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REVIEW

Contemporary Imaging of Aortic Stenosis

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Degenerative or fibrocalcific aortic stenosis (AS) is now the most common native valvular heart disease assessed and managed by cardiologists in developed countries.
Transthoracic echocardiography remains the quintessential imaging modality for the non-invasive characterisation of AS due to its widespread availability, superior assessment of flow haemodynamics, and a wealth of prognostic data accumulated over decades of clinical utility and research applications. With expanding technologies and increasing availability of treatment options such as transcatheter aortic valve replacements, in addition to conventional surgical approaches, accurate and precise assessment of AS severity is critical to guide decisions for and timing of interventions.
Despite clear guideline echocardiographic parameters demarcating severe AS, discrepancies between transvalvular velocities, gradients, and calculated valve areas are commonly encountered in clinical practice. This often results in diagnostically challenging cases with significant implications. Greater emphasis must be placed on the quality of performance of basic two dimensional (2D) and Doppler measurements (attention to detail ensuring accuracy and precision), incorporating ancillary haemodynamic surrogates, understanding study- or patient-specific confounders, and recognising the role and limitations of stress echocardiography in the subgroups of low-flow low-gradient AS. A multiparametric approach, along with the incorporation of multimodality imaging (cardiac computed tomography or magnetic resonance imaging) in certain scenarios, is now mandatory to avoid incorrect misclassification of severe AS. This is essential to ensure appropriate selection of patients who would most benefit from interventions on the aortic valve to relieve the afterload mismatch resulting from truly severe valvular stenosis.

Keywords Aortic stenosis • Echocardiography • Imaging • Assessment • Flow (or gradient)

Introduction

Aortic stenosis (AS) is the most commonly treated valvular heart disease in the industrialised world [1,2]. Echocardiography is the universally preferred diagnostic imaging modality in the assessment of AS and allows grading of haemodynamic severity, evaluation of valve morphology, and associated valvular or ventricular dysfunction [3–5]. Invasive haemodynamic assessment for AS in the cardiac catheterisation laboratory is no longer mandatory unless echocardiographic and clinical data are incongruent. Prognostically beneficial surgical (SAVR) or transcatheter (TAVR) aortic valve replacement is appropriately indicated in symptomatic severe AS [3,5–9]. As such, correct and precise evaluation of stenosis severity is critical to guide decisions for interventions and their timing.

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There is still no true gold standard for defining severe AS. Spectral Doppler assessment is the key echocardiographic technique for grading AS severity. Currently accepted haemodynamic parameters for severe AS include:

- AS jet peak flow velocity of (AV V_{max}) >4.0 $msec^{-1}$,
- transvalvular mean pressure gradient (MG) >40 mmHg
- calculated aortic valve area (AVA) by the continuity equation (CE) of <1.0 cm^2 (or <0.6 cm^2/m^2 indexed for body surface area (BSA; AVAi)) [3–5].

Ideally all three criteria would be met to confidently classify severe AS. However, it has been well-recognised that discordance between echocardiographic Doppler findings are commonly encountered in real world practice [10].

The focus of this review will be on the fundamentals of echocardiographic assessment of AS. The contribution of multimodality imaging (cardiac computed tomography [CCT] and magnetic resonance imaging [CMR]) will be addressed briefly where additional information may improve diagnostic confidence.

Recommended Standard Haemodynamic Assessment of AS Severity

The three primary spectral Doppler-derived parameters for determination of AS severity are AV V_{max}, transvalvular MG, and AVA calculated by the CE as defined above. Recommended cut-off values are detailed in Table 1 [4]. Importantly the degree of stenosis must not be decided based on a single criterion alone.

AS Peak Velocity and Mean Gradient

Continuous wave (CW) Doppler is a standard accepted technique to measure blood flow velocities across a stenotic (or regurgitant) valve orifice [11]. The simplified Bernoulli equation converts the measured velocity to a pressure gradient ($\Delta P = 4 \times (\text{Peak velocity})^2$) [12]. Due to this squared mathematical relationship, parallel alignment of the Doppler cursor with the direction of the stenotic jet is crucial to avoid underestimation of the peak velocity and true pressure gradient. Employing the non-imaging CW transducer (Pedoff probe) to interrogate multiple imaging windows and attaining the highest possible velocity envelope is mandatory [4]. Reporting the optimal imaging window is useful for serial studies. Failure to perform these basic techniques is a common source of underestimation of stenosis severity.

