When to use stress echocardiography in the evaluation of patients with valvular heart disease

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ABSTRACT

Stress testing and stress echocardiography are firmly established diagnostic tests in the evaluation of patients with suspected or known coronary artery disease, but less established in the evaluation of patients with valvular heart disease. However, there is emerging data supporting the incremental benefit of stress testing and stress echocardiography in patients with known valvular heart disease. Particular applications include hemodynamic assessment of valve function and pulmonary response during exercise-induced or chemically-induced stress to correlate with the patient's exertional symptoms. In addition, stress testing affords the opportunity for functional assessment of ventricular systolic function for prognostication and planning for surgery. SAHeart 2010; 7:94-105

INTRODUCTION

Valvular heart diseases are a major public health problem worldwide.[1,2] Rheumatic heart disease is the leading cause of valve disease in economically developing countries[3-5] and degenerative or aging-related valve diseases predominate in economically developed countries.[2,6] The majority of valve diseases are chronic and left-sided, affecting the mitral and aortic valves. The valves become stenosed or regurgitant. The development of symptoms (exertional dyspnoea, fatigue, angina, presyncope, syncope) typically occurs when the valve disease is severe and the symptoms are usually brought on by exertion. However, symptoms may be imperceptible because they can develop gradually and may not be reported by the patient, or the patient may be too sedentary to develop symptoms. Additionally, some patients with severe valve disease remain asymptomatic despite being active. Symptoms related to valve disease lead to decreased exercise tolerance and impaired quality of life. They may also indicate impending heart failure and death if the valve lesion is not corrected. The mainstay of treatment of severe valve disease is valvuloplasty (for mitral stenosis in suitable candidates) or surgery (valve replacement or repair).

Valve diseases come to attention because a murmur is detected on physical examination, but 2-D and Doppler echocardiography is superior to physical examination for detecting valve disease and should be utilised in the clinical evaluation of patients who have cardiac symptoms even in the absence of an audible or "loud" murmur on physical examination. Echocardiography is the single most useful test for determining the etiology and severity of valve disease and is the test of choice for guiding the management of patients with valve disease. Hemodynamic consequences of cardiac chamber remodelling with changes in ventricular and atrial size and function and/or pulmonary pressures commensurate with severe stenosis or regurgitation can be assessed by echocardiography and used for risk stratification and timing of therapeutic intervention. In addition, unsuspected coexistent heart diseases may be diagnosed during evaluation of valve disease.

In symptomatic patients, a resting echocardiogram that shows anatomically severe valve disease and associated hemodynamic abnormalities usually provides sufficient information to refer the patient to surgery.[7,8] Stress testing in those patients is not indicated unless there is a need to assess for hibernating myocardium

or left ventricular contractile reserve when planning for surgery. Stress testing and stress echocardiography are useful and indicated for patients who report exertional symptoms, but who only appear to have mild to moderate valve disease at rest that would not be expected to cause symptoms. Stress testing is also useful for assessing patients who are sedentary and who do not report symptoms despite having severe valve disease.

The discussion below will focus on left-sided native valve diseases and clinical situations where stress testing and stress echocardiography are useful for decision-making.

MITRAL STENOSIS

Mitral stenosis is caused by structural abnormalities of the mitral valve apparatus that lead to improper opening of the valve and subsequent obstruction to left ventricular filling during diastole.[7,9,10] The predominant cause of mitral stenosis is inflammation of the mitral valve from rheumatic fever which leads to valvular and/or subvalvular thickening and calcification and commissural fusion. As the valve narrows the left atrial pressure increases to continue driving blood into the left ventricle; a measurable pressure gradient develops across the valve during diastole.[7,11] The increased left atrial pressure is reflected back into the pulmonary circulation and may lead to pulmonary congestion and pulmonary venous and even pulmonary arterial hypertension. The associated symptoms are dyspnoea and fatigue or pulmonary oedema.[11,12] The normal mitral valve area is 4-6cm^2 and symptoms usually do not develop until the valve area is less than 2.5cm^2;[7,13] a valve area >1.5cm^2 usually does not produce symptoms at rest.[14] Development of symptoms or pulmonary hypertension in mitral stenosis is associated with a poor outcome if left untreated.[12]

TABLE 1: Grading of severity of mitral valve stenosis[7]

	Valve area	Mean gradient	Pulmonary artery systolic pressure
Mild	>1.5cm^2	<5mmHg	<30mmHg
Moderate	1-1.5cm^2	5-10mmHg	30-50mmHg
Severe	<1cm^2	>10mmHg	>50mmHg

