CHAPTER 1

Echocardiography in bicuspid aortic valve disease

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Introduction

Echocardiography is still the cornerstone imaging technique for evaluation of the aortic valve (AV). It is an essential imaging tool to: 1) describe valve anatomy and morphology; 2) quantify the degree of aortic valve dysfunction (regurgitation or stenosis) and its mechanisms; 3) assess the degree and localization of valve calcifications; 4) define the morphology and size of the aortic root and ascending aorta; 5) exclude aortic coarctation and other associated congenital lesions; and 6) determine the timing and feasibility of valve repair. In addition, the echocardiographic evaluation provides information on the status of cardiac involvement (staging of the disease).

Morphological evaluation of aortic valve

Transthoracic echocardiography (TTE) is the first line imaging tool for the evaluation of AV morphology. The morphological assessment of the AV is preferably performed in parasternal long axis (PLAX) and short axis (PSAX) views. The bicuspid aortic valve (BAV) is characterized by a typical "doming" movement of the aortic cusps during systole (Figure 1.1), particularly for right-left coronary cusp fusion, due to the commissural fusion. In addition, the presence of eccentric diastolic closure, better evaluated with M-mode, is suggestive of BAV. However, to establish the diagnosis, the valve should be preferably assessed in a short axis view. BAV is characterized by a fish-mouth appearance in systole with only two commissures reaching the valvular annulus (Figure 1.2). Diastolic evaluation of the valve can lead to a false tricuspid appearance due to the presence of

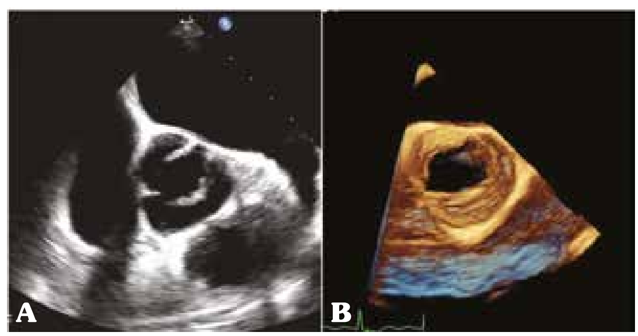
Figure 1.1. TTE PLAX view showing the systolic doming of the conjoint cusp (right/left coronary fusion, white arrow).

Figure 1.2. TTE PSAX view showing the typical fish-mouth appearance of BAV.

Figure 1.3. TEE mid-esophageal long axis view (~120°).

*The systolic doming of the conjoint cusp (right/left coronary fusion) is clearly visible.

Figure 1.4. A) TEE mid-esophageal short axis view of AV showing a BAV with the fusion of the coronary cusps and a fibrotic raphe. B) 3D TEE reconstruction of AV.



a fibrotic raphe between the two fused cusps. In BAV, the cusps usually have different sizes and the coaptation could be eccentric and/or incomplete. In cases with a suboptimal parasternal window, the subcostal short-axis view at the level of the AV, during maximal inspiration, can aid in the definition of aortic cusps morphology. In some cases, the distinction between tricuspid and BAV is still tricky, due to the presence of calcifications, a poor acoustic window, or the presence of incomplete fusion (*i.e.*, frustae BAV).[1] In these cases, transesophageal echocardiography (TEE) is superior to TTE in the evaluation of aortic valve morphology and can be of additional value in the diagnosis (Figures 1.3, 1.4). The presence of significant ascending aorta dilatation increases the likelihood of a BAV phenotype. It should be noted that in patients with extensive valve calcifications or rheumatic disease, without previous documentation of BAV and no significant ascending aorta dilatation, the bicuspid appearance of the valve is usually the result of an acquired calcification of the leaflets, while the valve was initially tricuspid. Surgical inspection and/or pathological examination may identify whether the fusion is congenital or not. This has clinical implications, as acquired BAV is not genetically determined nor associated with aortopathy. Fenestrations of the aortic cusps are common findings associated with both tricuspid and bicuspid aortic valves, with a higher prevalence in BAV.[2] Fenestrations alone are usually of little clinical significance and rarely have an influence on AV competence, but should be taken into account when a repairing surgical approach is considered. BAV is also associated with valve and left ventricular outflow tract (LVOT) calcifications. This is due to abnormal stress and turbulent flow. Stenosis of a BAV is typically due to superimposed calcifications, which often obscure the number of cusps and makes determination of valve morphology difficult. The evaluation of AV, LVOT and proximal ascending aorta calcification should routinely be part of a comprehensive echocardiographic evaluation, as it can affect the interventional approach. The severity of valve calcification is a predictor of clinical outcome[3] and can be graded semi-quantitatively, as mild (few calcifications with little acoustic shadowing), moderate, or severe (extensive thickening and increased echogenicity with a prominent acoustic shadow and restricted movement).[4]