Where spectral Doppler envelopes are suboptimal the off-label use of microbubble ultrasound contrast can be considered to enhance the CW signal and improve correlation with invasive haemodynamic values [13]. Measurements should be averaged from the one window with the highest velocity over three to five beats in sinus rhythm and at least five consecutive beats or more when there is an irregular rhythm. The simplified Bernoulli equation neglects the proximal left ventricular outflow tract (LVOT) velocity which is acceptable in the absence of subvalvular obstruction. However, if the LVOT velocity is >1.5 $msec^{-1}$, the expanded Bernoulli should be used to calculate a corrected peak gradient ($\Delta P = 4 \times (\text{AV peak velocity})^2 - (\text{LVOT peak velocity})^2$). This, however, does not apply to the mean velocity or gradient.

The transvalvular MG is derived from averaging the instantaneous gradients along the CW Doppler velocity curve over the ejection time period. Meticulous tracing of the velocity curve is critical to ensure accuracy and precision. The well-defined dense outer edge of the smooth CW Doppler envelope represents the true stenotic jet velocities. Overestimation of stenosis severity is frequently due to overenthusiastic tracing and inclusion of the fine linear signals or noise caused by the transit-time effect (Figure 1) [4]. Similarly, operator variation in outlining the shape of the Doppler velocity curve can significantly alter the absolute MG values [14].

Good Doppler ''hygiene'' ensures reproducibility and also avoids misdiagnosis of apparent ''rapid progression'' (increase in AV V_{max} ≥0.3 $msec^{-1}$/year) which has been correlated with worse outcomes [15].

For a given AV orifice area, transvalvular velocities and gradients are flow-dependent parameters. Co-existent systemic hypertension can result in a reduction in the AV V_{max} and MG [16,17]. Re-assessment of AS severity in a normotensive state is recommended if haemodynamic data is incongruent.

AVA by Continuity Equation (Effective Orifice Area [EOA])

The current preferred non-invasive estimation of the aortic valve area (AVA) is performed by the Doppler-derived CE, based on the law of conservation of mass [18,19]. Aortic valve

Table 1 Recommended primary haemodynamic parameters for grading aortic stenosis (AS) severity.

Parameter	Mild AS	Moderate AS	Severe AS
AS peak velocity (AV V_{max}, $msec^{-1}$)	2.6–2.9	3.0–4.0	>4.0
Mean gradient (MG, mmHg)	<20	20–40	>40
Aortic valve area (AVA, cm^2)	>1.5	1.0–1.5	<1.0
Indexed aortic valve area (AVAi, cm^2/m^2)	>0.85	0.60–0.85	<0.6

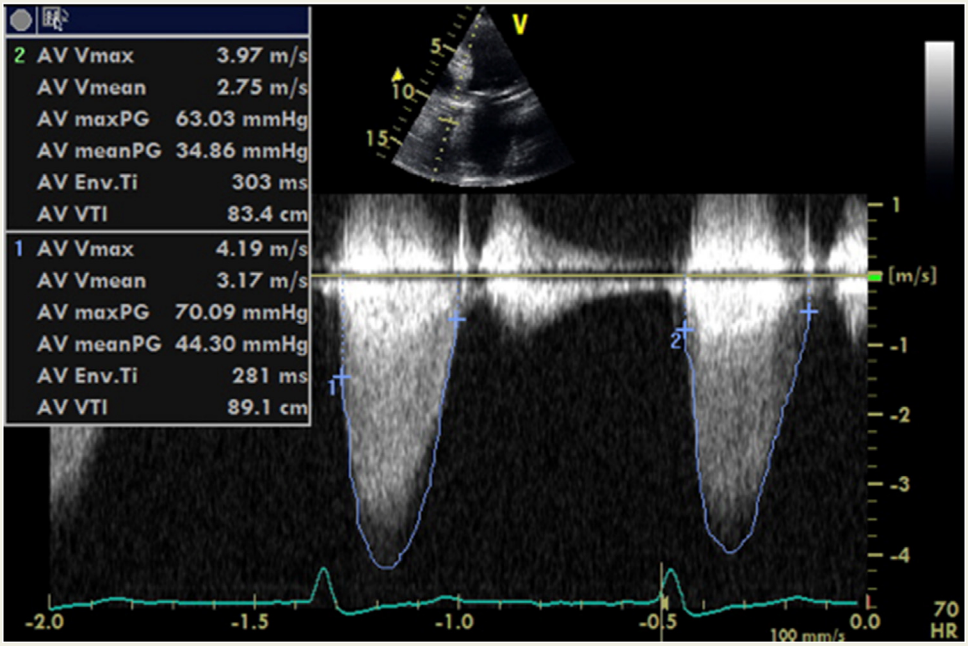

Figure 1 Example of a poorly overtraced CW spectral Doppler signal resulting in overestimation of the AV peak velocity (AV Vmax), mean gradient (AV mean PG), velocity-time integral (VTI), and ultimately overall AS severity. Abbreviations: CW, continuous wave; AV, atrioventricular; AS, aortic stenosis.

