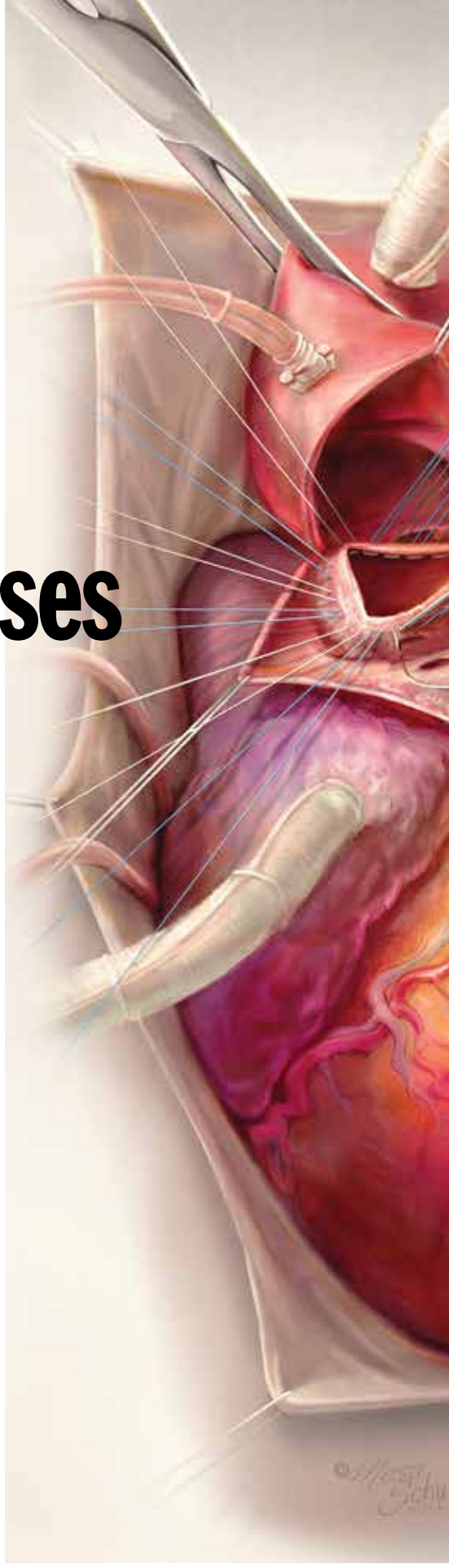
Diagnosing and managing common adult valvular heart diseases



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Generally, patients with valvular heart disease can be monitored clinically and with cardiac imaging until symptoms or ventricular enlargement or dysfunction appear. Optimal timing of valve surgery or intervention remains a crucial determinant of patient outcome.

Degenerative valve disease is the most common form of valvular heart disease (VHD) in developed countries, whereas rheumatic heart disease (RHD) occurs more often in developing nations. In Australia, acute rheumatic fever and the valvular heart disease resulting from it (RHD) continue to occur at very high rates in the Aboriginal and Torres Strait Islander community, predominantly affecting children and young adults.[1] It is therefore imperative for Australian general practitioners to have an understanding of the management of a wide array of valvular conditions. The diagnosis and management of the four most common adult valvular diseases – stenosis and regurgitation of the aortic valve and of the mitral valve – are summarised in this review.

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Aortic stenosis

Aetiology and pathophysiology

Aortic stenosis (AS) is the most common form of cardiovascular disease after hypertension and coronary artery disease.[2] It is usually caused by degenerative calcification of a trileaflet aortic valve or a congenitally abnormal bicuspid aortic valve leading to progressive stenosis of the valve – valvular AS. Less commonly, obstruction of left ventricle (LV) outflow can also occur below (subvalvular) or above (supravalvular) the valve.