Classification of bicuspid aortic valve

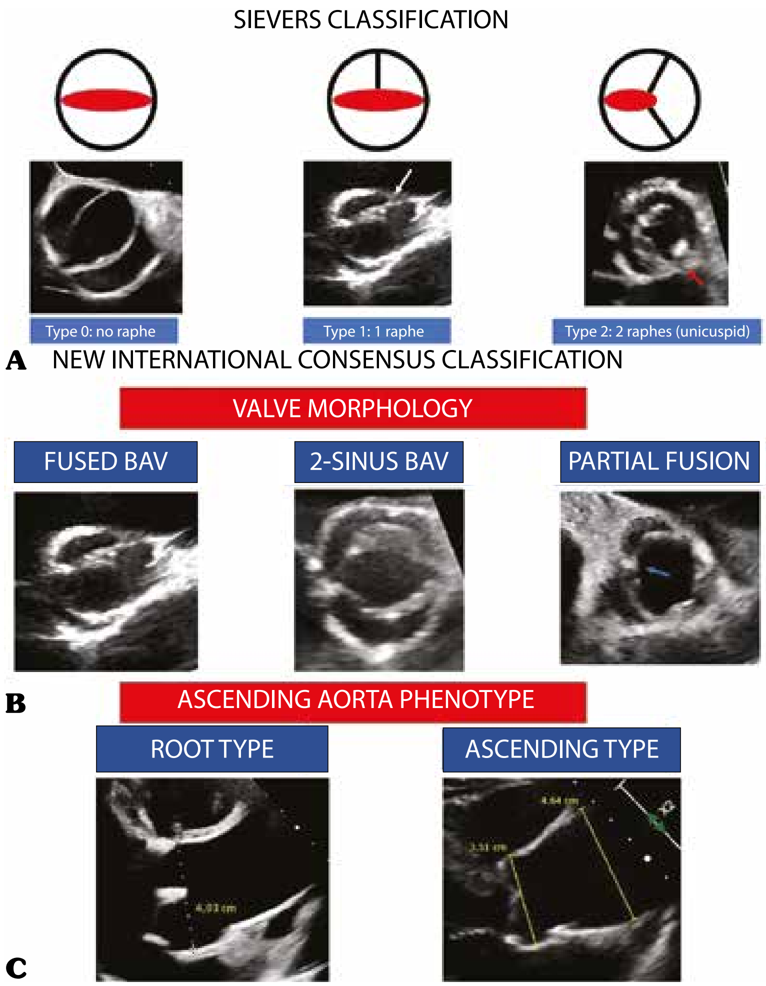
Sievers surgical classification system,[5] based on the number of raphes, is widely used to describe the BAV phenotype (Figure 1.5A). Three categories of BAV are described: type 0 (no raphe), type 1 (only one raphe, ~90%) and type 2 (two raphes, unicuspid valve). The most frequent type of BAV is characterized by fusion of the right and left cusps (~80%), also called anterior-posterior leaflet type, followed by the fusion of the right non-coronary cusp (~19%) and left non-coronary cusp (~1%). The "International consensus statement on nomenclature and classification of the congenital BAV and its aortopathy, for clinical, surgical, interventional and research purposes"[6] recently produced a new comprehensive classification system for BAV, not only including the valve phenotype and cusps fusion but also the degree of aortopathy, which is part of the BAV spectrum (Figure 1.5B, 1.5C). This new classification system recognizes three main types of BAV: 1) Fused BAV (3 aortic sinuses, 2 cusps, 2 commissure, common raphe); 2) 2-sinus BAV (2 aortic sinuses, 2 cusps, 2 commissures, no raphe); and 3) partial-fusion BAV (3 aortic sinuses, 3 cusps, 3 commissures of which one is fused <50%, small raphe). The fused-type BAV accounts for 90-95% of cases.[7]

Valve dysfunction

Aortic stenosis

Aortic stenosis (AS) represents the most common complication of BAV; only 15% of patients with BAV have a normal valve function in the fifth decade[8, 9] and BAV accounts for 50% of all valve replacements for AS in Europe and the USA.[8, 9] Patients with BAV and AS are usually younger than those with classic degenerative AS and BAV should be suspected in all patients aged <70 years with AS. Echocardiographic evaluation of AS in BAV does not differ from classic degenerative AS. In particular, a multiparametric approach is suggested by the current guidelines and is essentially based on the measurement of mean pressure gradient (the most robust parameter), peak transvalvular velocity (V_{max}) and valve area (Table 1.I).[10] It has to be kept in mind that when comparing Doppler-derived gradients with invasively

Figure 1.5. Comparison between Sievers surgical classification and the new International consensus statement classification of BAV.