area measured by this method represents the physiologic or effective orifice area (EOA).

$$\mathrm{SVAV} = \mathrm{SVLVOT}$$

$$\mathrm{AVA} \times \mathrm{AVVTI} = \mathrm{LVOTarea} \times \mathrm{LVOTVTI}$$

$$\mathrm{AVA} = \mathrm{LVOTarea} \times \mathrm{LVOTVTI}/\mathrm{AVVTI}$$

SV indicates the stroke volume. AV_{VTI} and $LVOT_{VTI}$ represent the velocity-time integrals (VTI) obtained from the tracing of the AV CW Doppler envelope and the LVOT pulsed-Doppler modal velocity respectively. $LVOT_{area}$ is calculated using:

$$LVOT_{area} = \pi \times (LVOT_{diameter}/2)^2$$

An $AVA \leq 1.0\ cm^2$ (and/or $AVAi < 0.6\ cm^2/m^2$) is predictive of adverse clinical outcomes including mortality in asymptomatic patients and is a well-defined threshold for triggering intervention in those who are symptomatic [3,5,20,21]. A major limitation of the AVA is that it is still not flow-independent and can be affected by changes in transvalvular flow rates [22–25]. This becomes relevant in the assessment of patients with low-flow low-gradient AS (LFLGAS) that will be discussed later. Aortic valve area calculations are also prone to measurement errors as it depends on the combined assessment of three separate parameters ($LVOT_{diameter}$, $LVOT_{VTI}$, and AV_{VTI}).

The $LVOT_{diameter}$ measurement by the two dimensional (2D) linear technique from the transthoracic echocardiography (TTE) parasternal long-axis view remains the Achilles heel in the CE. Any error in measuring the $LVOT_{diameter}$ is squared when entered into the CE. There still remains a lack of consensus within contemporary guidelines regarding the optimal anatomic site for the measurement of the $LVOT_{diameter}$ (i.e. 0.5–1 cm ''apical'' in the LVOT or at the level of aortic annulus). The ''annular'' $LVOT_{diameter}$ measured from the inner-to-inner edge of the right coronary cusp base to the posterior commissure has been proposed to:

- provide the best correlation with 3D transoesophageal echocardiography (TOE)-planimetered LVOT cross-sectional area (CSA) at the annular plane,
- result in better agreement with invasively-derived AVA, and
- be independent of variations in LVOT geometry [4,26–28].

The assumption of a circular LVOT geometry is also incorrect. Ellipticity of the LVOT has been well demonstrated by 3D imaging techniques with a smaller anterior-posterior (saggital) diameter that is conventionally callipered during 2D TTE/TOE, and a larger medial-lateral (coronal) dimension [29–31]. As such, there may be a systematic underestimation of the LVOT CSA, with a domino effect of erroneous SV and AVA calculations (may be ''smaller'' by up to 15–29%). So-called ''hybrid'' AVAs, where the $LVOT_{area}$ is planimetered using 3D TTE/TOE, CCT or CMR, and then incorporated into the CE with the echocardiographic $LVOT_{VTI}/AV_{VTI}$, has been suggested as a potential solution to overcome the geometric limitations of 2D imaging. However, hybrid AVAs have not been proven to better predict mortality over the conventional 2D echocardiographic AVA of $<1.0\ cm^2$. The proposed corresponding cut-off value for severe AS using the CCT-hybrid AVA was $<1.2\ cm^2$, which itself has not been validated with any clinical outcome studies [32,33].

Therefore, continued emphasis must be placed on optimising the routine 2D TTE $LVOT_{diameter}$ measurement, and a TOE should be considered for better visualisation if TTE images are suboptimal. Additionally, using the predicted $LVOT_{diameter}$ formula ($LVOT_{diameter}$ = (5.7 x BSA) + 12.1) as a reference, is a useful practical hint where a callipered 2 mm difference may imply an incorrect 2D measurement, [28,34,35].

Additional Useful Echocardiographic Considerations in the Assessment of AS Severity

AVA by Planimetry (Geometric Orifice Area [GOA])

Planimetry of the AV orifice is a reasonable surrogate for assessment of stenosis severity. It is a measure of the anatomic or geometric AVA (GOA) in contrast to the EOA [4,36]. The GOA can also be calculated by the Gorlin equation but EOA remains the tested predictor of clinical outcomes. Planimetry is potentially useful in situations where EOA by the Doppler CE may not be truly representative of the stenosis severity (e.g. concurrent subvalvular obstruction or an asymmetrical orifice with eccentric jets). The planimetered GOA is invariably larger, as blood flow will continue to accelerate downstream through the stenotic orifice to the level of the vena contracta where the EOA occurs [37,38].

