF probe or, when unavailable, a standalone probe. Accuracy of results demands proper optimization of trace gain and scale, with the sweep speed set between 50 mm/s and 100 mm/s. For patients with normal sinus rhythm, an average of at least 3 cardiac cycles should be taken, while patients with atrial fibrillation arrhythmia require a minimum of 5 to 10 consecutive cardiac cycles for accurate assessment. In all cases, it is essential to trace the dense outer edge of the spectral waveform while disregarding any transit time artifacts.[14]

In the presence of the pressure recovery phenomenon, the AVA can be adjusted to reclassify patients with discordant echocardiography findings, particularly in those with a small body and ascending aorta diameter <30 mm.[7]

Discordant grading due to discordant flow

The grading of AS severity can be complicated by the occurrence of discordance between AVA and MPG measurements. After the elimination of potential technical errors, moderate AS cases with discordance between Doppler echocardiographic findings (AV Vmax or AV MPG) and AVA can be categorized based on the stroke volume index (SVi), the mean transvalvular flow rate, and LVEF. A retrospective study conducted by Pio et al[25] found that approximately 19% of patients displayed discordant Doppler parameters, with an AVA of 1.0 to 1.5 cm^2 but a mean gradient <20 mm Hg.

Discordant grading for AS can be categorized into the following groups[26]:

1. Classical low-flow, low-gradient AS: This category is characterized by an SVi <35 mL/m² and an LVEF <50%.
2. Paradoxical low-flow, low-gradient AS: In this category, SVi is also <35 mL/m², but the LV maintains a preserved EF (≥50%).
3. Normal-flow, low-gradient AS: This category is defined by an SVi ≥35 mL/m², with a preserved EF (≥ 50%).

The categories of discordant grading for AS were identified and examined in various research studies, including the notable Discordant Echocardiographic Grading in Low Gradient AS (DEGAS Study) conducted by the Italian Society of Echocardiography and Cardiovascular Imaging Research Network.[27]

A recent study conducted by Stassen et al[18] revealed that discordant grading is a common occurrence among patients with moderate AS and is associated with a higher mortality risk than those with concordant moderate AS. In their study, the normal-flow, low-gradient pattern was found to be the most prevalent among discordant cases, accounting for 55% of such cases. Interestingly, only the paradoxical and classical low-flow, low-gradient patterns were independently linked to worse outcomes, whereas the normal-flow, low-gradient pattern was not.

These findings underscore the significance of a comprehensive evaluation and meticulous interpretation of echocardiographic findings when diagnosing moderate AS. Adhering to established guidelines and considering various factors influencing measurement accuracy are crucial to ensure precise diagnosis and appropriate management of patients with AS.

In the context of moderate AS with discordant grading, 2 primary scenarios may occur:

a) Severe AS is based on AVA, while moderate AS is indicated by the pressure gradient.
b) Moderate AS is based on AVA, whereas mild AS is based on the pressure gradient.

In some instances, patients may present with a combination of an AVA <1.0 cm², indicating severe AS, and an MPG <40 mm Hg, suggesting moderate AS. This phenomenon is commonly referred to as low-flow, low-gradient severe AS or pseudo-severe AS. Dobutamine stress echocardiography (DSE) is a valuable tool for distinguishing between true-severe and pseudo-severe (moderate) AS in cases with low-flow, low-gradient AS. By administering a low dose of dobutamine, DSE can increase transvalvular flow, thereby enhancing the accuracy of severity assessment. In cases of moderate AS with low blood flow, a combination of an AVA between 1.0 cm² and 1.5 cm² and an MPG <20 mm Hg may be observed. This scenario can present a diagnostic challenge, as the AS severity may be underestimated due to the low-flow state.

Although there are no specific studies examining the use of DSE in distinguishing between true-moderate and pseudo-moderate (mild) AS, it is reasonable to believe that DSE could also be beneficial in these situations.

In differentiating true-moderate and pseudo-moderate (mild) AS using DSE, it is important to define the criteria for each condition. True-moderate AS is characterized by an AVA that remains between 1.0 cm² and 1.5 cm² and an MPG that increases to 20 to 40 mm Hg during DSE. On the other hand, pseudo-moderate (mild) AS is defined as an AVA >1.5 cm² with a mean gradient <20 mm Hg. DSE is commonly employed for patients with reduced LVEF to assess the severity of AS. Still, it may also benefit patients with preserved LVEF, particularly if their flow rate normalizes with dobutamine. In instances where the flow rate across the AV is normalized to a value >210 mL/s during DSE, the discrepancy between AVA and MPG often resolves, which allows for a more accurate determination of the true severity of AS.

