The assessment of aortic stenosis: echocardiography and beyond

Aortic stenosis is the most common primary valve problem. This article describes its assessment and clinical interpretation using echocardiography and also shows how magnetic resonance, cardiac computed tomography and stress testing may be useful.

Aortic stenosis is defined by a thickened aortic valve with a transaortic peak velocity >2.5 m/s. In industrially developed countries the incidence rises sharply above the age of 55 years (Nkomo et al, 2006) and the predominant aetiologies are calcific degenerative disease and a bicuspid aortic valve. Moderate or severe aortic stenosis occurs in 0.4% of an unselected western population (Nkomo et al, 2006) or 3% aged ≥75 years but an ejection systolic murmur may be found in 20–30% of younger patients (Freeman and Levine, 1933) and over one half aged over 85 years (Griffiths and Sheldon, 1975). Echocardiography is the first-line technique to differentiate patients with aortic valve thickening from those with benign systolic flow murmurs and to assess the degree of stenosis and the ensuing adaptation of the left ventricle and the rest of the heart.

This article describes the echocardiography of aortic stenosis for the general cardiologist or physician. More detailed technical descriptions are available (Baumgartner et al, 2009; Chambers, 2009). It also describes how complementary imaging information is obtained using magnetic resonance and cardiac computed tomography and how exercise testing and biomarkers aid risk assessment (*Table 1*).

Transthoracic echocardiography

Transthoracic echocardiography is the mainstay of assessment (Baumgartner et al, 2009).

Imaging the valve

This may give a clue to aetiology (*Table 2*). The degree of thickening and immobility (*Figure 1*) also gives a useful guide to severity.

The left ventricle

The adaptation of the left ventricle affects outcome. Pressure overload causes left ventricular concentric remodelling then hypertrophy (Chambers, 2006b) and sometimes cavity dilatation at end stage. Left ventricular mass is only moderately related to the aortic gradient and is affected by gender and genetic factors (Carroll et al, 1992). Surgery is indicated even in asymptomatic aortic stenosis if the left ventricular ejection fraction is below 50% (Vahanian et al, 2012; Nishimura et al, 2014). Excessive hypertrophy is associated with a high risk of perioperative events and may make it difficult or impossible to position a transcatheter device.

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Table 1. Assessment of aortic stenosis

Modality	Indications
Transthoracic echocardiography	Essential in all
Transoesophageal echocardiography	Not routinely indicated but useful before and during transcatheter procedures or if endocarditis suspected
Treadmill testing	If asymptomatic and at low surgical risk
B-type natriuretic peptide	Breathlessness of uncertain origin
Low-dose dobutamine echo	Left ventricular ejection fraction <40% and mean gradient <40 mmHg
Exercise echocardiography	Moderate aortic stenosis and symptoms
Cardiac magnetic resonance	Echo images suboptimal or ascending aorta not imaged
Cardiac computed tomography	Work up towards transcatheter valve implantation or to assess ascending aorta if not seen on echocardiography or to assess coronary arteries in patients at moderate risk of coronary disease

Table 2. Clues to the aetiology in aortic stenosis

	Systolic bowing	Closure line	Associated features
Calcific disease	No	Central	Calcification of mitral annulus or aorta
Bicuspid	Yes	Eccentric	Ascending aortic dilatation, coarctation
Rheumatic	Yes	Central	Mitral involvement

Figure 1. Heavily calcified aortic valve. **a.** A zoomed parasternal long axis view and (**b**) a short-axis view. The valve remains virtually closed despite the image coinciding with systole.