When performing AVA planimetry, it is important to ensure that the measurement of the orifice area on a short axis en face view is parallel and corresponds to the true cusp edges. Only planimetry at the plane of maximal stenosis will avoid the potential overestimation of the AVA by incorrectly measuring the CSA beneath the doming leaflet tips as occurs in congenital or rheumatic aetiologies. Three dimensional (or at least biplane) TOE is preferred over conventional single plane 2D to compensate for the dynamic systolic aortic annular movement and ensure optimal alignment with the leaflet tips [39–41].

Aortic valve area planimetry by CCT and CMR are available non-invasive alternatives and have been validated against echocardiographic and invasive AVA values [42–47]. However, the feasibility and reliability of all of these approaches will remain limited by artefacts from valvular calcification. Cardiac computed tomography and CMR planimetry are further challenged by rhythm disturbances affecting electrocardiograph- gating (e.g. atrial fibrillation). CCT requires additional radiation exposure and need for intravenous contrast administration. Availability, cost, and general contraindications to CMR will restrict its routine use for this indication.

Dimensionless Severity Index (DSI)

The DSI is essentially the ratio of the $LVOT_{VTI} : AV_{VTI}$ [18]. There is a simplified version which uses the ratio of the peak LVOT : peak AV velocities but the VTI method is preferred. A DSI $<$ 0.25 is in keeping with severe AS where the AVA is conceptually $<$25% of normal (AVA = $LVOT_{area} \times$ DSI) [5,19].

The main advantage of the DSI is that it avoids the geometric assumptions inherent to the aforementioned $LVOT_{diameter}$ assessment, is not subject to incorrect $LVOT_{diameter}$ measurements, and is independent of the patient's body size. Where the DSI is most practically valuable is for the verification of the accuracy of the CE-derived AVA prior to implicating a LFLGAS scenario — a disproportionately small AVA with a DSI $>$ 0.25 should alert the sonographer or interpreting physician to the possibilities of underestimation of the $LVOT_{diameter}$ or $LVOT_{VTI}$ [48].

Pressure Recovery

Blood confined within a vessel accelerates as it approaches a stenotic valvular orifice due to reduction in the flow area. This increase in kinetic energy (dynamic pressure) is associated with a corresponding loss of potential energy (static pressure). The stenotic jet continues to ''constrict'' beyond the obstructing orifice to the level of the vena contracta (or EOA) where the minimum static pressure exists (i.e. maximal instantaneous pressure gradient). Downstream from the vena contracta, the jet then re-expands radially to ''re-attach'' to the vessel wall, kinetic energy is reconverted to potential energy, and the static pressure begins to rise i.e. pressure recovery (PR) [37,49].

Continuous wave Doppler measures the highest velocity or peak pressure gradient across the vena contracta while invasive catheterisation usually assesses the recovered pressure gradient (i.e. net pressure difference between the LV and the proximal ascending aorta) [50]. However, it is the latter which represents the physiologically important haemodynamic burden due to the valvular obstruction. Consequently, Doppler echocardiography may significantly overestimate invasively derived gradients in some cases of AS. The degree of pressure recovery is dependent on the transvalvular velocity (V), AVA (EOA), and size of the proximal aorta — narrowest area of the ascending aorta at or just distal to the sinotubular junction (AOA). The amount of pressure that needs to be ''recovered'' (i.e. to be deducted from the CW Doppler gradients to correct for this phenomenon) can be calculated using:

$$PR = [4 \times V^2] \times [2 \times (EOA/AOA)] \times [1 - (EOA/AOA)]$$

There is also a PR correction for the EOA to better represent the amount of energy loss as a result of the valvular obstruction [51–53]. The Doppler-based AVA by CE does not account for PR, whereas invasive AVA by Gorlin's equation incorporates catheter-based gradient measurements that have already undergone PR. A ''recovered'' EOA indexed for BSA (known as the energy loss index [ELI]) can be calculated and may offer incremental prognostic value over EOA alone [51,54]:

$$ELI = [(AOA \times EOA)/(AOA - EOA)]/BSA$$

Clinically relevant PR occurs when the ascending aorta diameter is <3.0 cm or if the ratio of EOA (cm^2) to ascending aorta diameter (cm) is $\geq$0.2 [50,55].

Acceleration Time/Ejection Time (AT/ET) Ratio

There has been renewed interest in the use of flow ejection parameters in the assessment of both prosthetic and native valvular AS. An AT $\geq$ 100 msec and AT:ET ratio of $\geq$0.37 was able to differentiate prosthetic aortic valve stenosis from normal function and patient-prosthesis mismatch, with a sensitivity/specificity of 86%/86% and 96%/82%, respectively [56]. This index was also noted to be angle-independent. In moderate or worse degrees of valvular AS, an AT:ET >0.35 identified symptomatic AS (sensitivity 77%, specificity 100%) and was associated with higher serum NT-proBNP levels [57]. The same optimal AT:ET cut-off of $\geq$0.35 was also able to reasonably differentiate severe AS from mild or moderate disease (sensitivity 59%, specificity 86%) in a larger cohort of patients [58]. Prolongation of the AT and an AT:ET >0.36 has been demonstrated to predict severe AS and is prognostically associated with increased mortality or need for AVR [59,60].