White arrow: complete fibrotic raphe of BAV with right/left coronary fusion; red arrow: single commissure of an unicuspid/unicommissural AV; blue arrow: partial raphe.

Table 1.I. Indices of severity in aortic valve stenosis.

Index name	Formula/method of measurement	Cut-off for severity
Peak velocity (m/s)	Direct measurement with CW Doppler	4 m/s
Mean gradient (mmHg)	Obtained from velocity curve and averaged	40 mmHg
Continuity equation AVA	AVA = (CSA-LVOT×VTI-LVOT)/VTI-AV	<1 cm^2 (0.6 cm^2/m^2)
Velocity ratio	LVOT-VTI/AV-VTI	<0.25

measured gradients, different values may be provided as the invasive method typically measures the peak-to-peak gradient (pressure difference between peak systolic LV pressure and peak systolic aortic pressure). Since the two pressure peaks do not occur at the same time, this pressure difference is actually lower than the Doppler-derived one, which instead measures the maximal instantaneous gradient. The mean gradients provided by echo and by catheterization are the preferred measurements and should be comparable. Although aortic valve area (AVA) is the theoretically ideal measurement for assessing severity, there are numerous technical limitations. In particular, 2D echocardiographic evaluation of AVA is essentially based on the continuity equation that depends on the measurement of LVOT cross-sectional area by the LVOT diameter from the TTE PLAX view, assuming the LVOT is a circle. However, studies showed that the real LVOT-CSA is rather elliptical, funnel-shaped or even hourglass-shaped and so this geometrical approximation unavoidably introduces size errors and poor reliability. Moreover, minor inaccuracies in LVOT diameter measurement would be squared for the calculation of LVOT cross-sectional area. To overcome such limitations, in discordant cases, current recommendations suggest direct planimetry of the LVOT cross-sectional area from cardiac computer tomography (CCT) or 3-dimensional transesophageal echocardiography (Figure 1.6).[4] However, AVA estimation by CCT does not improve the correlation with transvalvular gradient, the concordance gradient-AVA, or mortality prediction compared with echocardiography[11]

Figure 1.6. A) LVOT diameter measurement by 2D TTE. The estimated LVOT area according to the circle area formula is 4.52 cm^2. B) 3D TEE MPR of the LVOT in the same patient. The calculated planimetric area is 5.47 cm^2. C, D) This difference affects stroke volume estimation and continuity equation for aortic valve area estimation. Indeed, using the 2D imaging, calculated AVA by continuity equation is 0.9 cm^2 (severe range) while with 3D imaging 1.1 cm^2 (moderate range).

