POSITION PAPER

South African Heart Association Position Statement for the management of valvular heart disease – Part I

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ABSTRACT

The burden of valvular heart disease (VHD) remains high in South Africa and is associated with considerable morbidity and mortality. While a decline in acute rheumatic fever cases has been observed, chronic rheumatic VHD remains an important cause of index heart failure admission in South Africa. Additionally, with the increased longevity of the African population, degenerative VHD has emerged as an important aetiology. To date, data about VHD epidemiology, diagnosis, management, and patient follow-up remain scarce in this region. Patients with VHD and their physicians face unique challenges in the South African setting. Hence, in this Position Statement, we aim to provide the general cardiologist with a comprehensive review to complement existing guidelines on VHD for adequate patient management in the local setting. This document will comprise 2 parts. Part I focuses on the evaluation and management of native VHD. Part II will focus on prosthetic heart valves, infective endocarditis (IE), preoperative assessment of patients with VHD, VHD considerations in children, and future directions.

Keywords: valvular heart disease, management, South Africa.
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ABBREVIATIONS/ACRONYMS

AF: atrial fibrillation
AR: aortic regurgitation
AS: aortic stenosis
AVR: aortic valve replacement
CABG: coronary artery bypass grafting
CAD: coronary artery disease
CHA_2DS_2-VASc score: congestive heart failure, hypertension, age (≥ 75, 2 points), diabetes, stroke or transient ischaemic attack (2 points), vascular disease, age (65–74), and sex category
CMR: cardiac magnetic resonance
CT: computed tomography
ESC: European Society of Cardiology
EuroSCORE II: European System for Cardiac Operative Risk Evaluation II
HIV: human immunodeficiency virus
IE: infective endocarditis
INVICTUS: investigation of rheumatic atrial fibrillation treatment using vitamin K antagonists, rivaroxaban or aspirin studies
LFLG: low-flow, low-gradient
LMIC: low- to middle-income country
LOE: level of evidence
LV: left ventricular
LVEF: left ventricular ejection fraction
LVESD: left ventricular end-systolic diameter
MRAs: mineralocorticoid receptor antagonists
MR: mitral regurgitation
MS: mitral stenosis
NT-proBNP: N-terminal pro–B-type natriuretic peptide
OMT: optimal medical therapy
REMEDY: Global Rheumatic Heart Disease Registry
RHD: rheumatic heart disease
SAVR: surgical aortic valve replacement
SMR: secondary mitral regurgitation
SPAP: systolic pulmonary artery pressure

STS: The Society of Thoracic Surgeons
TAVI: transcatheter aortic valve implantation
TOE: transoesophageal echocardiography
TR: tricuspid regurgitation
TS: tricuspid stenosis
VHD: valvular heart disease
VKA: vitamin K antagonist

INTRODUCTION

VHD is a major global cause of morbidity and mortality, with varying epidemiology based on location.[1-3] Degenerative and functional valve disease predominates in high-income countries, while rheumatic heart disease (RHD) remains the leading aetiology of VHD in low- to middle-income countries (LMIC), affecting about 41 million people worldwide and contributing significantly to heart failure in endemic areas.[4,5] RHD is strongly associated with poverty and exposure to Group A *Streptococcus*.[6,7] In South Africa, heart failure incidence due to RHD increases with age, reaching over 53 per 100 000 per year in older adults, with a cumulative incidence of 23 per 100 000 per year.[8] Data from the Global Rheumatic Heart Disease Registry (REMEDY) and other studies show high mortality (16.9% at 2 years) and reveal that patients in resource-limited settings often present young with advanced disease and related complications.[9,10]

Given the high burden of RHD in sub-Saharan Africa, the potential rise in degenerative VHD due to increased life expectancy, and the rapid evolution of transcatheter techniques, medical management, and multimodality imaging in VHD, we deemed it necessary to formulate a location-specific Position Statement.[9-11] In Africa, human resources, expertise, and equipment limitations may not allow for dedicated heart valve centres and heart teams at all facilities. However, numerous referral centres offer specialist cardiologists and surgeons, and we urge clinicians involved in the care of patients with VHD to have a low threshold for consultation or referral.