Therefore, the AT:ET ratio represents a novel index that correlates with the physical examination findings of the late-peaking systolic murmur as the AS progresses and may be useful as an additional surrogate marker for severe AS when the primary haemodynamic parameters are discordant (Figure 2).

Specific Subgroups of AS With Low-Flow States

Classical Low-Flow Low-Gradient AS with Reduced Ejection Fraction (CLFLGAS)

Severe AS with concomitant LV systolic dysfunction accounts for 5–10% of the AS population and represents a high-risk and particularly challenging group of patients with a mean survival <1.5 years from the onset of symptoms [61,62]. LFLGAS with impaired LV ejection fraction (i.e. CLFLGAS) is defined by the constellation of an EOA < 1.0 cm^2, LV ejection fraction (LVEF) <50%, MG < 40 mmHg, and SV indexed <35 mL/m^2 [4,5]. A low-flow state has also been alternatively defined as a mean transvalvular flow rate (Q)<200 mLsec^{-1} which takes into consideration the ET in addition to SV [63–65].

CLFLGAS is comprised of two pathophysiologically and prognostically different clinical entities with very divergent treatment pathways and outcomes [3–5]. In true anatomically severe AS (TSAS) there is chronically elevated afterload and wall stress resulting in LV systolic dysfunction. Afterload reduction with AVR should therefore lead to LV functional recovery. The second situation involves those with mild or moderate AS with a coexisting cardiomyopathy responsible for the low-flow state. Here, there is insufficient energy or force to maximally open the aortic valve leaflets resulting in the apparent ''pseudo-severe'' AS (PSAS). Aortic valve replacement offers limited benefit in this scenario as it does not address the principal underlying contractile dysfunction.

Low-dose dobutamine stress echocardiography (DSE) is the recommended investigation to distinguish TSAS from PSAS as well as determining the presence of contractile or flow reserve (CR or FR) in patients with CLFLGAS [3–5,66]. The dobutamine infusion is commenced at 2.5–5.0 mcg/kg/min and the rate is increased at 3-5-minute intervals up to a maximum of 20 mcg/kg/min. After carefully establishing the optimal imaging window at baseline, both PW and CW Doppler interrogations of the LVOT and AV must be obtained at every stage to allow for AV V_{max}, MG, VTI (DSI) and AVA assessments. Target endpoints include a heart rate response >10–20 bpm above baseline or >100 bpm or if a diagnostic result is achieved.

Accepted criteria for TSAS includes a peak AV $V_{max} \geq$ 4.0 m/sec or MG $\geq$ 40 mmHg at any augmented flow rate with the provision that the calculated AVA does not exceed 1.0 cm^2 at any stage during the infusion. Conversely, if the AVA increases to >1.0 cm^2 (or a >0.2 cm^2 increment from baseline) with minimal change in the MG, then PSAS is the diagnosis. The reported prevalence of PSAS is in the order of 5–35% of patients with CLFLGAS [67]. The presence of CR or FR is defined as an increase in the SV or LVEF by >20% and is a powerful prognostic factor for improvement post-AVR [68]. When there is no significant augmentation in LV systolic function or SV with dobutamine (i.e. absence of CR) and no diagnostic threshold is achieved, the severity of AS remains ''indeterminate'', portending the worse overall clinical prognosis [69] [70].

Individual patients will have variable augmentation of flow in response to dobutamine. This introduces another confounder into the interpretation of the underlying AS severity which is based on haemodynamic parameters measured at different peak flow rates [67]. The authors of the multicentre Truly or Pseudo-Severe Aortic Stenosis (TOPAS) study proposed the novel index designated as the projected valve area (EOA_{proj}) as a potential solution to this limitation [71]. EOA_{proj}, conceptually, is the calculated EOA at a standardised flow rate (arbitrarily set as 250 mLsec^{-1}) and would, therefore, compensate for the unpredictable individual responses to dobutamine. EOA_{proj} is calculated from the following formula:

$$EOAproj = EOArest + VC \times (250 - Qrest)$$

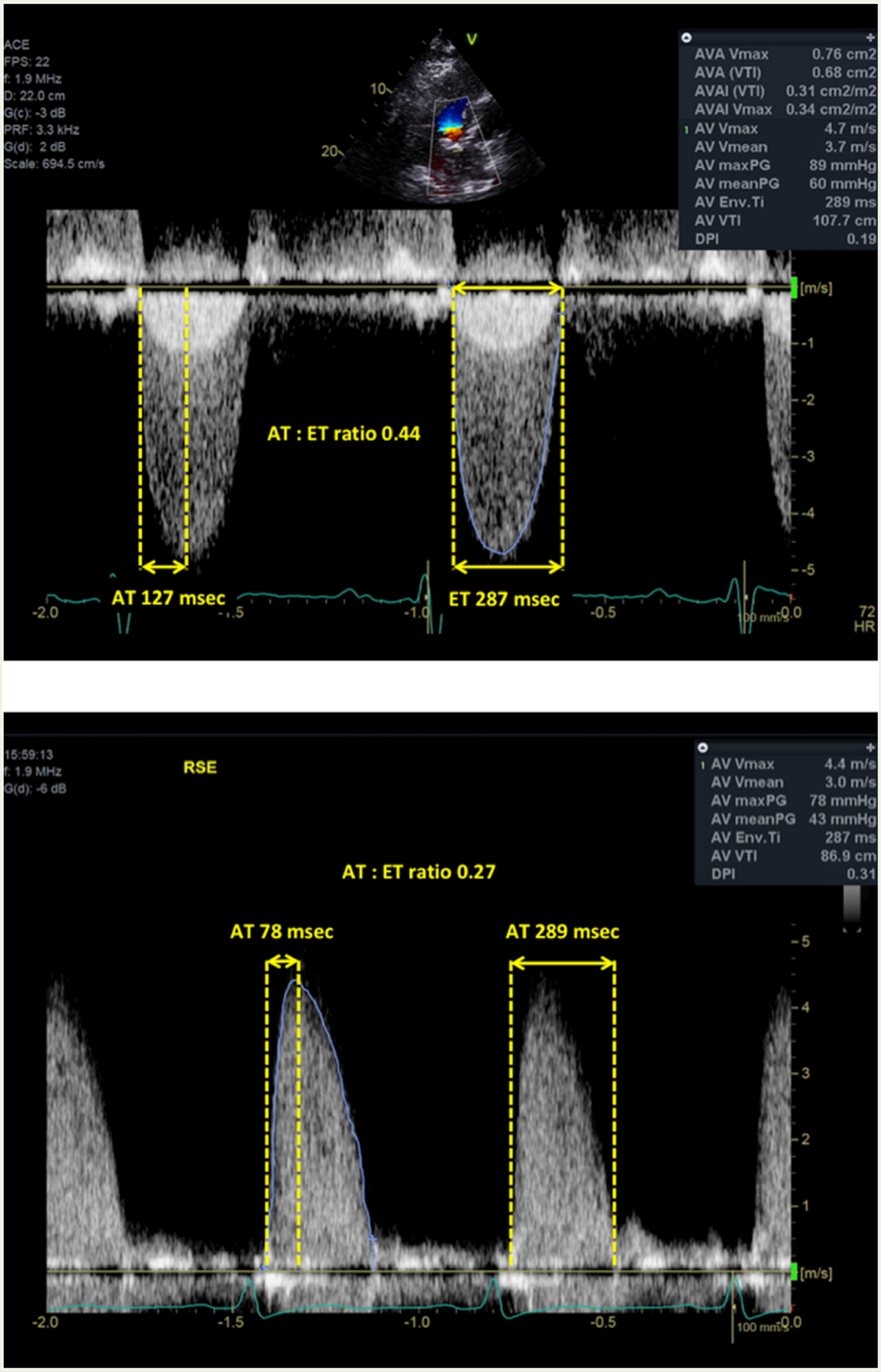

Figure 2 The top image demonstrates an AT:ET ratio of 0.44 consistent with severe AS. The bottom image illustrates a case of moderate AS with incongruent baseline haemodynamic data (AV V_{max} 4.4 msec^{-1}, PG/MG 78/43 mmHg, DSI 0.31) and a AT:ET ratio of 0.27 that is not in keeping with severe stenosis (Following pressure recovery there was improvement in concordance with a recovered PG/MG of 48/29 mmHg).

where EOA_{rest} and Q_{rest} are the baseline AVA and mean transvalvular flow rate (Flow = Stroke volume / Ejection time [Q = SV/ET]) respectively. Valve compliance (VC) is the rate of change in the EOA with increasing transvalvular flow during a dobutamine challenge and is extrapolated from the regression slope of the EOA vs flow curve plotted from data acquired during the incremental stages of the dobutamine infusion. In 23 patients with CLFLGAS (15 TSAS and 8