In valvular AS, there is an extended latent period during which the patient remains asymptomatic. As the severity of stenosis progresses, the LV adapts by increasing wall thickness to maintain chamber size (concentric hypertrophy) and cardiac output. Over time, the classic symptoms of angina, exertional dyspnoea and syncope develop because the LV compensatory mechanism cannot be maintained indefinitely, with

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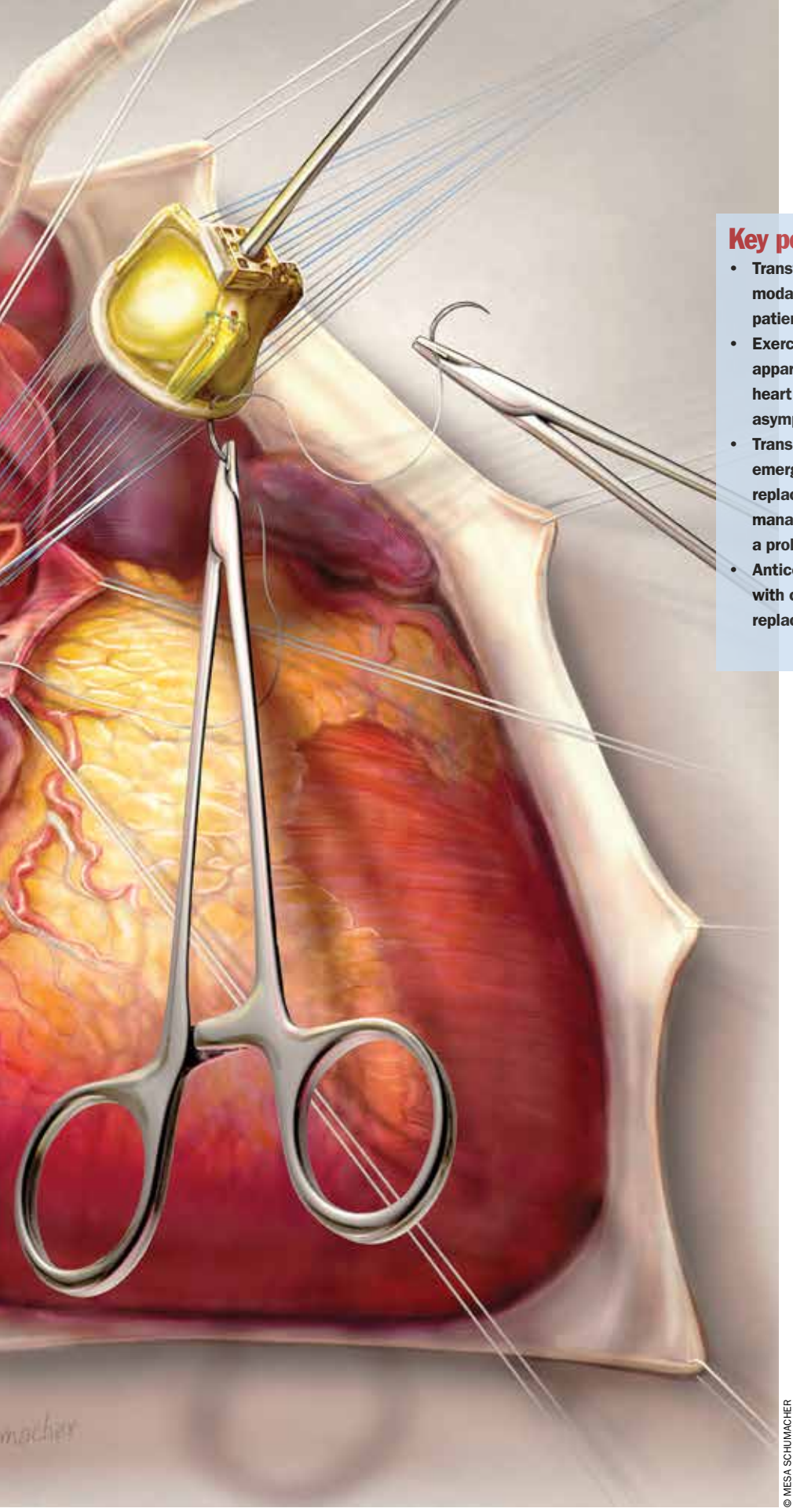

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Key points

- **Transthoracic echocardiography is the imaging modality of choice for diagnosis and follow up of patients with valvular heart diseases.**
- **Exercise testing has a role in evaluating apparently asymptomatic patients with valvular heart disease to identify whether they are truly asymptomatic.**
- **Transcatheter aortic valve implantation has emerged as an alternative treatment to valve replacement by open heart surgery for the management of aortic stenosis in patients with a prohibitive surgical risk.**
- **Anticoagulation for atrial fibrillation in those with concomitant valve disease (including valve replacement) is currently limited to warfarin.**

ensuing diastolic and ultimately systolic dysfunction. Physical examination findings are specific but not sensitive for evaluation of stenosis severity (Table 1).[3]