It is of utmost importance to accurately diagnose, quantify, assess the mechanism of, and identify complications in a VHD patient.[12] A baseline physical examination, 12-lead electro-cardiogram, chest X-ray, and cardiac imaging with a transthoracic echocardiogram, supplemented by transoeso-phageal echocardiography (TOE) if necessary, form the cornerstone of diagnosis.[14] Coronary artery imaging via computed tomography (CT) coronary angiography or invasive coronary angiography is recommended for coronary artery disease (CAD) assessment in men aged > 40 years, postmenopausal women, those with a history of cardiovascular disease, myocardial ischaemia, left ventricular (LV) systolic dysfunction, and ≥ 1 cardiovascular risk factors before valve surgery or a valve intervention (Class I, level of evidence [LOE] C). In low-risk cases, cardiac CT angiography has good negative predictive value for excluding CAD (Class IIa, LOE C).[12]

In the local context, resource and expertise limitations may preclude multimodality imaging assessment.[9] We advocate for diagnostic investigation, in which a centre has expertise for VHD assessment. The value of routine coronary angiography in the absence of cardiovascular risk factors before VHD intervention was investigated by Meel, et al. in a South African study.[13] They noted a low CAD prevalence (8.6%) in patients with VHD at Chris Hani Baragwanath Academic Hospital. The study's conclusion suggested individualising the decision to perform screening coronary angiography, considering age, symptoms, and cardiovascular risk factors for black patients scheduled to undergo valve replacement surgery in developing countries.

When managing a patient with VHD, their preferences must be considered.[12] The patients and their families must be extensively informed and guided in making the best decision and choosing the appropriate treatment option, considering the patient's life expectancy and expected quality of life. Comorbidities in the elderly should be considered, and therapeutic futility should be avoided, especially in a resource-limited setting such as South Africa. Appropriate patient risk stratification before surgery or intervention is required, using standard risk scores, such as The Society of Thoracic Surgeons (STS) predicted risk of mortality and the European System for Cardiac Operative Risk Evaluation II (EuroSCORE II). In the South African setting, with possible delays in definitive surgery, as shown in a recent study by Banderker, et al., patients with VHD and heart failure must be managed with optimal medical therapy (OMT) as a bridge to surgery.[14] Furthermore, patients who do not qualify for or decline surgery must be placed on optimal anti-failure pharmacotherapy.

IE prevention is crucial in high-risk patients, including those with prosthetic valves or material, previous IE, congenital heart disease, and ventricular assist devices, in which antibiotic prophylaxis is recommended.[12,15] Per the European Society of Cardiology (ESC) guidelines, antibiotic prophylaxis is not routinely indicated for intermediate risk groups, such as patients with RHD, degenerative valve disease, congenital valve abnormalities, cardiac devices, or hypertrophic cardiomyopathy. However, it may be considered on an individual basis. Strict oral hygiene is essential for both high- and intermediate-risk groups, especially in South Africa, where oral health among RHD patients is often poor, necessitating dental care education.[16] The South African Heart Association identifies RHD patients as high-risk and advises routine antibiotic prophylaxis for dental procedures involving gingival or mucosal manipulation. Additionally, increasing intravenous drug use increases IE risk in this population, requiring targeted prevention strategies.[17,18]

In patients with VHD and concomitant atrial fibrillation (AF), direct oral anticoagulants are preferred over vitamin K antagonists (VKA) for those with aortic regurgitation (AR), aortic stenosis (AS), or mitral regurgitation (MR).[12] However, they are not recommended for prosthetic valves or rheumatic moderate-to-severe mitral stenosis (MS).[12] The investigation of rheumatic AF treatment using VKAs, rivaroxaban or aspirin studies (INVICTUS) trial showed that VKAs were superior to rivaroxaban in reducing cardiovascular events and death in RHD without increasing the bleeding risk.[19] AF ablation should be considered during valve surgery, while evidence for routine left atrial appendage exclusion remains inconclusive.[20] Though large prospective trials are lacking, left atrial appendage resection is advised for patients with a CHA_2DS_2-VASc score ≥ 2 undergoing valve surgery, per ESC guidelines.[12]