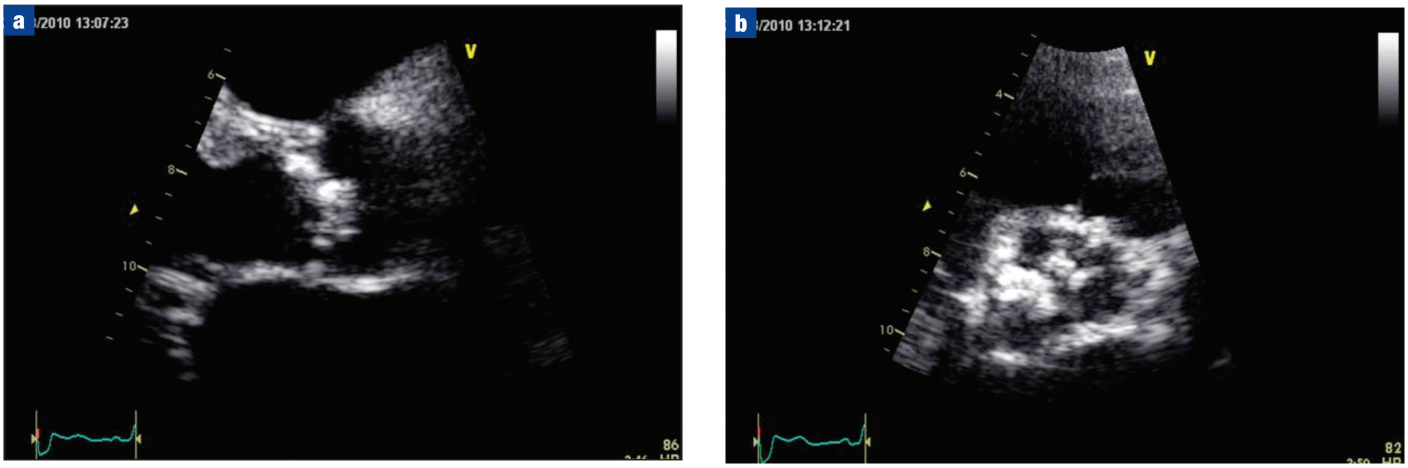


Figure 2. The modified Bernouilli equation. The sum of kinetic and potential energy in a closed system remains constant. Therefore as flow decelerates downstream from a stenosis kinetic energy falls and static pressure rises. By gathering terms on either side of the equation the difference in static pressure (the 'gradient') is the same as the difference in kinetic energy. Peak ΔP (mmHg) = $1/2\rho$ ($v_2^2 - V_1^2$) = $4v_2^2$ where ρ is blood density, v_1 is subaortic peak velocity and v_2 is transaortic peak velocity. When $v^2 >> v_1$ the subaortic term can be neglected. For human blood at body temperature, $1/2\rho$ is close to 4.

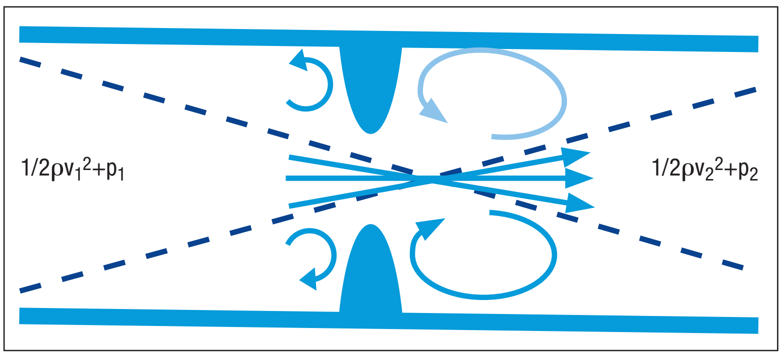
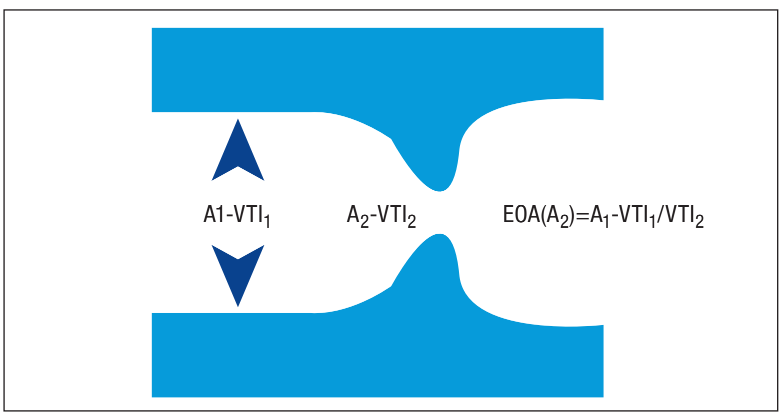