Paradoxical low-flow, low-gradient moderate AS, also known as pseudo-moderate AS, often involves a small, thick LV with restrictive physiology. This condition can pose challenges when using DSE to assess AS severity, as it may impede the normalization of the flow rate. Consequently, the grading discrepancy between AVA and MPG may persist even after DSE.

In such cases, an alternative approach to evaluating AS severity is to calculate the projected AVA using a normal flow rate of 250 mL/s, which falls within the median range of normal flow rates.[2, 28, 29]

When discrepancies between echocardiographic findings persist even after thorough echocardiographic studies, it is highly advisable to consider other imaging modalities for a more comprehensive evaluation. Cardiac computed tomography is strongly recommended in most guidelines and expert articles as a valuable tool in such cases.[2, 15, 16]

The diagnostic accuracy of AV calcium scoring has been well-established in various multicenter studies. These studies have demonstrated the excellent reproducibility of this method, making it a valuable tool for assessing the severity of AS. Based on the findings from these investigations, specific thresholds for AV calcium scores have been identified to help distinguish severe AS from less severe forms. In women, an AV calcium score >1,200 Agatston units (AU) indicates severe AS, while in men, a score >2,000 AU suggests severe AS. On the other hand, severe AS is less likely if the AV calcium score is <800 AU in women or <1,600 AU in men.

While it is true that non-contrast cardiac computed tomography can effectively quantify AV calcification, it is essential to acknowledge that this method does not account for valve leaflet fibrosis, which can contribute significantly to AS severity. As a result, in patients with predominant valvular fibrosis, the computed tomography calcium score may underestimate the true severity of AS. Furthermore, a low calcium score should not be used to definitively exclude moderate AS, particularly in patients with fibrotic AVs. In such cases, it is crucial to consider other diagnostic tools, such as transthoracic echocardiography, which can provide valuable information on valve leaflet thickness and hyperechogenic changes that may indicate significant fibrosis.[30-33]

Echocardiography is an essential diagnostic tool for evaluating the structure and function of the LV and other cardiac chambers, as well as for assessing the severity of AS. In a large registry-based cohort study involving 499,153 individuals who underwent first-time routine echocardiography between 2000 and 2019, the relationship between LVEF and mortality was examined. The study revealed that a truly normal LVEF was closer to 60% to 65%, rather than the commonly accepted 50%. At the 5-year follow-up, a significant improvement in cardiovascular-related and all-cause mortality was observed for both sexes within the LVEF range of 65.0% to 69.9%.[34] These findings challenge the traditional definition of normal LVEF and emphasize the importance of considering a higher threshold for defining normal cardiac function.

Numerous studies have demonstrated the significance of LVEF as an important prognostic marker in patients with moderate AS. In a study involving 696 patients with moderate AS (median AVA: 1.3 cm^2 and median age: 77 years), 40% of patients died during a median follow-up period of 3.4 years. The study found that decreased LVEF (<50%) and SVi (<35 mL/m^2) were associated with a worse prognosis, even when AV replacement was performed. These findings emphasize the significance of a comprehensive evaluation of LV function and individualized management strategies for patients with moderate AS, particularly those with reduced LVEF and SVi. The results of that study suggested that earlier intervention might lead to improved outcomes and reduced cardiac-related mortality in high- and intermediate-risk patients.[35]

The first phase of LVEF (EF1) is a novel parameter that evaluates the percentage change in LV volume from end-diastole to peak AV flow. EF1 has been proposed as a promising variable for the early identification of LV dysfunction in patients with AS. In a study involving 218 asymptomatic patients with at least moderate AS, the predictive value of EF1 was compared with that of conventional echocardiographic indices for clinical outcomes. The results demonstrated that EF1 was the most potent predictor of events across all patient subgroups. Additionally, a cutoff value of 25% for EF1 was associated with hazard ratios of 27.7 (unadjusted) and 24.4 (adjusted for other echocardiographic parameters, including global longitudinal strain [GLS]) for events at 2 years in all patients with asymptomatic AS. These findings suggested that EF1 was a simple and robust marker of early LV impairment, enabling the identification of patients at high risk of adverse events. Furthermore, the authors concluded that EF1 measurement could provide valuable information for the early detection and management of LV dysfunction in patients with AS.[36]

A recent study involving 508 patients with moderate AS and preserved LVEF (>50%) highlighted the increased risk of mortality in this patient population. The patients included in the study were either asymptomatic or had minimal symptoms and were grouped based on their age and sex.