The pressure gradient across the mitral valve is a function of the square of the flow across the valve and is dependent on the diastolic filling period.[7,11] Therefore, symptoms in mitral stenosis are usually precipitated by an increase in flow or heart rate and the degree of valve stenosis at rest may not reflect the true severity of obstruction with exercise.[7,14]

Guidelines for management of mitral stenosis are based on a point scale comprised of the mitral valve area, transmitral mean gradient and pulmonary artery systolic pressure (Table 1).[7] Severe mitral stenosis is defined as a mitral valve area <1cm^2, a transmitral mean pressure gradient >10mmHg or pulmonary artery systolic pressure >50mmHg. Patients with severe mitral stenosis benefit from mitral valvuloplasty or surgery.[7]

Mitral valve area (MVA) is determined by the pressure half-time (PHT) or continuity equation methods.[15-19] PHT refers to the time it takes for the transmitral gradient to reach half of the initial peak gradient and is determined by the slope of the continuous wave Doppler signal across the stenotic mitral valve. The initial peak gradient is higher and the PHT longer with worsening mitral stenosis. Mitral valve area is calculated by the formula:

$$MVA = 220/PHT$$

The PHT can be shortened in the presence of severe mitral stenosis if there is underlying decreased left atrial compliance since the high left atrial pressure may lead to more rapid equalisation of left atrial and left ventricular pressures during diastole.[20] Conditions that cause a rapid rise in left ventricular pressure during diastole such as the presence of decreased left ventricular compliance or severe aortic regurgitation may also lead to a shortened PHT and overestimation of mitral valve area (that is, underestimation of severity of mitral stenosis).[19] Calculation of the mitral valve area using the continuity equation (Figure 1) requires measurements of the forward stroke volume from the left ventricular outflow tract (LVOT) diameter (D), LVOT time velocity integral (TVI), and mitral valve TVI and using the following equation:

$$MVA = (LVOT\ D^2 \times 0.785 \times TVI_{LVOT})/TVI_{MV}$$

However, this equation should not be used in the presence of significant aortic regurgitation because it will result in underestimation of the severity of mitral stenosis.[21] Furthermore, severe

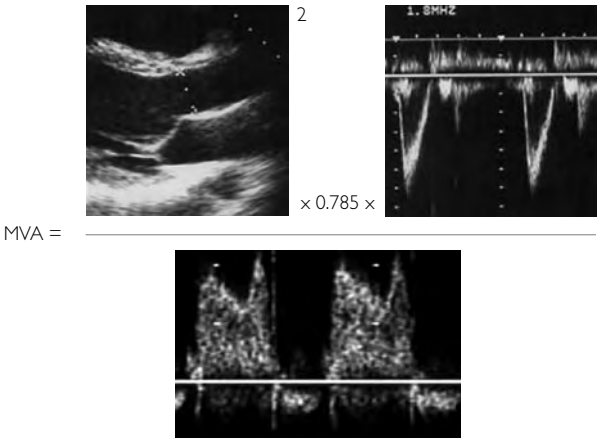

FIGURE 1: Example of calculation of mitral valve area by continuity equation

mitral regurgitation can cause overestimation of the severity of mitral valve stenosis if this equation is applied.[19] The mitral valve area can also be determined directly by planimetry of the mitral valve area at the tips of the mitral valve in the parasternal short-axis view. The mean transmitral gradient is determined by tracing the continuous wave Doppler signal across the stenotic mitral valve. If significant mitral regurgitation is present, the increased flow results in a higher transmitral gradient. Thus, a comprehensive evaluation of mitral stenosis should include assessment of the severity of mitral regurgitation.

Pulmonary artery systolic pressure (PASP) is estimated from the peak velocity of the tricuspid regurgitation (TR) continuous wave signal and right atrial pressure (RAP) using the modified Bernoulli equation:

$$PASP = 4 \times TR^2 + RAP$$

(RAP is estimated from the size of the inferior vena cava. If the diameter of the inferior vena cava decreases by 50% or more during inspiration, RAP is usually <10mmHg, and if the diameter decreases less than 50%, RAP is usually >10mmHg).[22]

Stress echocardiography for mitral valve stenosis

A symptomatic patient whose resting echocardiogram shows severe mitral stenosis is considered to have symptomatic severe mitral valve stenosis and stress echocardiography is not indicated.[23]

Patients who appear to have mild to moderate mitral stenosis at rest but who report symptoms of dyspnoea or fatigue may have another cause for their symptoms (such as lung disease or deconditioning), or may have hemodynamically severe mitral stenosis during exercise, since 2-D and Doppler hemodynamic determination of mild to moderate mitral stenosis at rest may not reflect the hemodynamic severity of the stenosis with exercise. Symptom-limited stress echocardiography (exercise or dobutamine) is useful in patients with mild to moderate mitral stenosis at rest to assess the transmitral mean gradient and pulmonary pressures at peak stress in order to establish a link between the patient's exertional symptoms and stress-induced hemodynamic abnormalities.[24-30]