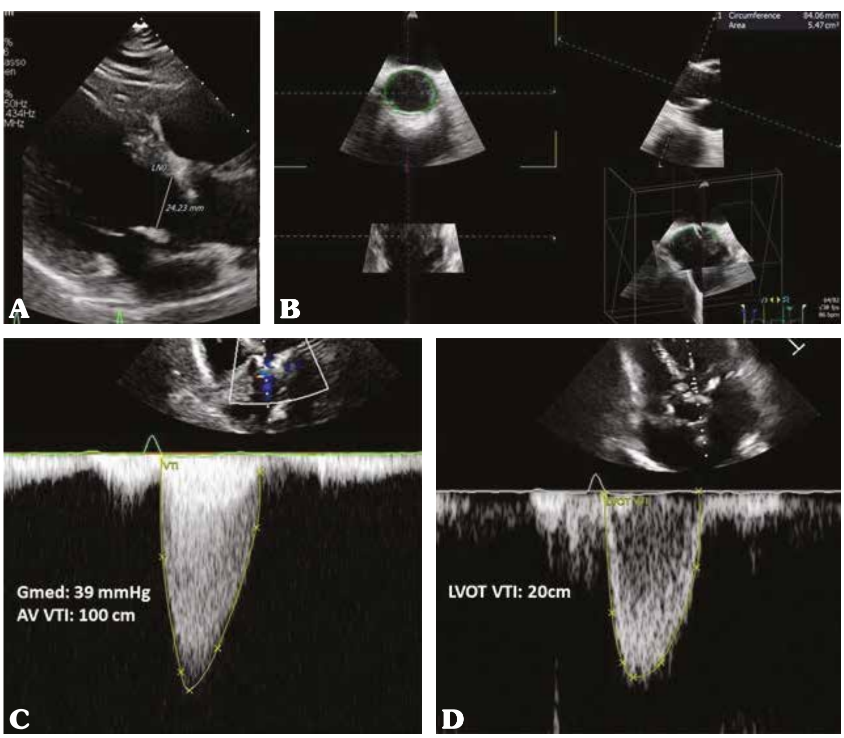
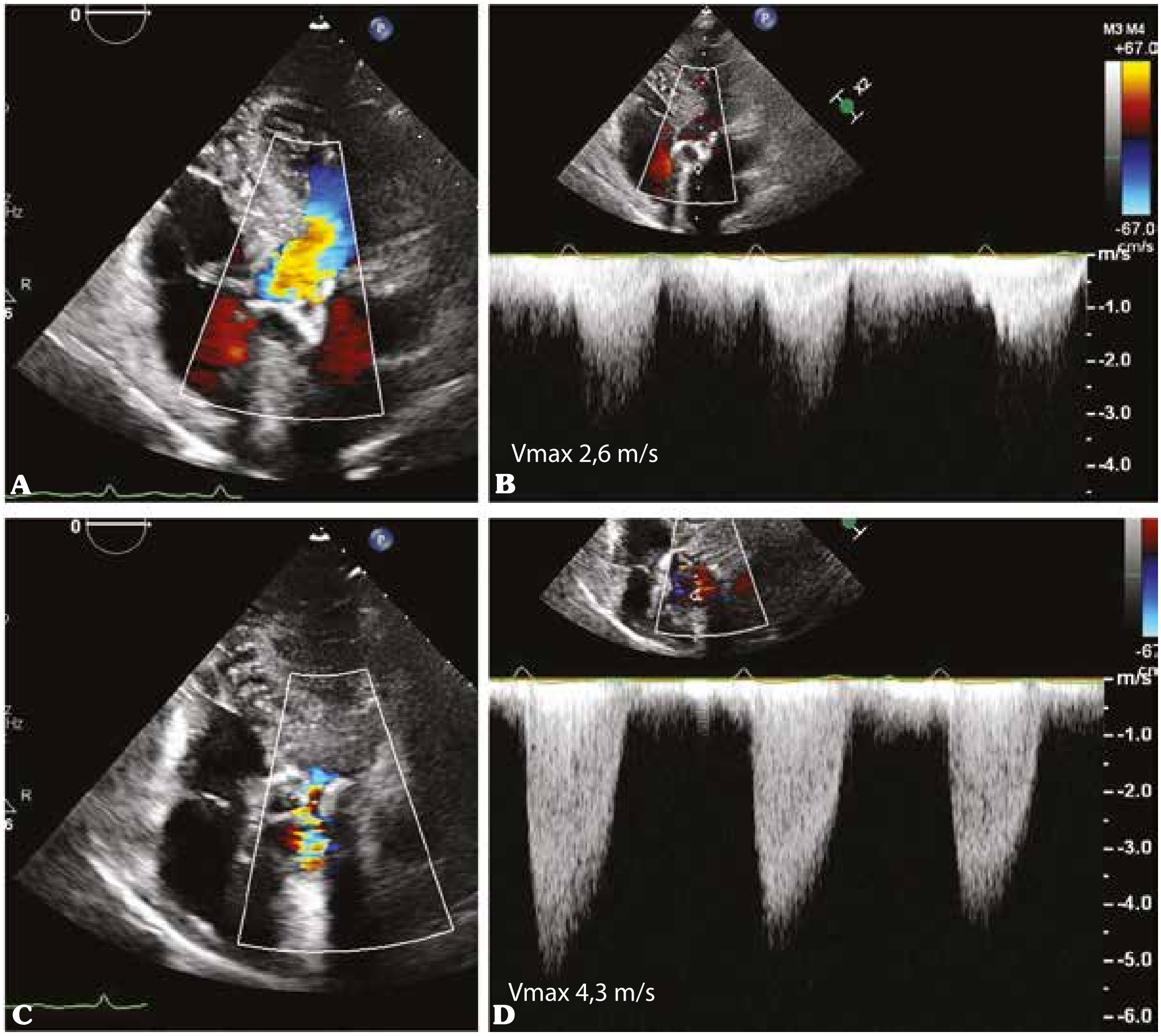