Figure 3. The continuity equation. This relies on the law of conservation of mass. The stroke volume must be the same on either side of the orifice. Rearranging the terms: EOA (cm^2) = CSA x VTI_1/ VTI_2. CSA is left ventricular outflow cross-sectional area (cm^2) calculated as πr^2 (r=radius of the left ventricular outflow tract), VTI_1 is subaortic velocity integral (cm) and VTI_2 is aortic velocity integral (cm). CSA = cross-sectional area; EOA = effective orifice area.



The rest of the heart

Pulmonary hypertension occurs in about 25% of patients with severe aortic stenosis and is associated with a poor outcome if aortic valve replacement is not performed (Pai et al, 2007). Mitral regurgitation is frequent and requires surgery if the mitral valve is anatomically abnormal (e.g. prolapsing) or if the regurgitation is more than moderate (Unger et al, 2010). Aortic root dilatation occurs in all types of aortic stenosis especially with a bicuspid aortic valve. Surgery may be indicated for aortic dilatation (often >55 mm) even if the aortic stenosis remains symptom-free (Vahanian et al, 2012).

Doppler measurements

Continuous wave Doppler records flow through the valve. The pulsed Doppler sample is placed in the left ventricle just below the aortic valve to allow calculation of the effective orifice area, stroke volume and, less commonly, of systolic flow. The minimum dataset is peak transaortic velocity and mean gradient (both derived from the continuous wave signal)(*Figure 2*) and effective orifice area using the continuity equation (*Figure 3*). Mean gradient is calculated automatically using the whole waveform and is more representative of the waveform than peak velocity or peak gradient which are maintained only instantaneously. Effective orifice area is relatively independent of flow.

The grade of aortic stenosis can then be determined (*Table 3*). Aortic valve surgery is primarily indicated for symptoms and severe aortic stenosis but may also be indicated on the findings at echocardiography without symptoms (*Table 4*). Discordance of the grade using these measurements occurs in about a third of cases. The shape of the waveform and appearance of the valve may then help decide whether peak velocity (and mean gradient) or the effective orifice area is the more representative. If the patient is particularly large or small it is also useful to index effective area to body surface area. An effective orifice area of 1.3 cm^2 (apparently moderate) in a small person (body surface area = 1.5) gives an indexed effective orifice area

Table 3. Grading severity in aortic stenosis

		Mild	Moderate	Severe
Main criteria	Transaortic Vmax (m/s)	2.6–2.9	3.0–4.0	>4.0
	Peak gradient (mmHg)	<40	40–65	>65
	Mean gradient (mmHg)	<20	20–40	>40
	Effective orifice area (cont eq) (cm^2)	>1.5	1.0–1.5	<1.0
Extra criteria	Valve appearance	Relatively mobile	Calcified but some residual mobility	Heavily calcified and immobile
	Waveform shape	Dagger	Dagger	Arch
	Indexed effective orifice area (cm^2/m^2)	>0.85	0.60–0.85	<0.60

of 0.86 cm^2 (mild aortic stenosis) while in a big person (body surface area = 2.5) the indexed effective orifice area is 0.52 cm^2 (severe aortic stenosis).

A common cause of a mean gradient in the moderate range and an effective orifice area in the severe range is low flow (*Figure 4*). Traditionally this has been recognized by a low ejection fraction <40%. However, it is now apparent that it can also occur with a normal left ventricular ejection fraction if the left ventricular cavity is small. This means that an insufficient volume can be ejected to maintain flow. This is usually defined by a stroke volume index <35 ml/m^2. In these patients left ventricular function is not normal despite the normal left ventricular ejection fraction and the outcome is poorer than for high gradient normal left ventricular ejection fraction aortic stenosis (Magne and Mohty, 2015).