During exercise, a rise in the transmitral mean diastolic gradient to >15mmHg along with a rise in pulmonary artery systolic pressure to >60mmHg associated with symptoms identifies a group of patients who have hemodynamically severe mitral stenosis and who would benefit from mitral balloon valvuloplasty or mitral valve surgery.[7,25,31,32] Some of these patients, however, may respond to more aggressive medical therapy, which is aimed at blunting the heart rate response to exercise. Therefore, exercise stress testing may be used to tailor medical therapy. A rise in pulmonary artery systolic pressure with exercise without a significant rise in the mean diastolic gradient suggests pulmonary disease.[33]

Supine bicycle exercise is preferable to treadmill exercise because hemodynamic data can be obtained during each stage of exercise.[28,31,33] The development of a mean gradient ≥18 mmHg with dobutamine stress in patients with non-severe mitral stenosis at rest identifies a group at high risk of developing subsequent dyspnoea or pulmonary oedema requiring hospitalisation, subsequent arrhythmias, or requiring mitral valve interventions.[34] Table 2 outlines variables that should be obtained at rest and during stress for clinical decision making. Additionally, colour flow imaging of the mitral valve is recommended because the severity of regurgitation can increase with exercise in patients with mixed mitral valve disease. The mitral valve area is not expected to change much from rest to stress, although it can be calculated accurately with the continuity equation or by planimetry.[30,35,36] The PHT during stress may be inaccurate for estimating valve area.[25,28,37-39] Exercise echo-

cardiography can also be used to assess haemodynamics after mitral valve balloon valvuloplasty.[40]

MITRAL REGURGITATION

Unlike mitral valve stenosis, which is almost always caused by rheumatic carditis, the predominant causes of mitral valve regurgitation differ between developing and developed countries. Rheumatic carditis remains the major cause of mitral regurgitation in developing countries and is the predominant cause of heart failure in children and young adults with active rheumatic carditis.[41] In developed countries, mitral regurgitation is most commonly related to degenerative mitral valve disease often associated with aging.[2] Another important cause of mitral regurgitation is functional mitral regurgitation related to ischaemic or non-ischaemic cardiomyopathy, but the relative global distribution of this etiology of mitral regurgitation is unknown.

Severity of mitral valve regurgitation is determined by a variety of methods including qualitative, semi-quantitative, and quantitative measurements (Table 3).[42] The reader is referred to the American Society of Echocardiography Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography[42] for complete details of the criteria including their utility, advantages, and limitations. In asymptomatic patients, quantitative grading of mitral regurgitation is a powerful predictor of subsequent atrial fibrillation, heart failure, or death where the effective regurgitant orifice (ERO) surpasses all other qualitative or quantitative measurements as a prognosticator.[43]

TABLE 2: Key data to be acquired at rest and during stress during assessment of severity of mitral valve stenosis

	Rest	Stress
Blood pressure	×	×
Heart rate	×	×
MVA	×	
Mean gradient	×	×
TR velocity	×	×
Symptoms	×	×
Exercise duration		×

Stress echocardiography in mitral valve regurgitation

Rheumatic mitral regurgitation

Severe mitral regurgitation from rheumatic carditis is typically associated with symptoms of dyspnoea, fatigue, or heart failure. Surgery is indicated for symptomatic patients with severe rheumatic mitral regurgitation and there is no role for stress testing.

Patients who report symptoms, but who appear to have mild to moderate mitral regurgitation at rest should undergo symptom-limited exercise echocardiography to determine whether the mitral regurgitation severity increases with exercise and if pulmonary hypertension develops (pulmonary artery systolic pressure >60 mmHg).[7,33] An increase in the severity of mitral regurgitation correlates well with elevation of pulmonary artery systolic pressure.[44,45]

TABLE 3: Qualitative and quantitative parameters for grading mitral regurgitation severity (with permission from the American Society of Echocardiography)[42]

	Mild	Moderate	Severe
Structural parameters			
LA size	Normal	Normal or dilated	Usually dilated
LV size	Normal	Normal or dilated	Usually dilated
Mitral leaflets or supporting structures	Normal or abnormal	Normal or abnormal	Abnormal/flail leaflet/Ruptured papillary muscle
Doppler parameters			
Colour flow jet (at Nyquist limit of 50-60cm/s)	Small central jet (usually <4cm^2 or <20% of LA area)	Variable	Large central jet (usually >10cm^2 or >40% of LA area) or variable size wall-impinging jet swirling in LA
Mitral inflow-PW	A-wave dominant*	Variable	E-wave dominant* (E usually >1.2 m/s)
Jet density-CW	Incomplete or faint	Dense	Dense
Jet contour-CW	Parabolic	Usually parabolic	Early peaking-triangular
Pulmonary vein flow	Systolic dominance	Systolic blunting may be present	Systolic reversal may be present
Quantitative parameters			
VC width (cm)	<0.3	0.3-0.69	≥0.7
R Vol (ml/beat)	<30	30-59	≥60
RF (%)	<30	30-49	≥50
ERO (cm^2)	<0.20	0.20-0.39	≥0.40