Figure 1.7. A, B) Incorrect alignment across AV and the absence of a clearly visible jet through the valve leads to a faint continuous-wave Doppler signal and an underestimation of the AV velocity and gradient. C, D) correct Doppler alignment in the same patient with an optimal signal and a correct estimation of AV velocity and gradient.



and a higher cut-off of severity of 1.2 cm^2 has been proposed when hybrid imaging is used.[12, 13] For an accurate measurement of the transaortic jet velocity (and the derived gradients), the Doppler beam needs to be aligned with the AV jet and the jet should be clearly visible across the valve (Figure 1.7C, 1.7D). Alignment errors and the absence of the color-Doppler signal below the valve lead to an underestimation of the true velocity and consequently of AS severity (Figure 1.7A, 1.7B). To avoid such mistakes, the Doppler study should include apical windows, as well as right parasternal, suprasternal and sometimes subcostal approaches. It is not uncommon in BAV that the transaortic flow rate is high due to co-existing aortic regurgitation and valve area may be >1.0 cm^2 despite velocity and mean gradient in the range of severity. When the accuracy of measurements is confirmed and there is no evidence for a reversible clinical high flow state (*i.e.*, sepsis, hyperthyroidism, anemia), the patient with a BAV velocity of >4 m/s and a valve area of >1.0 cm^2 most likely has combined moderate aortic regurgitation. In this case, BAV velocity and mean gradient are better predictors of clinical outcome than valve area and should be used to grade the valve disease as severe.[14] Finally, blood pressure should be routinely measured during echocardiographic evaluation of AS, as the valve gradient in hypertensive patients can be underestimated. Ventriculo-arterial impedance calculation [Zva = (systolic arterial pressure + mean aortic gradient)/indexed stroke volume] expresses the real hemodynamic burden on the left ventricle and a value >4.5 is associated with increased mortality.

Aortic regurgitation

Aortic regurgitation (AR) is a common finding in patients with BAV with a prevalence of about 60% and is more frequent in men.[15] The most common mechanisms of AR in BAV are: 1) altered and incomplete cusp coaptation; 2) cusp fibrosis and calcification; 3) cusp prolapse; 4) dilatation of the ascending aorta; and 5) endocarditis (Figure 1.8). The quantification of AR, as for AS, is based on an integrated approach including qualitative, semi-quantitative and quantitative parameters (Table 1.II)[16] and can be particularly challenging in BAV due to presence of multiple/eccentric jets, extensive valve calcifications and mixed mechanisms. New parameters obtained by 3D TEE echocardiography may be useful to overcome some limitations of traditional