The survival of patients with severe AS is nearly normal until the onset of symptoms, from which point the average survival without surgical intervention is only two to three years because of increased heart failure-related death and sudden cardiac death.[4-7] Some patients with severe AS remain asymptomatic and prognosis is hard to predict; these patients, however, have a high likelihood of developing symptoms over the course of three to five years because of the progressive nature of the disease.[8]

Diagnosis

Echocardiography

Transthoracic echocardiography (TTE) is the imaging modality of choice to diagnose AS (Figures 1a and b). It provides an accurate assessment of the aortic valve area and the transvalvular gradient, measurements used in the estimation of the severity of AS.[9] The normal aortic valve area is 2.5 cm^2. A valve area of less than 1.0 cm^2 or a mean gradient of more than 40 mmHg represents severe stenosis capable of causing symptoms or, rarely, sudden cardiac death (Table 2).[10] Echocardiography is also used to diagnose left ventricular hypertrophy and estimate the left ventricular ejection fraction (LVEF).

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Table 1. Key physical examination findings in valvular heart disease

Valvular condition	Heart sounds		Murmur	Signs of severity
	S1	S2		
Aortic stenosis	Normal	Soft or single	Ejection systolic murmur radiating to the neck	Late-peaking murmur, diminished/ delayed carotid upstroke amplitude
Mitral stenosis	Loud	Loud	Opening snap followed by a diastolic rumble Presystolic accentuation in sinus rhythm	Signs of pulmonary hypertension: loud P2, right ventricular heave, right heart failure
Aortic regurgitation	Soft (acute AR)	Soft	Diastolic murmur ± systolic flow murmur	Longer murmur, wide pulse pressure, bounding peripheral pulses
Mitral regurgitation	Soft	Normal	Apical pansystolic murmur	S3, signs of pulmonary hypertension
Mitral valve prolapse	Loud	Normal	Mid-systolic click followed by murmur	S3, signs of pulmonary hypertension

Abbreviations: AR = aortic regurgitation; MVP = mitral valve prolapse.

Cardiac catheterisation

Given the accuracy of echocardiography in the assessment of AS, cardiac catheterisation is generally only performed to identify coronary artery disease rather than to confirm haemodynamic findings. However, invasive haemodynamic measurements of catheter-derived valve area and transvalvular gradient can be performed if noninvasive tests are inconclusive or provide discrepant results regarding AS severity. Coronary angiography is recommended before surgical aortic valve replacement (AVR) in men aged over 40 years, postmenopausal women and individuals at risk of coronary artery disease.

Exercise stress testing

Exercise testing has a role in evaluating apparently asymptomatic patients with severe AS to identify whether they are truly asymptomatic.[11] Many patients do not recognise the gradual development of symptoms and cannot distinguish dyspnoea from ageing and physical deconditioning.[2] Such testing should only take place under the careful supervision of an experienced physician.

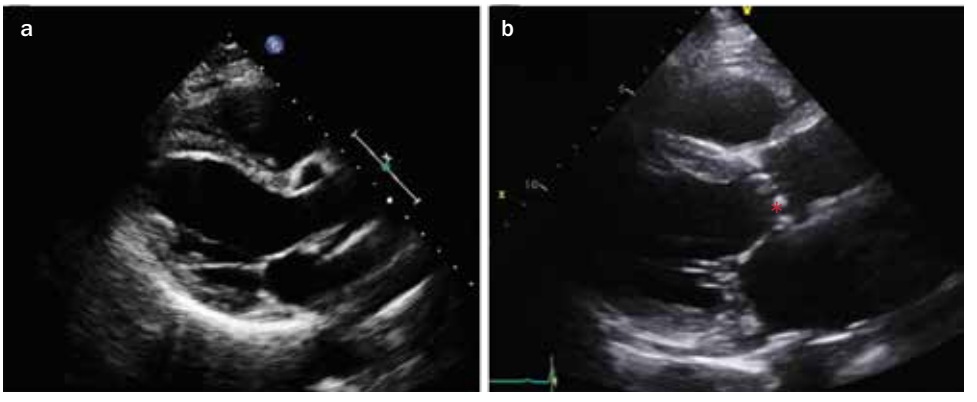
Cardiac magnetic resonance

Cardiac magnetic resonance imaging (CMR) can be used to measure anatomical valve area and transvalvular velocity. However, the role of this modality is currently not well defined.