CW = continuous-wave. LA = left atrium. ERO = effective regurgitant orifice. LV = left ventricle. PW = pulsed-wave. RF = regurgitant fraction. R Vol = regurgitant volume. VC = vena contracta.

** Usually above 50 years of age or in conditions of impaired relaxation, in the absence of mitral stenosis or other causes of elevated LA pressure.*

Supine bicycle exercise is the preferred stress testing modality because the severity of mitral regurgitation can be assessed at every stage of exercise. Qualitative and semi-quantitative measurements are easier to obtain during stress testing, but attempts should be made to assess severity of regurgitation by quantitative measurements as well.[42]

Tischler et al. reported a high incidence of exercise-induced worsening of mitral regurgitation in a group of patients with exertional dyspnoea but with only mild rheumatic mitral valve disease at rest (mild stenosis and mild regurgitation).[44] The mechanism responsible for this increase in severity of mitral regurgitation in patients with rheumatic mitral valve disease is unclear.

Degenerative mitral regurgitation

Symptomatic patients with severe mitral regurgitation due to mitral valve prolapse or flail mitral valve leaflets should be referred to surgery. The preferred mode of surgical correction is mitral valve repair instead of mitral valve replacement.[7,43,46] There is no indication for stress echocardiography in symptomatic patients with severe degenerative mitral regurgitation. Asymptomatic patients with overt signs of left ventricular dysfunction (left ventricular ejection fraction ≤60% and left ventricular end-systolic dimension ≥40mm) should also be referred for mitral repair; there is no role of stress testing in these patients.[7,8]

There is some debate regarding whether asymptomatic patients with severe degenerative mitral valve regurgitation and preserved left ventricular size and systolic function (not meeting and exceeding guideline cut-off values) should be referred to surgery. We favour mitral valve repair in these patients given the unavoidable consequences if left unoperated and the extremely low operative risk and excellent long term outcome of these patients. However, the surgery should be performed at centres with expertise and high success rates in mitral valve repair.[43,47-50]

Exercise testing in asymptomatic patients with severe mitral regurgitation with preserved left ventricular size and systolic function may help identify those with decreased exercise capacity due to mitral regurgitation and those with latent left ventricular dysfunction. The goal of stress testing in these patients is therefore to assess functional capacity and response of left ventricular size and systolic function to exercise. Decreased exercise capacity in asymptomatic patients (peak VO2 <84% predicted), as assessed by cardiopulmonary exercise testing, identifies a subgroup at higher risk of developing subsequent heart failure or dying.[51] Exercise duration of <15 minutes on a modified Bruce protocol in asymptomatic patients with severe mitral regurgitation is associated with a much higher risk of developing left ventricular dysfunction or symptoms (average annual event risk of 23.5% versus 4.6% in those with exercise duration ≥15 minutes).[52]

The inability to increase left ventricular ejection fraction ≥4% with exercise (that is, lack of contractile reserve) identifies patients with latent left ventricular dysfunction.[53-55] These patients are at higher risk of developing overt left ventricular dysfunction when treated medically and at higher risk of developing postoperative heart failure.[54,55] An exercise left-ventricular systolic volume index >25ml/m^2 in minimally symptomatic patients identifies those at risk of developing postoperative heart failure. Depressed longitudinal myocardial function assessed by 2-D speckle tracking at rest and during exercise was able to identify a subgroup of patients with latent left ventricular dysfunction and predicted postoperative left ventricular dysfunction.[56]

Ischaemic mitral regurgitation

The mechanism of ischaemic mitral regurgitation is related to global and regional remodelling of the left ventricle from ischaemia or infarction. This leads to apical and posterior displacement of the papillary muscles, tenting of the mitral valve leaflets, loss of annular contraction and resultant mitral leaflet malcoaptation and regurgitation.[57,58] Mitral regurgitation is present in up to 50% of patients following myocardial infarction[59] and is associated with poor long term outcome even when the regurgitation is mild; the outcome is worse still when the regurgitation is moderate or more.[60] Lesion severity in terms of the ERO and regurgitant volume that impact negatively on survival in ischaemic mitral regurgitation is much less than that of organic or degenerative mitral regurgitation (ERO≥20mm^2 and regurgitant volume ≥30ml are considered severe regurgitation in ischaemic mitral regurgitation).[60] Mitral valve surgery is recommended in patients who have severe mitral regurgitation and impaired left ventricular ejection fraction who are to undergo coronary bypass surgery.[8]