For established, chronic RHD, long-term secondary prophylaxis against rheumatic fever with intramuscular benzathine benzylpenicillin every 3–4 weeks for 10 years is recommended.[12] Lifelong prophylaxis should be considered in high-risk patients, based on the severity of their valve disease and streptococcal exposure. Primary prevention during acute rheumatic fever focuses on treating Group A *Streptococcus* infection, while echocardiographic screening and secondary prophylaxis in subclinical RHD are under investigation to reduce the prevalence in endemic regions. However, studies such as REMEDY and a recent South African single-centre study highlight the low uptake of secondary prophylaxis, possibly due to older patient populations, a reported decline in acute rheumatic fever incidence, underdiagnosis of latent carditis in chronic RHD, and supply issues in the public sector.[9,14,21]

Sliwa, et al. reported a high prevalence of comorbidities, including renal dysfunction, AF, and anaemia in patients with RHD.[8] Banderker, et al. and Meel, et al. found a high prevalence of comorbidities in patients with rheumatic mitral valve disease.[14,22] Arterial hypertension and human immunodeficiency virus (HIV) infection were the most common concomitant diseases in these studies. Patients with dual HIV and RHD have threefold higher odds of suffering a stroke or transient ischaemic attack than those with isolated RHD.[23] Timely recognition and appropriate management of comorbidities are essential in these patients.

AORTIC REGURGITATION (AR)

Aetiology

AR can be caused by primary aortic valve disease or pathology of the ascending aorta (idiopathic root dilatation, Marfan syndrome, aortic dissection, collagen vascular disease, or syphilis). The most common cause in high-income countries is calcific aortic valve disease.[24]

Assessment

Clinically, AR may be difficult to ascertain or grade. Signs suggestive of severe AR include a longer diastolic murmur with a rougher quality, pronounced peripheral signs (particularly Hill's and Duroziez's signs), an Austin Flint murmur, and signs of increased LV size/LV dysfunction, such as a displaced apex beat or a third heart sound.[25] Patients with suspected AR need to undergo echocardiography to assess its mechanism and severity, and evaluate the LV size and function. Echocardiographic features suggestive of severe AR are summarised in Table I.[26] A CT scan may be required to accurately assess the dimensions of the aortic root and the ascending aorta. If there is doubt, TOE and cardiac magnetic resonance (CMR) imaging are useful alternative modalities to assess the morphological features and AR severity.[12]

TABLE I: Features of severe aortic regurgitation.

Dilated left ventricle, LVEDD > 65 mm
Dense regurgitant jet on CW Doppler profile
Jet area ≥ 65% of LVOT
Vena contracta > 6 mm
Pressure half-time < 200–250 ms, CW max velocity > 3–3.5 m/s
Holodiastolic flow reversal with an end-diastolic velocity ≥ 20 cm/s in the descending aorta

CW: continuous wave, LVEDD: left ventricular end-diastolic diameter, LVOT: left ventricular outflow tract.

Management

Surgical aortic valve replacement (SAVR) is recommended for all symptomatic patients with severe AR. The ESC guidelines advise SAVR for all such patients, regardless of LV function.[12] Even patients with extreme LV enlargement and significant LV dysfunction experience symptomatic and survival benefits from aortic valve intervention.[27,28] SAVR carries a higher risk in this setting, but in the modern surgical era, peri-operative outcomes are acceptable.[29]

In asymptomatic patients with severe AR, surgery should be performed if the left ventricular end-systolic diameter (LVESD) is > 50 mm (indexed LVESD > 25 mm/m^2), the left ventricular ejection fraction (LVEF) is ≤ 50%, or if serial imaging indicates significant disease progression. Moreover, patients with incidental, significant AR who are undergoing cardiac surgery for another indication (e.g. coronary artery bypass grafting [CABG]) should undergo SAVR.[12]