Treatment

Patients with AS who are asymptomatic should be followed clinically, with careful attention paid to any change in symptoms. There are currently no satisfactory medical treatments to halt the progression of aortic stenosis. Replacement of the aortic valve is the only effective, long-term treatment to relieve this mechanical obstruction. The decision to perform AVR is based on the presence of severe aortic stenosis with either symptoms or evidence of left ventricular – systolic dysfunction (LVEF below 50%).[9]

In carefully selected patients, the prognosis following AVR is excellent, even in the elderly population. However, as AS predominantly affects the elderly, many patients have medical comorbidities that make them poor candidates for surgical AVR. In the past decade, transcatheter aortic valve implantation (TAVI; also known as percutaneous aortic valve implantation) has emerged as an alternative treatment for the management of patients with a high or prohibitive surgical risk (Figures 2a to d). This is commonly performed through the transfemoral approach; other access options include transapical,



Figures 1a and b. Normal aortic valve and aortic stenosis transthoracic echocardiogram (parasternal long axis view).
a (left). Normal aortic valve with normal leaflet mobility.
b (right). Aortic stenosis, showing calcified and thickened aortic valve leaflets with severely restricted systolic opening (red asterisk).

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transaortic and transsubclavian approaches. Trials have demonstrated improvements in survival after TAVI compared with medical therapy, and similar survival compared with surgical AVR for high-risk patients with AS.[12,13] The evaluation of the potential candidate for TAVI is a complex process based on clinical and anatomical criteria. A meticulous clinical assessment must be performed and cases discussed by a multidisciplinary heart valve team, including a geriatrician, to appropriately select the patients who are most likely to benefit.

Percutaneous balloon valvuloplasty of the aortic valve may be a reasonable option as a bridge to AVR in the near future in patients with AS who are highly symptomatic or as a palliative procedure in those who are not AVR candidates. Because of its high rate of restenosis, it is not the procedure of choice in patients who are good AVR candidates.[14]

Mitral stenosis

Aetiology and pathophysiology

Rheumatic fever is the leading cause of mitral stenosis (MS) worldwide. This multisystem inflammatory disease, a complication of a group A streptococcus infection of the throat that usually has onset in childhood, primarily affects women, leading to valvular fibrosis, calcification and commissural fusion leading to mitral stenosis. Other causes of MS are relatively rare and include congenital abnormalities, severe mitral annular calcification and atrial myxoma.

Table 2. Echocardiographic criteria for the definition of severe valve stenosis*

Measurement	Aortic stenosis	Mitral stenosis
Valve area (cm^2)	<1.0	<1.0
Indexed valve area (cm^2/m^2)	<0.6	–
Mean gradient (mmHg)	>40†	>10‡
Maximum jet velocity (m/s)	>4.0†	–
Velocity ratio	<0.25	–
Pulmonary artery systolic pressure (mmHg)	–	>50

* Adapted from Baumgartner et al. (reference 10).
† In patients with normal cardiac output.
‡ Useful in patients with sinus rhythm, to be interpreted according to heart rate.

A normal mitral valve area is 4.0 to 6.0 cm^2. Symptoms develop when the valve area decreases below 1.5 cm^2, due to increased left atrial pressure and decreased cardiac output.[3] Increased left atrial pressure eventually causes pulmonary arterial intimal hyperplasia and medial hypertrophy, often resulting in pulmonary hypertension and right ventricular (RV) dysfunction.