Mitral valve repair, however, does not appear to be superior to mitral valve replacement in patients with ischaemic mitral regurgitation.[61,62] Surgery solely for mitral regurgitation in patients with ischaemic mitral regurgitation and impaired left ventricular systolic function does not seem to offer survival benefit,[63-65] but may be considered for relief of symptoms in those with associated heart failure refractory to medical therapy.[66]

In some patients, mild to moderate ischaemic mitral regurgitation may become severe with exercise and these patients are at higher risk of heart failure or death.[67-69] Ischaemic mitral regurgitation that worsens with exercise and the development of pulmonary hypertension with exercise are indeed important causes of acute pulmonary oedema in patients with left ventricular systolic dysfunction.[69] Exercise Doppler echocardiography may therefore be helpful in elucidating the etiology of exertional symptoms or acute pulmonary oedema in patients with mild to moderate mitral regurgitation at rest.[69-72] Worsening of the degree of mitral regurgitation during exercise is related to changes in local left ventricular remodelling and more deformation of the mitral valve apparatus leading to systolic expansion of the mitral annulus which increases the regurgitant orifice.[67]

Dobutamine stress testing in patients with ischaemic mitral regurgitation is useful for determining the presence and extent of hibernating viable myocardium[73] since treatment of viable hibernating myocardium with revascularisation or medical therapy or cardiac resynchronisation may improve both left ventricular systolic function and mitral regurgitation.[74-77]

Non-ischaemic functional mitral regurgitation

The mechanism of mitral regurgitation in non-ischaemic dilated cardiomyopathy has also been described and is related to mitral leaflet tethering, annular expansion, and decrease in left ventricular driving forces that close the mitral valve leaflets.[78] Mitral regurgitation is common among patients with non-ischaemic dilated cardiomyopathy and its presence impacts negatively on survival with the worst survival being in those patients with moderate to severe regurgitation.[79] Even patients with mild degree or regurgitation have a less favourable outcome compared to those without any mitral regurgitation.[79] As in ischaemic mitral regurgitation, a potential reason for why even mild degrees of functional mitral regurgitation are associated with poor outcome may be related to the dynamic nature of mitral regurgitation, where mitral regurgitation worsens with exercise.[58] Yamano et al., using exercise echocardiography, demonstrated exercise-induced changes in functional mitral regurgitation in patients with non-ischaemic dilated cardiomyopathy (Figure 2) and this correlated strongly with exercise intolerance.[80]

Dobutamine changes loading conditions and usually decreases the severity of mitral regurgitation by, among other things, decreasing mitral ERO[81] and increasing forward left ventricular stroke volume.[82] Dobutamine is therefore not considered a useful stress testing modality for the assessment of mitral regurgitation. Exercise, and not dobutamine, should be the stress modality when assessing whether the severity of mitral regurgitation, regardless of etiology, increases with stress.

AORTIC STENOSIS

Aortic valve stenosis may be caused by rheumatic carditis, but it is more commonly caused by an atherosclerotic and inflammatory process related to aging and cardiovascular risk factors (commonly referred to as degenerative aortic valve stenosis).[2,6,83-87] Criteria for severity of aortic valve stenosis are outlined in Table 4.

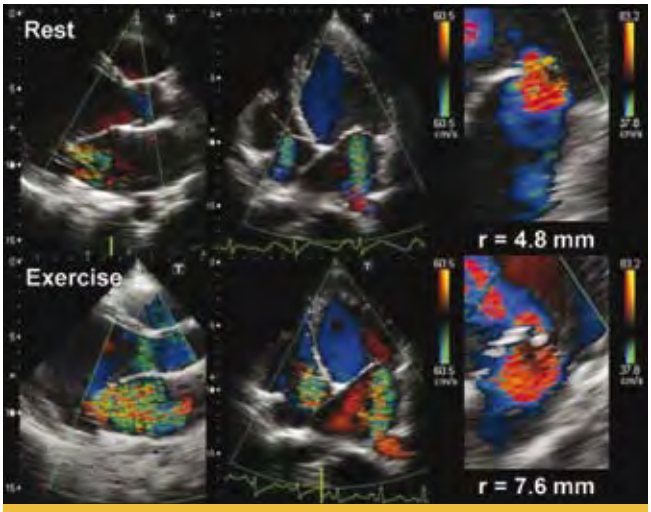

FIGURE 2: Colour Doppler echocardiograms of a patient who showed an increase in functional MR severity during exercise. The radius of the proximal isovelocity surface area (r) increased from 4.8 to 7.6mm (right) and the ERO from 14.2 to 29.1mm^2 (with permission)[80]