Over a follow-up period of approximately 47 months, 113 patients (22.2%) underwent AV replacement for severe AS, while 255 patients (50.2%) passed away. The study concluded that patients with moderate AS and preserved LVEF were at a higher risk of mortality than the general population due to associated comorbidities.[37] These results suggest that LV GLS may be a more accurate marker than LVEF in detecting subtle structural and functional changes in patients with moderate AS.[3, 38]

A recent study highlighted the utility of LV GLS in predicting patient outcomes in cases of moderate AS. The study involved 760 patients with moderate AS and preserved LVEF, divided into 3 groups based on their LVEF and LV GLS values. The primary aim of the study was to assess all-cause mortality rates over a 50-month follow-up period. The findings revealed that patients with LVEF<50% and LVEF>50% but LV GLS<16% had significantly higher mortality rates at 1-, 3-, and 5-year follow-up periods than those with LVEF>50% and LV GLS>16%.[38] These results emphasize the significance of incorporating LV GLS alongside LVEF and clinical assessment in diagnosing and evaluating the severity of AS, as well as determining prognosis.

A study by Zhu et al[39] further emphasized the importance of LV GLS in assessing the prognosis of patients with moderate AS and preserved LVEF. The researchers employed the speckle-tracking method to select patients with moderate AS and LVEF≥50% and aimed to determine their all-cause mortality rate based on the median GLS value. The study involved 287 patients with a median age of 76 years, of which 47% were male. The mean AVA was 1.25 cm², and LVEF was 62%. The median GLS was −15.2%. During a median follow-up period of 3.9 years, 103 deaths (36%) were reported. This study, along with others in the field, highlights the significance of incorporating comprehensive echocardiographic assessments, including LV GLS, in managing patients with AS.

LV diastolic function

AS frequently leads to concentric LV remodeling or LV hypertrophy due to the pressure overload imposed on the LV by the stenotic valve.[40] Other factors such as systemic hypertension or increased arterial stiffness may also contribute to this process. Physiologically, AS can cause LV pressure overload, potentially leading to LV systolic or diastolic dysfunction.[41]

Stassen et al[42] conducted a retrospective analysis of data from a comprehensive registry of patients with moderate AS and preserved LV systolic function across 3 academic centers from October 2001 through December 2019. The study included 1247 patients with moderate AS, categorized into 3 groups based on their diastolic function: normal, indeterminate, and dysfunctional. The primary objective was to assess the prevalence of diastolic dysfunction and its prognostic implications in patients with moderate AS and preserved LV systolic function. The primary outcome was all-cause mortality, while the secondary outcome was a composite of all-cause mortality and surgical or transcatheter AV replacement. The study revealed that a significant proportion of patients with moderate AS exhibited diastolic dysfunction (normal: 32%; indeterminate: 25%; and dysfunctional: 43%). Over a median follow-up period of 53 months, 39% of the patients died, with a 1-year survival rate of 91% and a 5-year survival rate of 65%. After adjustments for several clinical variables, diastolic dysfunction was independently associated with all-cause mortality (hazard ratio [HR]: 1.37; 95% confidence interval [CI]: 1.09 to 1.73) and the composite endpoint of all-cause mortality and AV replacement (HR: 1.24; 95% CI: 1.04 to 1.49).

Stobe et al[43] conducted a study involving 131 patients with moderate AS, divided into 2 groups based on the number of pathophysiological changes in their condition. Group I included 79 participants with fewer than 2 changes, while Group II consisted of 52 participants with 2 or more changes. The pathophysiological changes considered in the study included LV hypertrophy, indicated by an increased LV mass index (males: ≥115 g/m² and females: ≥95 g/m²); diastolic LV dysfunction, characterized by an increased E/e' (≥14 in sinus rhythm or ≥11 in atrial fibrillation); and right ventricular load, denoted by an increase in the tricuspid regurgitation jet maximal velocity (TR Vmax) ≥2.8 m/s in the apical 4-chamber view. The primary aim of the study was to determine the duration patients could survive without the need for AV replacement. Group II experienced a more pronounced decrease in AVA (mean = −0.24 cm²) than Group I (mean = −0.06 cm²). Furthermore, Group II showed an increase in MPG (6.29±7.13 mm Hg) relative to Group I (2.89±6.35 mm Hg) and a decrease in GLS (1.57±3.42%) compared with Group I (0.8±2.56%). The study conducted a follow-up of the patients for 30 months, and the findings indicated that patients with 2 or more pathophysiological changes in their condition were associated with a worse prognosis in moderate AS. Moreover, the survival rate without AV replacement was 82% for Group I and 56% for Group II (HR: 3.94; 95% CI: 1.74 to 8.94).