There is increasing recognition that the left ventricular outflow tract is often oval and not circular, resulting in underestimation of the effective orifice area using the continuity equation (Chin et al, 2014). Three-dimensional echocardiography can measure left ventricular outflow area (Gutierrez-Chico et al, 2008) to improve the accuracy of the continuity equation and also improving the sizing of transcatheter devices.

Table 4. Echocardiographic indications for surgery in asymptomatic aortic stenosis

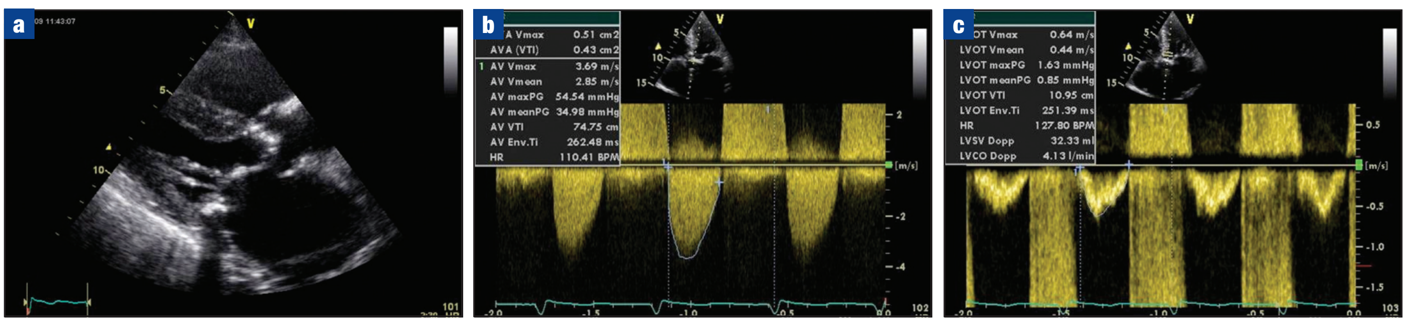
Moderate or severe aortic stenosis having coronary artery bypass graft or aortic replacement	
Severe aortic stenosis and left ventricular ejection fraction <50% with no other cause	
Peak transaortic velocity >5.0 m/s or effective orifice area <0.6 cm^2	
Severe coexistent aortic dilatation	
Less accepted indications*	■ Increase in peak transaortic velocity ≥0.3 m/s in 1 year associated with severe calcification ■ Severe left ventricular hypertrophy in the absence of systemic hypertension ■ Increase in mean gradient >20 mmHg on exercise

** these are based on little data, sometimes only one study, and must be interpreted in the whole clinical context. From Vahanian et al (2012); Nishimura et al (2014)*

Stress echocardiography

The main indication is a combination of effective orifice area in the severe range (<1.0 cm^2) but with a mean gradient in the moderate range (<40 mmHg) and reduced left ventricular ejection fraction (<40%). In this situation there is either severe aortic stenosis causing left ventricular systolic dysfunction or there is moderate aortic stenosis with another cause of left ventricular dysfunction (e.g. myocardial infarction or alcohol). To resolve this requires low dose dobutamine stress echocardiography. The endpoints are the change in gradient and whether there is left ventricular contractile reserve (Garbi et al,