SAVR is the preferred intervention method. Transcatheter aortic valve implantation (TAVI) is reserved for carefully selected patients and should be performed only in experienced centres. Although some evidence exists for the symptomatic benefit of renin–angiotensin–aldosterone system inhibitors and dihydropyridines, the role of pharmacotherapy remains adjunctive.[30] Beta blockers and other negatively chronotropic agents must be used with caution in patients with severe, chronic AR. Pharmacotherapy has no established role in delaying AR progression.

It is important to diagnose any significant pathology of the aortic root and ascending aorta. In the absence of traditional risk factors for aortopathy, syphilis should be ruled out as a cause. Dilatation of the aortic root or ascending aorta may need to be addressed at the time of surgery, and should be strongly considered if the aortic diameter measures ≥ 55 mm.[12]

The South African perspective

Any of the AR causes that are prevalent in the developed world could apply in the South African context. However, RHD remains an important cause of valve pathology, with an estimated incidence of 23.5 cases per 100 000 per year in our region.[8] While significant aortic valve disease due to RHD is generally associated with other valve pathology, it can occur in isolation.[31,32] Another important cause in LMICs is IE.

Although access to echocardiography may be limited, it remains essential for confirming the diagnosis and guiding management. Specifically in the context of AR, it is important to rule out functional or presystolic MR, as additional mitral valve replacement is usually not required in these cases.[32]

AORTIC STENOSIS (AS)

Aetiology

The most common cause of AS in developed countries is calcific aortic valve disease.[33-36]

Assessment

Clinical features suggestive of severe AS include a systolic murmur (grade 4/6 or greater), central *pulsus parvus et tardus* or a late-peaking murmur, a diminished or absent second heart sound, paradoxical splitting of S2, and a fourth heart sound.[25] Echocardiography supplemented by TOE is required to assess AS morphology and severity.[12] The main determinants of severe AS are summarised in Table II. In patients with diagnostic uncertainty regarding AS severity based on the parameters listed in Table II, LV systolic function, marked aortic valve calcification, and a Doppler velocity time index < 0.25 (LV outflow tract time integral/aortic valve time integral) may be of incremental value.

In the presence of an impaired LVEF, care should be taken not to miss the presence of low-flow, low-gradient (LFLG) AS.[12] It is characterised by a mean transvalvular gradient < 40 mmHg, a valve area ≤ 1 cm^2, a LVEF < 50%, and an indexed LV stroke volume ≤ 35 ml/m^2.[12] Dobutamine stress echocardiography is required for these patients to rule out pseudo-stenosis. A CT scan with a high aortic valve Agatston score (> 1 200 for females, > 2 000 for males) is further evidence that AS is severe in the setting of LFLG AS.

Further investigations that may help determine the need for surgery, particularly in asymptomatic patients with severe AS, include conventional exercise stress testing to confirm the absence of symptoms and identify blood pressure drop during exercise, a CT scan to assess the severity of aortic valve calcification, and serum N-terminal pro–B-type natriuretic peptide (NT-proBNP) levels.[12]

TABLE II: Features of severe aortic stenosis.

Mean transvalvular gradient ≥ 40 mmHg
Peak velocity ≥ 4 m/s
Valve area (according to the continuity equation) ≤ 1.0 cm^2, indexed < 0.6 cm^2/m^2
Time to peak velocity > 100 ms*

** Kamimura D, Hans S, Suzuki T, et al. Delayed time to peak velocity is useful for detecting severe aortic stenosis. J Am Heart Assoc. 2016;5(10):e003907. https://doi.org/10.1161/JAHA.116.003907.*