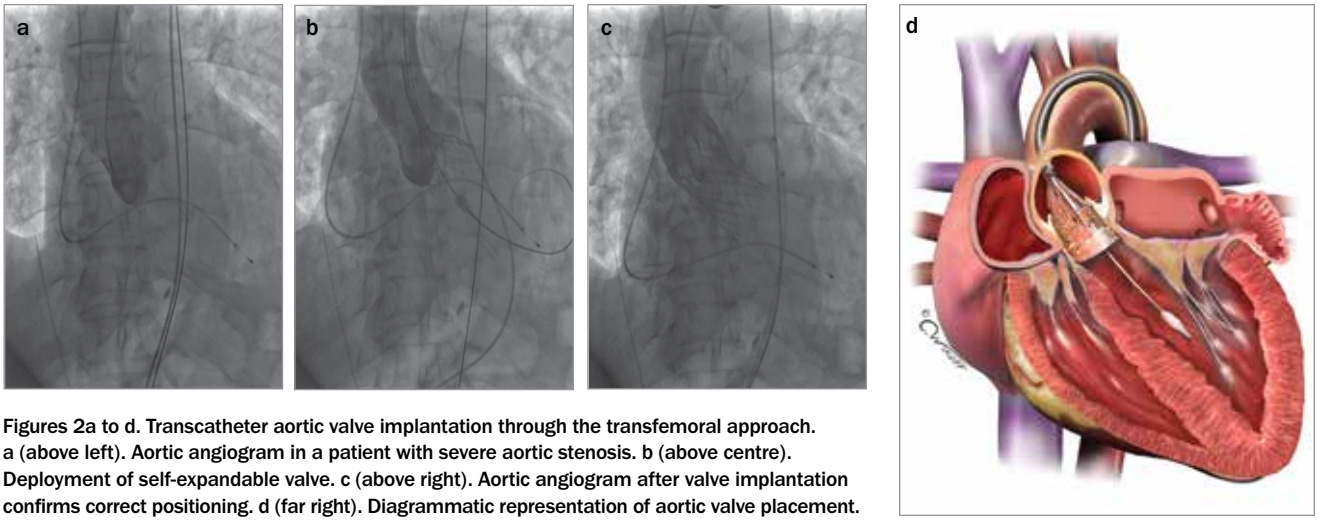
Patients develop symptoms if the time of diastolic filling decreases and/or transmitral flow increases, as is the case with exercise, atrial fibrillation, pregnancy or infection. Symptoms are generally those of left-sided heart failure, including dyspnoea, orthopnoea and paroxysmal nocturnal dyspnoea, but patients can also develop signs of right-sided failure such as peripheral oedema (Table 1).

Diagnosis

Echocardiography

Echocardiography is the modality of choice to assess the severity and consequences of MS (Table 2).[10] TTE provides sufficient information for routine follow up, including valve morphology, area, mean gradient, left atrial size and ventricular function (Figure 3). Transoesophageal echocardiography (TOE) with 3D imaging is used to determine suitability for percutaneous balloon mitral valvuloplasty (PBMV).

Stress echocardiography can be used to obtain valuable valvular and pulmonary haemodynamic data during exercise. Stress testing is also useful for assessment of functional capacity, especially if it is difficult to determine on clinical history.



Figures 2a to d. Transcatheter aortic valve implantation through the transfemoral approach. a (above left). Aortic angiogram in a patient with severe aortic stenosis. b (above centre). Deployment of self-expandable valve. c (above right). Aortic angiogram after valve implantation confirms correct positioning. d (far right). Diagrammatic representation of aortic valve placement.

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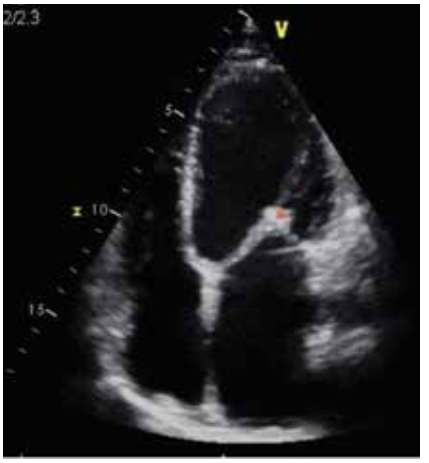

Figure 3. Mitral stenosis. Transthoracic echocardiogram (four chamber view) demonstrating a rheumatic mitral valve with severe stenosis (red asterisk).