TABLE 4: Grading of severity of aortic valve stenosis[7]

	Valve area	Valve area index	Peak velocity	Mean gradient
Mild	>1.5cm²		<3m/s	<25
Moderate	1-1.5cm²		3-4m/s	25-40mmHg
Severe	<1cm²	<0.6cm²/m²	>4m/s	>40mmHg

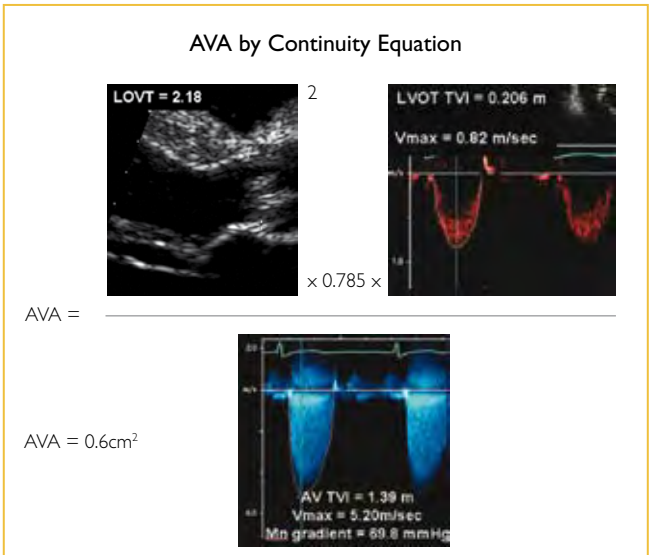

FIGURE 3: Example of aortic valve area calculation

Aortic valve area (AVA) (Figure 3) is calculated from the continuity equation which requires measurements of the forward stroke volume from LVOT diameter (D), LVOT TVI, and transvalvular TVI using the following equation:

$$AVA = (LVOT\ D^2 \times 0.785 \times TVI_{LVOT})/TVI_{AV}$$

A dimensionless index TVI_{LVOT}/TVI_{AV} can also be used in cases where the diameter of the LVOT is difficult to measure. A TVI_{LVOT}/TVI_{AV} <0.25 is consistent with severe aortic stenosis.[7] Symptoms related to aortic stenosis (dyspnoea, angina, and syncope being the classic triad)[88] typically develop when the degree of aortic stenosis is severe. Prompt surgery is indicated in symptomatic severe aortic stenosis[89] and there is no indication for stress testing.[7,8] Surgery is also recommended for patients with asymptomatic severe aortic stenosis with left ventricular systolic dysfunction (left ventricular ejection fraction <50%).[7,8] Patients with moderate aortic stenosis should undergo aortic valve replacement if they are having open heart surgery for other reasons.[7,8]

Stress echocardiography in aortic valve stenosis

Aortic stenosis with normal left ventricular systolic function

Surgery is not generally recommended for asymptomatic patients with severe aortic valve stenosis until they develop symptoms. However, about 30% of asymptomatic patients will develop symptoms or heart failure within two years of diagnosis.[90,91] The risk of sudden death in asymptomatic patients with severe aortic stenosis is <1% per year[92,93] and some asymptomatic patients with severe aortic stenosis may develop irreversible left ventricular dysfunction, although there is no reliable data to suggest that irreversible left ventricular dysfunction develops as a result of severe aortic stenosis in the absence of symptoms.[8] The risk of adverse outcomes with aortic valve replacement on the other hand is about 3-5% and therefore aortic valve replacement is not recommended routinely for asymptomatic patients with severe aortic stenosis.[7,8] Several predictors of progression of aortic stenosis and poor outcome in initially asymptomatic patients have been described and include the degree of aortic valve calcification (moderate or more),[94] peak jet velocity across the aortic valve (peak velocity >4.0m/sec),[92,95] and a higher rate of hemodynamic progression (increase in peak velocity across the aortic valve >0.3m/s per year or decrease in aortic valve area >0.1cm² per year.[94,95]

Exercise testing is useful in asymptomatic patients with severe aortic stenosis to help identify those patients at higher risk of developing symptoms and heart failure during follow up. Moreover, this may identify patients who are not truly asymptomatic. Exercise treadmill testing has been shown to be safe in patients with asymptomatic severe aortic stenosis, but it has to be performed under careful and close physician supervision.[96-101] Predictors of the development of symptoms include symptoms during exercise testing, an abnormal blood pressure response to exercise (<20mmHg increase in systolic blood pressure) and the development of ST segment depression ≥2mm.[98,99]