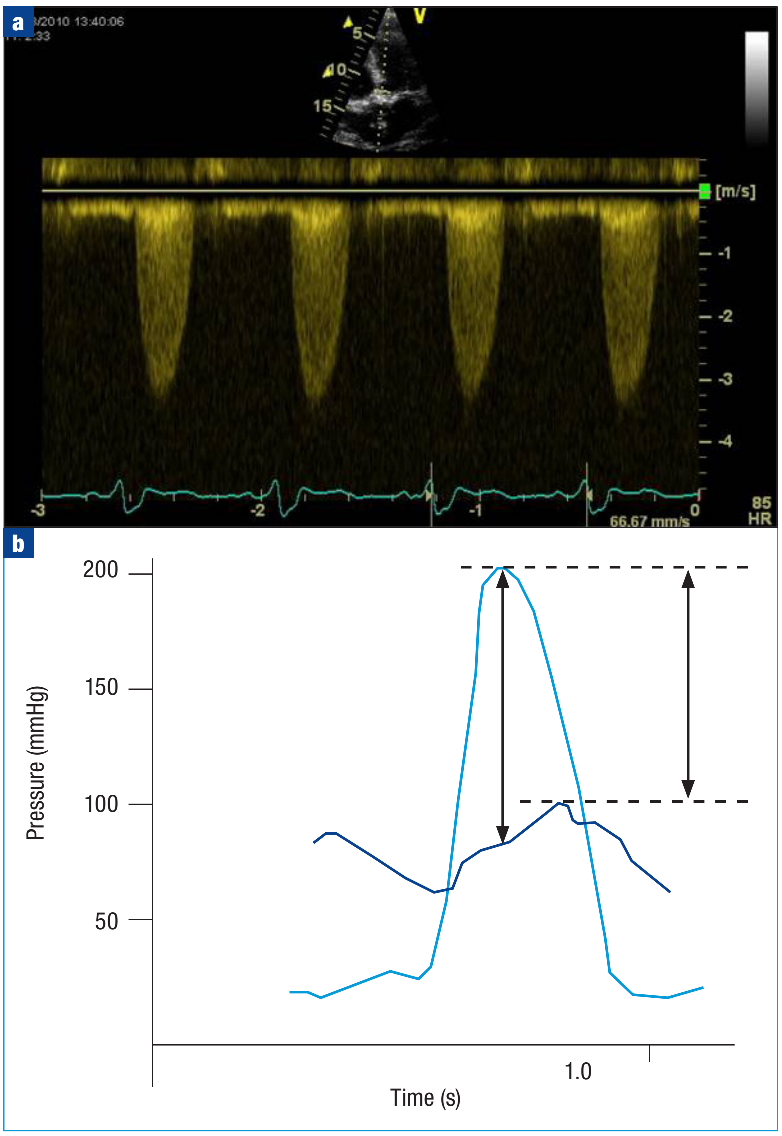
Figure 4. Low flow aortic stenosis. **a.** The left ventricle caught in systole shows normal end-systolic size and the estimated left ventricular ejection fraction was 55%. **b.** However, the mean gradient on continuous wave was only 35 mmHg. **c.** Low flow was confirmed by a low subaortic VTI of 11 cm and the effective orifice area using the continuity equation was 0.4 cm^2.



2015). Mortality at surgery is substantially higher in the absence of contractile reserve – about 35% compared to 5% with contractile reserve. If the patient without contractile reserve survives surgery the left ventricle can still recover function in the mid and long term (Quere et al, 2006).

Stress echocardiography is also indicated if there are symptoms despite only moderate aortic stenosis. The aim is to determine if there is coexistent coronary disease (shown by the development of a wall-motion abnormality) or a poorly compliant aortic valve. If the aortic valve is poorly compliant (fails to open on exercise) then the gradient may increase disproportionately with stress, usually taken as an increase in mean gradient of >20 mmHg (Garbi et al, 2015). Finally stress echo may be indicated in patients before major non-cardiac surgery who are not able to exercise to determine whether prior aortic valve intervention is needed.

Figure 5. A comparison of pressure wave **(a)** measured directly and **(b)** derived from Doppler.