Cardiac catheterisation

Cardiac catheterisation with right heart haemodynamics is not now considered essential in the routine follow up of patients with mitral stenosis. It can, however, provide valuable data if there is a discrepancy between clinical and echocardiographic findings.[3]

Treatment

Indigenous Australians who have RHD should receive antibiotic prophylaxis prior to invasive procedures to prevent infective endocarditis.[15] Non-Indigenous Australians who have RHD and are at significant socioeconomic disadvantage are at higher risk of infective endocarditis and should also be considered for antibiotic prophylaxis.

Anticoagulation therapy is indicated in all patients with atrial fibrillation, previous systemic embolism or documented left atrial thrombus.[3] It is important to note that for patients with atrial fibrillation and significant valvular disease, particularly rheumatic mitral valve disease, conventional stroke risk stratification scores such as the CHA_2DS_2-VASc risk score do not apply. Additionally, anticoagulation for atrial fibrillation in those with concomitant valve disease including valve replacement is limited to warfarin as current data do not support the use of novel anticoagulants in these patients.[16]

In asymptomatic patients with mild to moderate MS, annual clinical and regular echocardiographic examinations are recommended, with no need for specific medical therapy. Diuretics may be helpful in reducing left atrial pressure and relieving symptoms in those with mild symptoms. Beta blockers or rate-lowering calcium channel blockers can improve exercise tolerance.[9]

Symptomatic patients with severe MS or those with pulmonary hypertension (more than 50 mmHg at rest) should be considered for PBMV. Unlike valvuloplasty for aortic stenosis, PBMV provides excellent mechanical relief with long-term benefit, obviating the need for cardiac surgery. Patients with significant mitral regurgitation (MR) or severely thickened and calcified mitral valve leaflets and/or subvalvular apparatus are not optimal candidates for this procedure and require surgical mitral valve replacement.[3,9]

Aortic regurgitation

Aetiology and pathophysiology

Aortic regurgitation (AR) results from disease affecting the aortic leaflets, their supporting structures in the aortic root or both, preventing normal closure. Common aetiologies include RHD, dilatation of the aortic root, congenital leaflet abnormalities, age-related degeneration, endocarditis, connective tissue disease or collagen vascular disease. Congenitally abnormal bicuspid valve is often associated with thoracic aortic dilatation.

There is both LV preload and afterload excess in chronic AR. The stroke volume is increased into the high-impedance aorta, which leads to systolic hypertension, high pulse pressure and increase in afterload.[2] The excess preload leads to increased LV end-diastolic volume, which in turn increases LV wall stress and further increases LV afterload. Compensatory eccentric hypertrophy and chamber dilatation preserves LV systolic function for many years, allowing patients to remain asymptomatic.[3,17]

With progression of disease, LV systolic dysfunction ensues as compensatory mechanisms are exhausted and patients present with symptoms of left-sided failure such as dyspnoea and orthopnoea. Systolic dysfunction is reversible in the early stages of AR and can improve after normalisation of loading conditions by AVR. With time however, progressive chamber enlargement leads to irreversible LV dysfunction, highlighting the need for careful follow up of these patients.

Diagnosis

Echocardiography

Echocardiography provides key information about aortic valve morphology, aortic size, ventricular size and function and severity of regurgitation. TOE may be performed to more precisely define the aortic valve anatomy in those with a suboptimal TTE study or in patients being considered for aortic valve repair. Myocardial strain imaging, a relatively novel echocardiographic technique measuring longitudinal function, may have a role in the future to detect early signs of LV decompensation.[18]

Cardiac computed tomography/ magnetic resonance imaging

Cardiac CT or CMR scanning provides excellent visualisation of the aorta and is recommended for its evaluation if abnormalities are suspected on the basis of echocardiography.[19] CMR can also provide accurate assessment of LV volume and LVEF in addition to estimating regurgitant volumes.

Cardiac catheterisation

Cardiac catheterisation is not necessary in the routine assessment of patients with aortic regurgitation. It is performed if noninvasive imaging is inadequate and is often performed to assess coronary anatomy prior to AVR.