PSAS) undergoing both DSE and then surgical AVR, EOA_{proj} was superior to the traditional stress MG and final EOA in distinguishing TSAS from PSAS (For TSAS - Stress MG > 30 mmHg: sensitivity 80%, specificity 63%, %Correct classification 74%; Stress EOA $\leq 1.0\ cm^2$: 67%, 63%, 65%; ΔEOA <0.3 cm2: 87%, 13%, 61%; $EOA_{proj} \leq 1.0\ cm^2$: 93%, 63%, 83%). Indexed $EOA_{proj} \leq 0.55\ cm^2/m^2$ provided additional discriminatory power (sensitivity 100%, specificity 83%, %Correct classification 95%). Unfortunately, when the increase in flow rate is <15%, the accuracy of VC calculations is less reliable, therefore limiting the value of EOA_{proj}.

There is a simplified version of the EOA_{proj} where VC was calculated using:

$$VCsimpl = (AVApeak - AVArest)/(Qpeak - Qrest)$$

where AVA_{rest} and Q_{rest} are measured from baseline haemodynamics and AVA_{peak} and Q_{peak} are obtained at peak dose dobutamine. VC_{simpl} can then be substituted into the EOA_{proj} equation above [72]. There was good correlation ($r = 0.95$, $p < 0.001$) and agreement ($0.004+/-0.07\ cm^2$) between both the conventional and simplified approaches with similar accuracy in distinguishing TSAS from PSAS (ROC [AUC] 0.89 vs 0.86, and %Correct classification ($EOA_{proj} \leq 1.0\ cm^2$) was 94% vs 92% respectively). The simplified EOA_{proj} is relatively uncomplicated to calculate and only requires the additional measurement of the ET at rest and peak dose dobutamine (Figure 3). EOA_{proj} may reduce the frequency of ''indeterminate'' AS severity cases based on conventional criteria alone.

Paradoxical Low-Flow Low-Gradient AS with Preserved Ejection Fraction (PLFLGAS)

The syndrome of PLFLGAS accounts for up to 25–35% of unselected AS cases [73]. In a retrospective analysis of 512 patients with severe AS (based on indexed AVA $\leq 0.6\ cm^2/m^2$) and preserved LVEF (≥50%), Hachicha et al. first described the observations noted in 181 patients (35%) with a paradoxical low-flow state (defined as a SV index $\leq 35\ mL/m^2$), and made comparisons to those with normal flow (NF) [74]. PLFLGAS was associated with a female preponderance, smaller concentrically remodelled LV cavities, higher degree of LV global afterload as measured by the valvulo-arterial impedance ({Z_{va} ($mmHg\ mL^{-1}\ m^{-2}$) = [Systolic arterial pressure + AV MG]/SV index}) and lower survival. PLFLGAS was regarded as a more advanced stage of the disease where chronic afterload excess exceeds LV compensatory mechanisms, impairs myocardial function, reduces cardiac output, pseudonormalises peripheral blood pressure, and consequently carries a poorer prognosis. A prospective cohort of 187 PLFLGAS patients case-matched with an equal number of moderate AS (MAS) and severe AS with high gradient (HG-SAS) demonstrated that those with PLFLGAS had a 1.71 and 2.09-fold increase in total and cardiovascular mortality respectively [75]. Five-year (5-year) survival was 64 ± 4% for PLFLGAS, 81 ± 3% for MAS, and 82 ± 3% for HG-SAS. Aortic valve replacement improved outcomes in the PLFLGAS group.