An increase in the mean systolic Doppler gradient ≥18mmHg during exercise echocardiography was shown to have incremental prognostic value over resting echocardiography and exercise

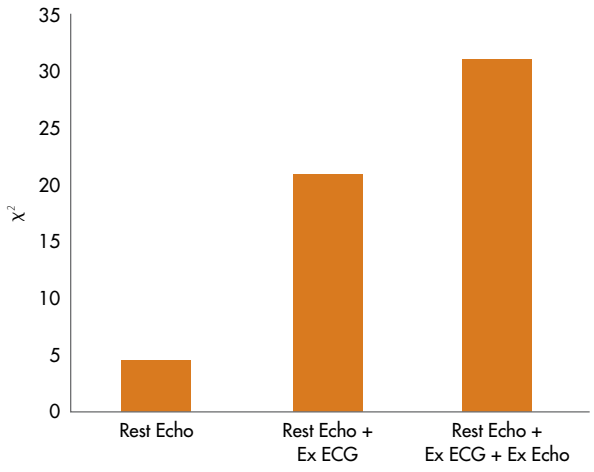

FIGURE 4: Incremental prognostic value of exercise Doppler echocardiography over resting echocardiographic and exercise electrocardiographic parameters in patients with asymptomatic aortic stenosis (with permission)[101]

χ^2 = chi-square. Echo = echocardiography. Ex = exercise. ECG = electrocardiogram.

treadmill data in predicting higher risk of developing symptoms, heart failure, needing aortic valve replacement, or cardiac death.[101] (Figure 4)

Aortic stenosis with reduced left ventricular systolic function

As previously mentioned, patients who have severe aortic valve stenosis (AVA <1cm^2 and mean gradient >40mmHg) and reduced left ventricular systolic function (LV EF <50%) should be referred for surgery.[7,8]

However, some patients with reduced left ventricular systolic function (EF <40%) may present with a calculated AVA ≤1cm^2 and a low transvalvular mean gradient (<30mmHg), a situation termed low gradient, low output aortic stenosis where the transvalvular gradient is discordant with the calculated valve area.[102] In this setting, there may be fixed, severe aortic stenosis which has resulted in left ventricular systolic failure with reduced contractility and stroke volume and a low transvalvular gradient. On the other hand, both the calculated aortic valve area and transvalvular mean gradient may be low because of reduced left ventricular contractility and stroke volume from other causes and the stenosis is only mild or moderate ("relative" aortic stenosis).[102] The two situations can be distinguished from each other by use of low to intermediate dose dobutamine echocardiography. In fixed, severe aortic stenosis an infusion of dobutamine will result in increased contractility and stroke volume and a higher mean transvalvular gradient, while the calculated aortic valve area does not change significantly. If the aortic stenosis is not severe, with the increased left ventricular contractility and stroke volume the aortic valve will open more and the valve area increases, while the mean gradient remains unchanged or only increases modestly. It is important to make the distinction between these two types of patients because those with fixed, severe aortic stenosis will benefit from aortic valve surgery, while those with relative aortic stenosis will not.[102] Therefore, dobutamine echocardiography is particularly helpful in patients with aortic stenosis with left ventricular systolic dysfunction and low transvalvular mean gradients.[103]

Since the main purpose of using dobutamine in this situation is to increase transvalvular flow and not to induce myocardial ischaemia,[73] the incremental infusion of dobutamine stops at 20ug/kg/min. Longer dobutamine infusion stages (up to 5 to 8 minutes) are recommended to avoid rapid increases in heart rate and also to allow for steady-state conditions to be reached and for careful data acquisition.[73] Patients who have true fixed, severe aortic stenosis and left ventricular contractile reserve, defined as an increase in stroke volume ≥20% during dobutamine echocardiography, have a much better postoperative outcome than those without contractile reserve (stroke volume increase <20%).[104-106] However, patients without left ventricular contractile reserve should still be considered for aortic valve replacement surgery, even though their surgical risk is higher,[107,108] since the outlook without surgery is dismal. A significant number of patients with aortic stenosis will have coronary artery disease[109] and assessment for coexistent coronary artery disease in these patients should be by coronary angiography.