Treatment

In asymptomatic patients with chronic severe AR, the likelihood of adverse events is low. However, when LV end-systolic diameter (LVESD) exceeds 50 mm, the risk of developing symptoms of LV dysfunction or death is approximately 19% per year.[20,21] No satisfactory medical therapy exists to attenuate progression of aortic regurgitation.[22] Therefore, the use of vasodilator and β-blocking agents should be restricted to patients with concurrent hypertension.

Asymptomatic patients with severe AR and normal LV size and function should have clinical and echocardiographic

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examinations every 12 months. Patients should be considered for AVR when symptoms develop, LV dilatation is severe (LVESD more than 50 mm) or LV systolic dysfunction develops (LVEF below 50%).[9]

Patients should also be referred for surgery regardless of AR severity if maximal ascending aortic diameter is 55 mm or greater (or 50 mm or greater with bicuspid aortic valve and risk factor; 50 mm or greater with Marfan syndrome and no risk factors; or 45 mm or greater with Marfan syndrome and risk factors).[9] Risk factors in patients with bicuspid aortic valve include family history of dissection, systemic hypertension, coarctation of the aorta or increase in aortic diameter of more than 2 mm each year in repeated examinations, using the same technique and confirmed by another technique. Risk factors in patients with Marfan syndrome include family history of acute cardiovascular events (aortic dissection, sudden death), severe AR, desire to become pregnant and size increase exceeding 2 mm per year as mentioned above.

Mitral regurgitation

Aetiology and pathophysiology

Mitral regurgitation (MR) is caused by abnormalities of the mitral valve leaflets, the structures forming the subvalvular apparatus, or both. Common aetiologies of primary MR include mitral valve prolapse (MVP) from degenerative valvular disease (myxomatous disease and fibroelastic disease), RHD and infective endocarditis. In secondary MR (also termed 'functional' MR), the valve leaflets and chordae are structurally normal with regurgitation caused by LV remodelling due to cardiomyopathy or ischaemic heart disease. Left ventricular remodelling leads to restriction of leaflet closure from apical tethering due to displaced papillary muscles, mitral annular dilatation, and reduced closing force of the leaflets.[23] Less common causes of MR include mitral annular calcification, congenital abnormalities, appetite suppressing drugs and radiation therapy.

Chronic MR leads to volume overloading of the LV, leading to progressive dilatation and eccentric hypertrophy. The left atrium also enlarges to accommodate the increasing regurgitant volume, predisposing to atrial fibrillation. The compensated phase of mitral regurgitation may last many years before the prolonged state of overload eventually leads to decompensation and left heart failure. The LVEF in patients with MR is initially supranormal because of the increase in preload and the afterload-reducing effect of emptying into the low-impedance left atrium. Therefore, the LVEF can be a misleading measure of LV contractility. This needs to be taken into account when considering optimal timing of mitral valve surgery.

Diagnosis

Echocardiography

Transthoracic echocardiography is the principal investigation in patients with MR and provides information on MR severity, mechanism, repairability, chamber size and function.[3,9] Echocardiographic findings have been shown to be important predictors of outcomes.[24]

TOE with 3D imaging is often performed

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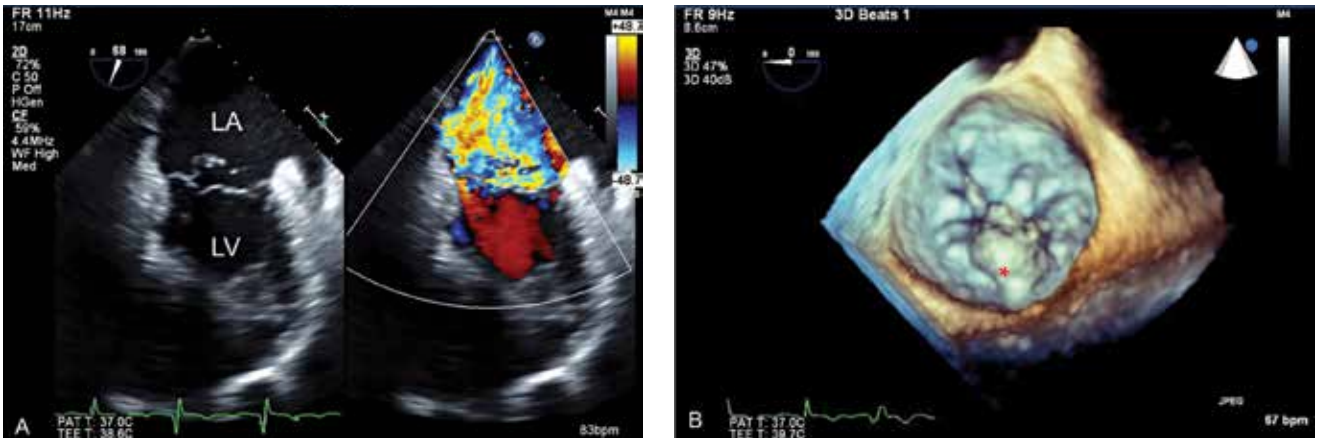