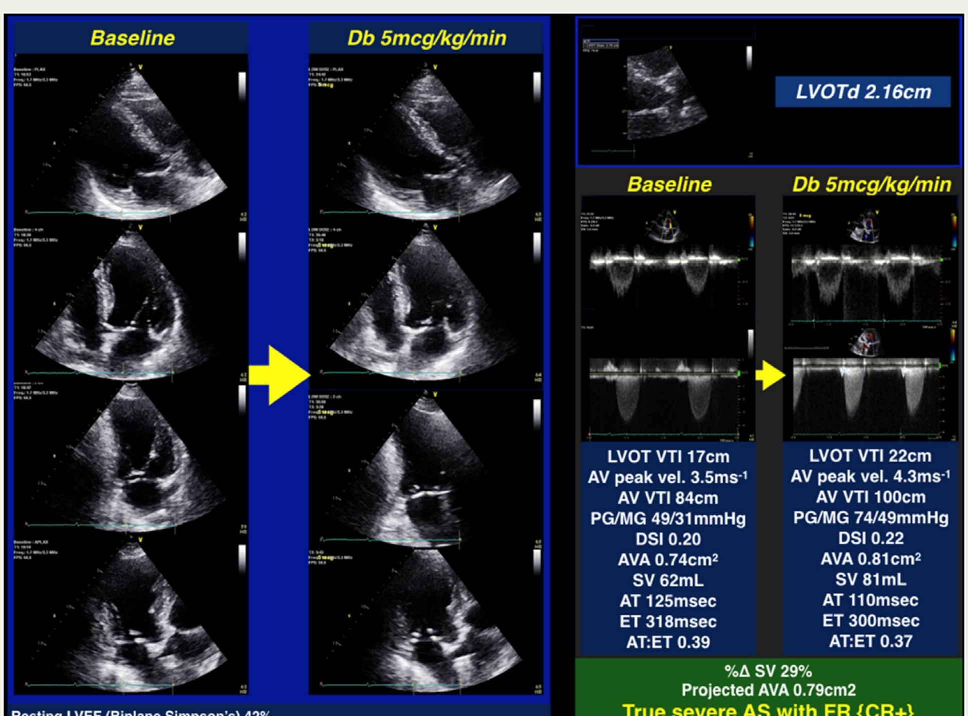

Figure 3 Example of a low-dose DSE for assessment of CLFLGAS (diagnostic targets for TSAS were achieved at an infusion dose of 5 mcg/kg/min, demonstrating the presence of CR, and the calculated EOA_{proj} confirming the true severity of AS).

As with CLFLGAS, up to 30% of patients in this cohort of PLFLGAS may have PSAS instead of TSAS. Although the use of low-dose DSE and calculation of EOA_{proj} have theoretical advantages in this syndrome, attempting to augment flow in these patients with pre-existing small LV cavities and low SV would be difficult. Data advocating this is also limited to one study with a relatively small number of patients [76]. Highlighted in many reviews and current guidelines on this subject is the absolute need to firstly ensure measurements of all variables used in the CE for AVA and SV calculations are accurate. As previously discussed, the underestimation of the $LVOT_{diameter}$ resulting in a ''falsely'' small AVA or low SV is a common error. In patients with a small body size it is also important to calculate the indexed AVA.

Leaflet calcification is the predominant pathophysiological lesion in degenerative AS. Quantification using AV calcium (AVC) scoring by CCT (Agatston method) may be able to corroborate stenosis severity in challenging cases when Doppler parameters remain inconclusive. Atrioventricular calcium score using a 16-slice CT defined an optimal threshold of 1651 Agatston units (AU) to differentiate severe from non-severe AS in patients with an LVEF $\leq$ 40% (sensitivity 80% and specificity 87%) [77]. Using a different approach, establishing AVC thresholds for severe AS in a cohort with LVEF 64 $\pm$ 6% and concordant haemodynamic data (Indexed AVA $\leq$ 0.6 cm^2 and MG $\geq$ 40 mmHg; Absolute AVC $\geq$ 1274 AU (AVC indexed to annulus CSA $\geq$ 292 AU/cm^2) in women and $\geq$2065 AU ($\geq$476 AU/cm^2) in men), Clavel et al observed that 45–66% of the included subset of patients with discordant AS (Indexed AVA $\leq$ 0.6 cm^2 and MG $\leq$ 40 mmHg) had ''severe'' stenosis levels of AVC [78]. Although AVC scoring is a form of anatomic severity assessment, it is predictive of haemodynamic AS severity and mortality [79]. However, underestimation of the degree of AS by AVC can occur when there is significant leaflet fibrosis contributing to the stenosis as is the case in younger patients with bicuspid aortic valves. The latest recommendation from the European Association of Cardiovascular Imaging and American Society of Echocardiography have set categorical cutoffs for very likely/likely/unlikely severe AS of $\geq$3000/$\geq$2000/<1600 AU in men and $\geq$1600/$\geq$1200/<800 AU in women [4].

Despite all of the above, there is still no absolute defining parameter that has been prospectively assessed to reliably determine the true severity of AS in the PLFLGAS state. Therefore, in the discrepant setting of a severe AVA and moderate transvalvular MG, an integrated approach with comprehensive Doppler assessment, consideration of complementary data from other imaging modalities, or even biomarkers (e.g. plasma BNP) may be necessary to clarify the true degree of AS [80–84].

Conclusion

Contemporary imaging assessment of AS requires a multiparametric approach that must first begin with attention to detail when performing and analysing all components of the fundamental echocardiographic haemodynamic criteria (AV V_{max}, MG and AVA). Where discordance persists, understanding and appropriately applying additional considerations including the GOA, DSI, PR, and systolic timing intervals may help resolve the question of stenosis severity. In LFLGAS, additional functional testing in the form of a DSE to augment flow is necessary to confirm the haemodynamic severity of AS, but should only be performed in experienced centres. When the low-flow state cannot be adequately ''corrected'' and the degree of stenosis remains indeterminate, additional anatomic quantification of AVC with CCT may have a role to facilitate clinical decision-making.

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