Other echocardiographic measurements

The haemodynamic effect of aortic stenosis is imperfectly described by the simple basic formulae in everyday use. One effect is pressure recovery (Baumgartner et al, 1999). Blood flow decelerates beyond a stenosis (*Figure 2*) and as it loses kinetic energy the static pressure (as measured with a manometer) must rise. This rise is limited because energy is also lost as a result of turbulence causing heat. The recovered pressure is maximal about 10 orifice diameters downstream from the stenosis at which point the pressure drop (compared with the left ventricular cavity) is lower than measured at the valve orifice. This pressure difference is thought to better reflect the strain on the left ventricle and may better determine left ventricular hypertrophy and clinical events. A cardiac catheter tends to measure the recovered pressure difference while Doppler echocardiography estimates the maximal pressure difference at the orifice (*Figure 5*). These measurements may differ because:

- Doppler estimates pressure at the vena contracta just beyond the aortic orifice while the catheter estimates the difference between the left ventricle and a point in the aorta downstream from the valve where pressure is usually completely recovered. This effect is most important in mild aortic stenosis
- Doppler estimates peak instantaneous pressure while cardiac catheterization estimates peak to peak gradient
- Unless the aortic stenosis is severe the short form of the modified Bernoulli equation underestimates gradient by neglecting subaortic peak velocity
- Errors may occur. If the aortic signal is not optimized, the aortic stenosis will be underestimated. However, coronary angiography introduces major systematic errors based on the limitations of fluid-filled system.

Another effect is total left ventricular outflow impedance (Briand et al, 2005). The stress on the left ventricle is the summation of the transaortic resistance and the aortic compliance. The effect on left ventricular function of a combination of moderate valve stenosis and low aortic compliance is similar to the effect of severe aortic valve stenosis. Valve and aortic resistance are combined in the Z index with a value >4.5 often taken as severe (Baumgartner et al, 2009).

These effects are the subject of research and are not used in routine clinical practice. They may occasionally be needed to explain discrepant clinical findings and help determine whether the left ventricle may recover after aortic valve intervention.

Other methods of assessment

Cardiac catheterization

Coronary angiography is needed before aortic valve surgery but the valve should almost never be crossed. The risk of death, stroke or pulmonary oedema is about 7% crossing the valve (Chambers et al, 2004). Catheter- and Doppler-derived gradients are related but different and not directly comparable (*Figure 5*).

Multislice computed tomography and cardiac magnetic resonance

The ascending aorta may not be well imaged on transthoracic echocardiography and then computed tomography or cardiac magnetic resonance should be used. It is increasingly common to check the aortic diameter using computed tomography or cardiac magnetic resonance if it is close to a surgical threshold. It may be better to use computed tomography when considering referral for aortic valve surgery since this can also detect calcium in the ascending aorta and identify porcelain aorta as an indication for a transcatheter procedure instead of conventional surgery. Coronary computed tomography angiography can also produce an assessment of the coronary arteries in patients at moderate risk of coronary disease. Those at higher risk still require conventional invasive contrast angiography. Computed tomography is also widely used to assess the size and shape of the left ventricular outflow tract and annulus for valve sizing in the work up towards transcatheter aortic valve implantation. It provides additional information such as the degree of calcification of the leaflets, the distance to the coronary arteries and the calibre, tortuosity and calcific burden of the peripheral vessels (Achenbach et al, 2010).

If echocardiographic image quality is poor, computed tomography or cardiac magnetic resonance can be used to image the valve while cardiac magnetic resonance can measure velocities across the valve. Anatomical area on computed tomography or cardiac magnetic resonance can be useful and, although not the same as effective orifice area, it is possible that a combination of anatomical area and calcium score will give a reliable measure of the grade of stenosis. Qualitative assessment of valve calcification on transthoracic echocardiography predicts events and aids the decision for surgery. Computed tomography calcium scoring is quantitative and predicts disease progression (Clavel et al, 2014) better than on transthoracic echocardiography. It is likely that myocardial fibrosis detected by cardiac magnetic resonance (Shah et al, 2014b) will predict events, but further work is required before this can be recommended clinically. Cardiac magnetic resonance is far more accurate than transthoracic echocardiography for quantifying left ventricular mass and is therefore useful in research studies to document the regression of left ventricular hypertrophy after surgery, although it has not yet been shown to be a prognostic marker.

Risk assessment

Aortic stenosis is common with a relatively higher risk of sudden death than other valve disease. It is therefore important to determine whether the risk of sudden death is particularly high (*Table 5*).