Left atrial (LA) volume and LA strain

An enlarged LA may signify longstanding diastolic dysfunction and advanced disease in AS. A recent study included 324 patients with moderate to severe AS, with an average age of 69 years. Among the participants, 61% were men, and AS was moderate in 99 patients (30.6%) and severe in 225 (69.4%). The LA volume was measured using apical 4- and 2-chamber views and indexed to BSA using the biplane Simpson's method. An increased left atrial volume index (LAVI) to BSA was defined as >34 mL/m². The study reported a mean LVEF of 64±8%, a LAVI of 35±14 ml/m², and a flow rate of 244±70 mL/s. Adverse events were associated with an increased LAVI (45% [n=145]), independent of age, smoking, diabetes, atrial fibrillation, LVEF, LV mass, AVA, and low flow rate (<200 mL/s) (HR: 1.86; 95% CI: 1.24 to 2.82; P=0.003).[44] These findings suggest that an increased LAVI could serve as a significant predictor of adverse events in patients with AS.

Apart from conventional echocardiographic parameters for assessing diastolic function, LA strain imaging could enhance prognostic evaluation for moderate AS cases with preserved LV systolic function. Although preliminary studies have shown promise, the efficacy of LA strain as an imaging biomarker for AS still requires further validation.

A recent study investigated the predictive utility of phasic LA strain in patients with moderate to severe AS who were asymptomatic or minimally symptomatic and had an LVEF >50%. Speckle-tracking echocardiography was employed to measure left atrial reservoir strain (LASr), conduit strain (LAScd), and contractile strain (LASct) in conjunction with clinical and echocardiographic variables, as well as N-terminal pro-B-type natriuretic peptide. The primary outcome of the study was a composite endpoint that included all-cause mortality, hospitalization due to heart failure, progression to New York Heart Association functional class III or IV, acute coronary syndrome, or syncope. The authors enrolled 173 patients with a mean age of 69 years and a mean peak transaortic velocity of 4.0 m/s. The median values for LASr, LAScd, and LASct were 27%, 12%, and 16%, respectively. Over a median follow-up period of 2.7 years, 66 patients (38%) experienced the primary composite endpoint. To predict the primary outcome, the researchers identified the optimal cutoffs for the 3 LA strain parameters: LASr <20%, LAScd<6%, and LASct<12%. Risk analyses conducted in the study demonstrated that models incorporating LA strain parameters outperformed other echocardiographic variables in predicting clinical outcomes. Notably, LA strain parameters emerged as significant predictors of adverse events when combined with N-terminal pro-B-type natriuretic peptide. Among the 3 LA strain parameters, LAScd with a cutoff value of <6% demonstrated the highest specificity (95%) and positive predictive value (82%) for the primary composite endpoint. The authors' competing risk models that incorporated LAScd with a cutoff value of <6% demonstrated the best discriminative value, suggesting that LA strain imaging could be an essential tool in the prognostic evaluation of AS. The study findings highlighted the importance of LA strain evaluation in patients with moderate to severe AS and preserved LVEF, as LA strain variables are superior predictors of risk compared with other echocardiographic measures and N-terminal pro-B-type natriuretic peptides. Moreover, LAScd <6%, LASr <20%, and LASct <12% were identified as markers indicating a higher risk for adverse outcomes in this patient population.[45]

Hemodynamic progression of moderate AS

Although AS is a progressive disease, data are scarce on the progression of moderate AS. This lack of understanding regarding its progression patterns has contributed to a lack of consensus among experts on managing and monitoring moderate AS.