AORTIC REGURGITATION

Aortic regurgitation may be due to the sequelae of rheumatic carditis or may be secondary to congenital abnormalities of the valve such as bicuspid aortic valve with prolapse or quadricuspid aortic valve. Diseases of the aorta that lead to dilatation or inflammation of the aorta may also result in aortic regurgitation. Acute severe aortic regurgitation, which may occur as a result of aortic valve endocarditis or aortic dissection or blunt trauma,

needs to be treated promptly with aortic valve surgery. On the other hand, chronic severe aortic valve regurgitation is usually well tolerated and the patient may remain asymptomatic for a long time. Surgery is recommended for patients with symptoms attributable to severe aortic regurgitation whether or not there is left ventricular systolic dysfunction. In asymptomatic patients, surgery is recommended when there are signs of left ventricular systolic dysfunction defined as left ventricular ejection fraction ≤50% or when there is severe left ventricular dilatation (left ventricular end-diastolic diameter >75mm or end-systolic diameter >55mm)[7] Several qualitative and quantitative measurements are used to grade severity of aortic regurgitation (Table 5). The reader is referred to the American Society of Echocardiography's Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography[42] for complete details of the criteria including their utility, advantages, and limitations.

Stress echocardiography in aortic regurgitation

Aortic valve replacement is not indicated in patients with severe aortic regurgitation who are asymptomatic and who have normal left ventricular systolic function and no evidence of severe left ventricular dilatation. These patients can however develop latent left ventricular systolic dysfunction even in the absence of decreased systolic function at rest or significant ventricular dilatation. The response of left ventricular ejection fraction to exercise or dobutamine has been shown to be an important determinant of later development of overt left ventricular systolic dysfunction and a predictor of left ventricular functional recovery following aortic valve surgery.[110-112] Therefore, stress echocardiography can be a useful adjunct in the serial evaluation of patients with asymptomatic severe aortic regurgitation. Wahi et al showed that contractile reserve on exercise echocardiography was a better predictor of subsequent left ventricular decompensation in patients treated medically and correlated better with resting left ventricular ejection fraction following aortic valve surgery.[110] Impaired left ventricular contractile reserve assessed by low dose dobutamine echocardiography has also been shown to be a marker of irreversible left ventricular systolic dysfunction in patients undergoing aortic valve replacement for minimally symptomatic chronic severe aortic regurgitation.[111]

TABLE 5: Qualitative and quantitative parameters useful in grading aortic regurgitation severity (with permission from the American Society of Echocardiography)[42]

	Mild	Moderate	Severe
Structural parameters			
LV size	Normal	Normal or dilated	Usually dilated
Aortic leaflets	Normal or abnormal	Normal or abnormal	Abnormal/prolapse or wide coaptation defect
Doppler parameters			
Jet width in LVOT-Colour Flow	Small in central jets	Intermediate	Large in central jets. Variable in eccentric jets
Jet density-CW	Incomplete of faint	Dense	Dense
Jet pressure half-time, ms	Slow >500	500-200	<200
Diastolic flow reversal in descending aorta	Brief, early diastolic reversal	Intermediate	Prominent holodiastolic reversal
Quantitative parameters			
VC width (cm)	<0.3	0.3-0.60	≥0.6
Jet width/LVOT width (%)	<25	25-64	≥65
Jet CSA/LVOT CSA (%)	<5	5-59	≥60
R Vol (ml/beat)	<30	30-59	≥60
RF (%)	<30	30-49	≥50
ERO (cm2)	<0.10	0.10-0.30	≥0.30

AR = aortic regurgitation. CSA = cross sectional area. CW = continuous wave doppler. EROA = effective regurgitant orifice area. LV = left ventricle. LVOT = left ventricular outflow tract. PHT = pressure half-time. PW = pulsed wave doppler. R Vol = regurgitant volume. RF = regurgitant fraction. VC = vena contracta.

CONCLUSION

Stress echocardiography can be a very useful, integral part of the evaluation of patients with valvular heart disease. Its main applications are to evaluate the hemodynamic response to stress to help link exertional symptoms to underlying valve disease in patients who appear to have mild to moderate disease at rest, or, in the case of an "asymptomatic" patient with severe valve disease, to determine if limiting symptoms are indeed present. Stress echocardiography can unmask latent left ventricular systolic dysfunction in seemingly normal left ventricles at rest, determine whether there is contractile reserve in those with reduced left ventricular systolic function, and determine the presence and extent of viable hibernating myocardium in patients with depressed left ventricular systolic function, particularly in patients with ischaemic mitral regurgitation. An abnormal left ventricular response to exercise is an important predictor of subsequent systolic dysfunction and left ventricular recovery following valve surgery.

There are however, several stress modalities and protocols in the literature pertaining to the utility of stress testing and stress echocardiography in patients with valvular heart disease. Additionally, patients studied are not uniform, and there have not been any randomised studies. As a result, Class I indications for stress testing in patients with valvular heart disease are few, limited mainly to mitral stenosis when there is discrepancy between resting echocardiographic findings and clinical findings[7] or asymptomatic patients with severe aortic stenosis.[8] Emerging data supports the integration of stress testing and stress echocardiography into decision making for optimal management of patients with valvular heart diseases.

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