The resting echocardiogram

Critical aortic stenosis (Vmax ≥5.0 m/s) is associated with a 36% risk of events by 1 year and 75% by 3 years (Rosenhek et al, 2010). A fast rate of progression taken as >0.3 m/s per annum in the presence of calcification (Rosenhek et al, 2000) is a class 2b indication for surgery in Europe although it is possible that in the future an objective calcium score using computed tomography may be used.

Exercise is routinely indicated in all patients with asymptomatic severe aortic stenosis who are low risk for surgery. The history alone is remarkably insensitive and non-specific. Patients tend to slow up to avoid experiencing overt symptoms and exercise testing can bring out symptoms in about one half (Das et al, 2005). International guidelines (Vahanian et al, 2012; Nishimura et al, 2014) suggest a role for routine exercise echocardiography although the evidence base is still small. The most likely group in which this might be useful are those with a resting mean gradient >35 mmHg in whom a rise in mean gradient >20 mmHg confers a particularly high risk of events (Marechaux et al, 2010) and in whom early surgery might be indicated.

Computed tomography calcium scoring is quantitative and predicts disease progression (Clavel et al, 2014) better than transthoracic echocardiography. There is conflicting evidence about the value of biomarkers notably B-type natriuretic peptide (Steadman et al, 2010).

Conclusions

Echocardiography is the mainstay of assessment (*Table 6*) but there are a number of emerging trends. Magnetic resonance and cardiac computed tomography are increasingly used if echocardiography is suboptimal or to provide complementary information. Complete assessment of the aortic valve may require integration of left ventricular function and aortic physiology. Stress echocardiography is increasingly used as the grading of aortic stenosis and left ventricular function may differ on exercise compared with resting conditions. There is increasing emphasis on risk assessment using echocardiography, stress testing and biomarkers. BJHM

Table 5. Markers of a high risk of events

Transthoracic echo	Vmax >5.0 m/s Rapid progression (>0.3 m/s per annum) with calcification
Stress echo	Increase in mean gradient >20 mmHg (especially if resting mean gradient >35 mmHg) Reduced contractile reserve (<4% increase on exercise)
Exercise testing	Symptoms and possibly a blunted blood pressure rise
B-type natriuretic peptide	Raised >500 pg/ml
Cardiac computed tomography	High calcium score

KEY POINTS

- The minimum Doppler dataset is peak transaortic velocity, mean gradient and effective orifice area using the continuity equation.
- Discrepancies in grade between gradient or velocity and effective orifice area are common and have many causes including low flow as a result of a small left ventricle cavity.
- Stress echocardiography is indicated mainly for patients with left ventricular ejection fraction <40% and severe aortic stenosis on effective orifice area (<1.0 cm^2) despite moderate gradient (<40 mmHg).
- Risk assessment is based on serial echocardiograms, treadmill exercise, stress echocardiography and B-type natriuretic peptide levels.
- Multimodality imaging including magnetic resonance and cardiac computed tomography is increasingly helpful especially to image the ascending aorta.

Table 6. Checklist report in aortic stenosis for the non-echocardiographer
Appearance and movement of the aortic valve. Is this description consistent with the grade? If the valve is bicuspid check for aortic dilatation and coarctation
Grade of stenosis. Is there a discrepancy between gradient and effective orifice area?
Grade of associated regurgitation. High flow rates cause by severe regurgitation may increase the mean gradient even in moderate aortic stenosis
Has the aorta been measured both at the root (sinus) and the ascending aorta?
Left ventricular dimensions and systolic function. If the ejection fraction is low the mean gradient may underestimate the grade of stenosis. If the left ventricle is hypertrophied with a small cavity systolic flow is likely to be low
State of the mitral valve. Mitral involvement is common in rheumatic disease. Mitral regurgitation may need operation if moderate in association with abnormal valve function or if functional and more than moderate
Pulmonary artery pressure. This is common in severe aortic stenosis and associated with a poor prognosis if aortic valve surgery is not performed

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Conflict of interest: none.

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