Management

The first step is to assess whether aortic valve intervention is required. If so, a decision must be made between TAVI and SAVR.[12] Symptomatic patients with severe AS (including LFLG AS) should generally undergo intervention.[12] The decision is more challenging in asymptomatic patients, where expectant management until symptom development before proceeding to intervention has been the traditional approach. Generally, asymptomatic patients with severe AS and a LVEF < 55% should undergo intervention, as should patients with another indication for cardiac surgery (e.g. CABG) who also happen to have significant AS requiring aortic valve replacement (AVR).[12] Preliminary data suggest that asymptomatic patients with a normal LVEF could benefit from early aortic valve intervention; however, a conservative approach is still required for most patients with severe, asymptomatic AS.[34]

Based on currently available evidence, AVR can be considered in patients at low surgical risk who, in addition to having severe AS, manifest: (1) systolic blood pressure decrease > 20 mmHg during exercise stress testing; (2) a mean transvalvular gradient ≥ 60 mmHg or a maximal transvalvular velocity (V_{max}) > 5 m/s; (3) annual V_{max} progression ≥ 0.3 m/s; (4) severe aortic valve calcification on CT scan; or (5) significantly elevated NT-proBNP levels.[12,37] Once the decision regarding aortic valve intervention has been made, the heart team must weigh numerous factors to determine whether TAVI or SAVR best serves the patient.

The South African perspective

AS can be caused by tricuspid or bicuspid degenerative calcific aortic valve disease or RHD. Although rarely the cause of isolated AS, RHD contributes significantly to the burden of AS in South Africa.[36,37] It is usually accompanied by mitral valve involvement. Despite limited resources, the ESC guidelines should be followed regarding indications for aortic valve intervention; SAVR remains the gold standard. Most patients aged < 70 years, particularly if the aetiology is bicuspid aortic valve disease, should undergo SAVR. TAVI is not currently recommended in younger patients with RHD-related AS. As a general guide, patients with a EuroSCORE II or STS score ≥ 4% are at least intermediate risk or higher, and the final risk assessment resides with the heart team. Limited femoral access, bicuspid aetiology, multivessel CAD, and low coronary origins above the annulus favour SAVR.

The decision to forego SAVR in favour of TAVI is complex and should be made by a heart team. TAVI should be considered in the following scenarios: (1) all patients aged ≥ 70 years (regardless of surgical risk); (2) expected, technically difficult open-heart surgery (e.g. previous radiation, porcelain aorta, previous CABG where potential damage to the grafts is anticipated); (3) a very frail patient; (4) major comorbidity (the most common being chronic obstructive pulmonary disease); or (5) a younger patient with a high operative risk.[38,39]

MITRAL REGURGITATION (MR)

Aetiology

MR can be primary or secondary (SMR). Primary MR arises from disease of one or more components of the mitral valve apparatus.[12] RHD is the most common MR aetiology in low-income countries, whereas degenerative MR dominates in high-income countries.[12] IE remains an important MR aetiology. SMR arises from left atrial or ventricular remodelling rather than primary leaflet disease.[12] Atrial SMR is linked to AF and enlargement of the annulus (often with heart failure with preserved ejection fraction).[12] Ventricular SMR is associated with LV dilation and resultant papillary muscle displacement in heart failure with reduced ejection fraction.[12]

Assessment

Severe MR presents with dyspnoea, fatigue, orthopnoea, and palpitations due to AF and LV volume overload. Clinical signs of severe MR include a left atrial lift, high-grade pansystolic murmur at the apex radiating to the axilla, a displaced apex beat, a third heart sound, and, in late stages, signs of pulmonary oedema and right heart failure.[40] Transthoracic echocardiography supplemented by TOE is the recommended first-line modality for MR evaluation.[12] An integrated approach using qualitative, semi-quantitative, and quantitative assessments is crucial for an accurate assessment of MR severity (Table III).[12]

MR mechanism evaluation is important for decision-making regarding surgical or transcatheter mitral valve repair. In cases where two-dimensional echocardiography is insufficient to evaluate mitral valve anatomy or MR severity, additional imaging is indicated, such as advanced echocardiography (strain, three-dimensional, TOE), exercise echocardiography, and CMR imaging.[12] Right heart catheterisation has utility in accurately quantifying systolic pulmonary artery pressure (SPAP), and where there is discordance between echocardiographic MR severity assessment and symptoms. It is also useful to exclude pulmonary hypertension from coexisting lung pathology.