Figures 4a and b. Mitral regurgitation. Transoesophageal echocardiogram. a (left). Mitral valve prolapse with flail and severe mitral regurgitation. b (right). Three-dimension echocardiography demonstrating prolapse and flail P2 scallop of the posterior mitral valve leaflet (asterisk). LA = left atrium, LV = left ventricle.

when planning for surgery (Figures 4a and b). Preoperative assessment of valve repairability requires experience and should be performed in a high-volume centre.[25]

Exercise testing

Stress testing can be useful for assessment of functional capacity in patients with MR, especially if it is difficult to clarify symptoms on clinical history.

Cardiac magnetic resonance

Cardiac magnetic resonance imaging can be used to accurately quantify regurgitant volume and LV function, and to predict postsurgical LV remodelling.[26] The role of this modality is currently not well defined and hence routine use of CMR is not recommended.

Cardiac catheterisation

Cardiac catheterisation is not necessary in the routine assessment of patients with MR.[3] It is, however, performed to assess valvular haemodynamics if noninvasive imaging is inadequate, and often to assess coronary anatomy prior to mitral valve surgery.

Treatment

Asymptomatic patients

Patients with severe chronic MR can be asymptomatic for years. Because LV dysfunction can develop in the absence of symptoms, six- to 12-monthly clinical and echocardiographic follow up is needed.

Surgery is indicated in these patients if the LVEF is 60% or lower or LVESD is 45 mm or greater. Surgery should also be considered in asymptomatic patients with atrial fibrillation or pulmonary hypertension (systolic pulmonary artery pressure above 50 mmHg).[9] Repair rather than replacement should be performed wherever possible. This removes the need for anticoagulant therapy in patients in sinus rhythm and avoids possible failure of the prosthetic valve.

Symptomatic patients

Surgery is indicated in patients with MR before the development of irreversible myocardial dysfunction, which is suggested by LVEF below 30% or LVESD greater than 55 mm.[9]

Patients with mitral valve prolapse

No accepted medical therapy has been shown to delay the need for surgical intervention in asymptomatic patients with severe MR due to MVP and preserved LV function. Routine antibiotic prophylaxis prior to invasive procedures is no longer recommended.[15] Surgery in an experienced centre should be considered even in asymptomatic patients if there is a high likelihood of successful repair and low perioperative risk.[9] Catheter-based interventions have been developed to correct MR percutaneously with some success; however, more experience and longer-term follow up is required.

Antibiotic prophylaxis for infective endocarditis

Prophylaxis for infective endocarditis prior to certain invasive procedures is now only recommended in certain groups of patients.[15] These include patients with a history of valve replacement/repair with prosthetic material or unrepaired/incompletely repaired cyanotic congenital heart disease, those with recently repaired congenital heart disease, those who have undergone cardiac transplantation with valvulopathy and those with rheumatic heart disease and who are at high risk for infective endocarditis (as discussed earlier under the treatment of mitral stenosis).

Summary

A spectrum of valvular heart conditions is seen in Australia, these being caused predominantly by degenerative valvular conditions or rheumatic heart disease. Echocardiography is the diagnostic modality of choice, not only to determine valvular haemodynamics but also to assess compensatory mechanisms of the cardiac chambers. Management of these patients has improved with the advent of novel imaging and procedural techniques. Optimal timing of intervention or surgery remains a crucial determinant of patient outcome. **CT**

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References

A list of references is included in the website version of this article (www.cardiologytoday.com.au).

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