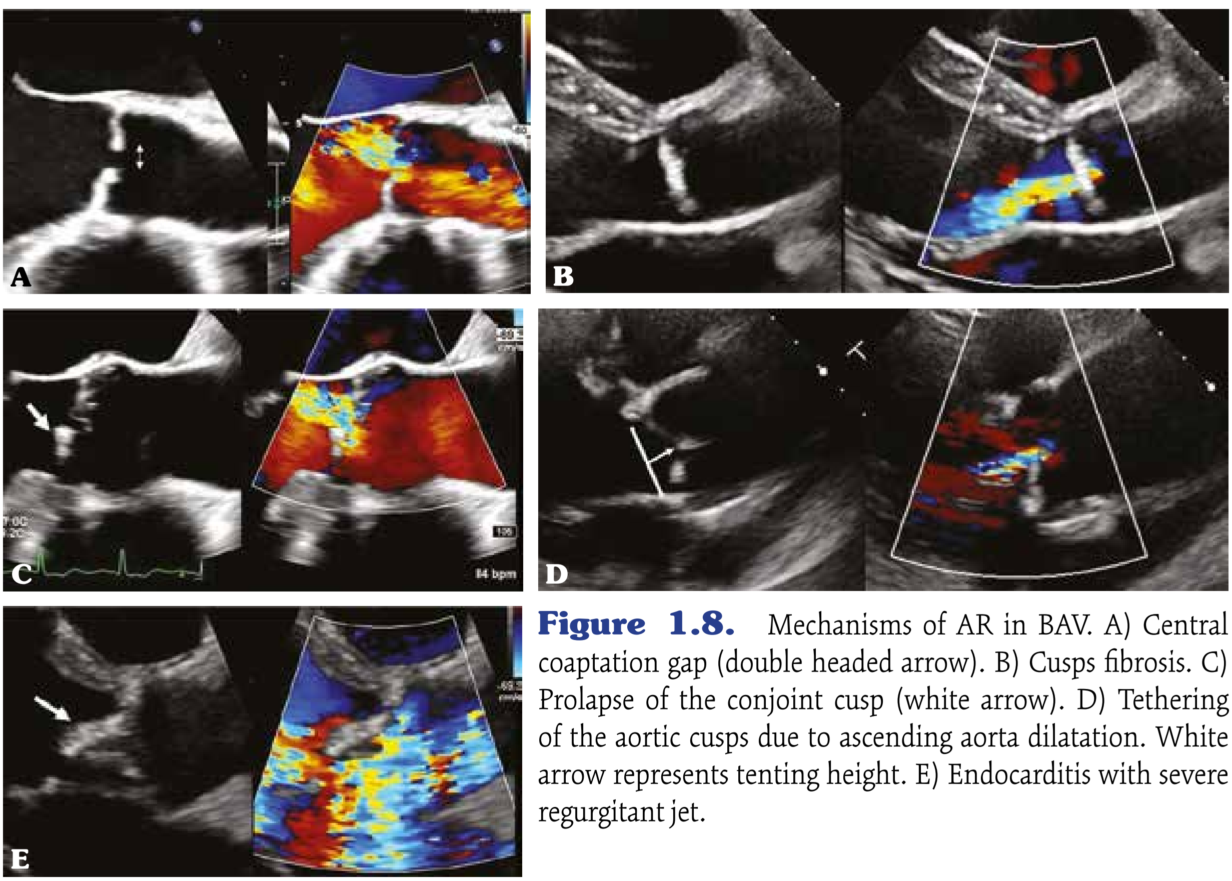


Figure 1.8. Mechanisms of AR in BAV. A) Central coaptation gap (double headed arrow). B) Cusps fibrosis. C) Prolapse of the conjoint cusp (white arrow). D) Tethering of the aortic cusps due to ascending aorta dilatation. White arrow represents tenting height. E) Endocarditis with severe regurgitant jet.

Table 1.II. Parameters of quantification for AR. Modified from: Vahanian *et al.*[16]

Parameter	Value for severity	Advantages	Limitations
Valve morphology	Flail valve/cusp	Flail is specific for severity.	Other morphological abnormalities are not specific for severe AR.
Color flow regurgitant jet	Large regurgitant jet in the LV	Ease to assess.	Underestimation in eccentric jets.
CW signal of regurgitant jet	Dense, holodiastolic	Ease to assess.	Underestimation in eccentric jets and severely calcified valves.
Flow reversal in descending aorta	Holodiastolic, (EDV>20cm/s)	Highly specific for severe AR.	Need adequate suprasternal window; affected by aortic compliance.
Vena contracta width	>6 mm	Quick and easy; relatively independent of hemodynamic factors.	Not valid for multiple jets; intermediate values need confirmation.
Pressure half-time (ms) <200	<200 ms	Quick and easy.	Affected by LV compliance, blood pressure, acuity, other valve pathology. Not reliable in chronic severe AR.
PISA method	EROA>30 mm^2	Can be used in eccentric jet; not affected by the etiology of regurgitation or other valve disease; gives a quantitative parameter.	Errors in PISA radius are squared; not validated for multiple jets; limited by aortic valve calcifications.
	RV>60 mL		

2D echocardiography. In particular, quantitative assessment of the regurgitant volume and regurgitant fraction by 3D volumetric approach may aid in the evaluation of AR severity. Direct planimetry of the vena contracta area (3D VCA), derived by 3D color-Doppler TEE echocardiography, has been proposed as an alternative method for the quantification of the EROA and the derived regurgitant volume (Figure 1.9).[17] However, no cut-off values of severity have been provided by published reports. If an eccentric jet is difficult to quantify and LV dilation is disproportionate to the degree of AR, cardiac MRI might provide a better way to quantity AR and LV volumes.[18] Finally, if aortic valve repair or valve-sparing surgery is considered, the morphology of the aortic valve cusps and suitability for valve repair should be provided by preoperative TEE.

Ascending aorta evaluation

Echocardiographic evaluation of BAV should routinely include evaluation of the LVOT and ascending aorta as aortopathy and coarctation have important implications on the therapeutic approach and prognosis. CT or CMR have an additional role in assessing the aortic vessel. Aortopathy may lead to aortic aneurysm, dissection