A recent study sought to address this knowledge gap by investigating the hemodynamic progression of AS and its association with risk factors and clinical outcomes. The study identified 2 distinct groups of patients with moderate AS, each characterized by different hemodynamic trajectories based on serial systolic MPG measurements. The primary outcomes of interest in that study were all-cause mortality and AV replacement. The study included 686 patients and analyzed 3093 transthoracic echocardiography reports to identify the hemodynamic progression patterns of AS. The final class model identified 2 distinct AS trajectory subgroups: slow progression (44.6%) and rapid progression (55.4%). At the onset of the study, the MPG was significantly higher in the rapid progression group than in the slow progression group (28.2 mm Hg vs 22.9 mm Hg; P>0.001). The slow progression group had a higher prevalence of atrial fibrillation than the rapid progression group, although there were no significant differences in the prevalence of other comorbidities. The results revealed that patients with a higher initial MPG (≥24 mm Hg) were associated with a more rapid progression of AS and higher rates of AV replacement. Further, the rapid progression group had a significantly higher AV replacement rate, but there was no difference in mortality between the groups. Therefore, the researchers concluded that MPG could be an applicable predictive value for managing the disease.[46]

Recommended simplified algorithm for diagnosing moderate AS

In light of the studies and insights discussed in this review, a stepwise approach is proposed for the diagnosis of suspicious moderate AS. This systematic method intends to effectively identify AS, mitigate the risk of complications, and ultimately enhance patient outcomes (Figure 1).

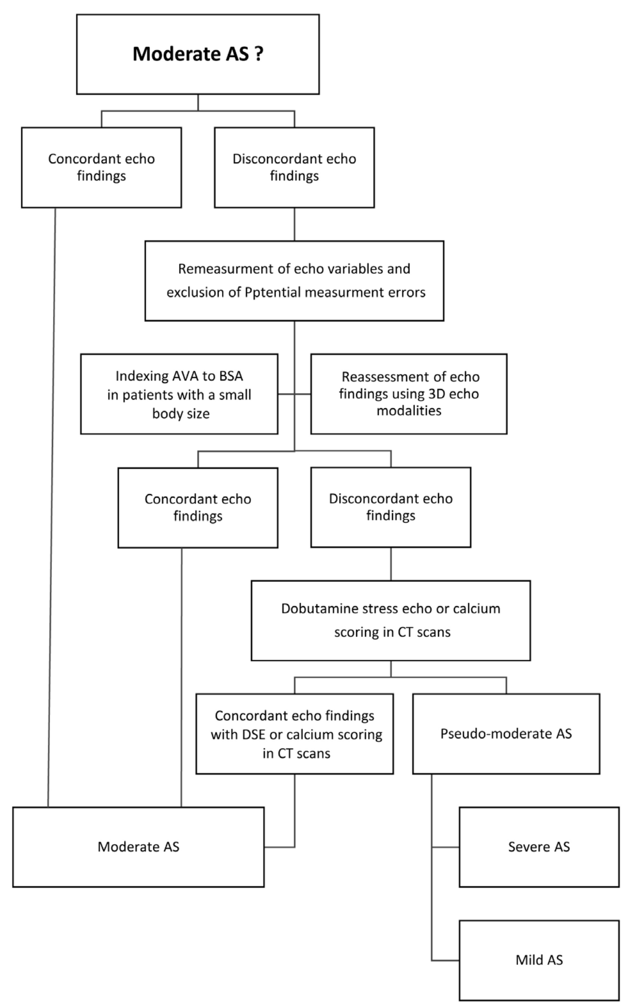

Figure 1. The image depicts the recommended simplified algorithm for diagnosing moderate AS.
AS, Aortic valve stenosis; CT, Computed tomography; DSE, Dobutamine stress echocardiography; AVA, Aortic valve area; BSA, Body surface area

Conclusion

Diagnosing and managing moderate AS necessitates meticulous consideration. Research has demonstrated that moderate AS is a progressive condition with adverse impacts on the survival rate. It is essential to acknowledge that AS significantly affects other heart structures. Echocardiography remains the primary imaging modality for the diagnosis, grading, and prognostication of AS. Still, there are notable gaps in the guidelines for the diagnosis and management of moderate AS, some of which may be resolved with the implementation of new echocardiographic technologies.

It is essential to recognize the inherent limitations of echocardiography. Indeed, in certain cases, additional imaging techniques may be required for optimal management. To this end, closer scrutiny of the LV and the interplay between the stenotic valve, ventricle, and arterial vasculature is vital. The utilization of multi-modality imaging can facilitate the differentiation of moderate AS, aid in the improved risk stratification of patients, and ultimately contribute to superior outcomes.

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