Management

Urgent surgery is advised in acute, severe MR.[12] Surgery is indicated for chronic, severe, symptomatic, and primary MR (Class I, LOE B). In the absence of symptoms, a LVEF ≤ 60% (Class I, LOE B), a LVESD ≥ 40 mm (Class I, LOE B), a left atrial volume ≥ 60 ml/m^2 or diameter ≥ 55 mm (Class IIa, LOE B), SPAP > 50 mmHg (Class IIa, LOE B), and AF (Class IIa, LOE B) portend a poor prognosis, and these patients must be considered for intervention. Watchful waiting is considered safe in asymptomatic patients who do not meet these criteria. Mitral valve repair is favoured over mitral valve replacement depending on the complexity of the lesion (Class I, LOE B) and the availability of surgical expertise.[12]

Management per ESC 2025 guidelines prioritises OMT for heart failure and AF control for SMR, with cardiac resynchronisation therapy indicated for eligible patients.[12] Interventions are considered for symptomatic, severe SMR despite OMT and device therapy, following heart team evaluation. Transcatheter repair is recommended for non-surgical candidates who meet echocardiographic criteria, while surgery is considered primarily during concomitant CABG.[12] In advanced cases unresponsive to

TABLE III: Quantification of severe primary and secondary mitral regurgitation.[12]

	Parameter	Criteria
Qualitative assessment	Mitral valve morphology	Primary: Flail leaflet or prolapse, large coaptation defect, retracted leaflet Secondary: Normal leaflets with severe tenting, poor leaflet coaptation
Qualitative assessment	Colour flow jet area	Primary: Large central jet (≥ 50% of LA) or eccentric wall impinging jet of variable size Secondary: Small to moderate central jet (< 50% of LA) or eccentric jet along the wall
Qualitative assessment	Flow convergence	Primary: Large throughout systole Secondary: Small to absent in late systole
Qualitative assessment	Continuous wave Doppler jet	Primary: Holosystolic/dense/triangular Secondary: Late systolic/decreased intensity/parabolic
Semi-quantitative assessment	Vena contracta width (cm)	Primary: ≥ 0.7 cm (≥ 0.8 cm for biplane) Secondary: ≥ 0.7 cm (biplane)
Semi-quantitative assessment	Pulmonary vein flow pattern	Primary: Systolic flow reversal, blunted S wave in one pulmonary vein may be normal if other criteria are met Secondary: Systolic blunting
Semi-quantitative assessment	Mitral inflow pattern	Primary: E wave dominant (> 1.2 m/s) Secondary: E wave dominant (> 1.2 m/s)
Semi-quantitative assessment	TVI MV/TVI aortic	Primary: > 1.4 Secondary: > 1.4
Quantitative assessment	EROA (2D PISA, mm^2)	Primary: EROA ≥ 40 mm^2/R Vol ≥ 60 ml Secondary: ≥ 30 mm^2/R Vol ≥ 45 ml

Note: Enlargement of the left ventricle and left atrium is a sign of severe mitral regurgitation.
2D: two-dimensional, EROA: effective regurgitant orifice area, LA: left atrium, MV: mitral valve, PISA: proximal isovelocity surface area, R Vol: regurgitant volume, TVI: time velocity integral.

therapy, LV assist device implantation or cardiac transplantation may be options.

Medical therapy is useful to reduce LV filling pressure and decrease afterload in acute MR.[12] Inotropic support and intra-aortic balloon pump insertion are indicated for hypotension and haemodynamic instability. There is a limited role for medical therapy in chronic MR with preserved LV function. Patients presenting with overt heart failure should be managed per standard guidelines.[41]

In the absence of symptoms, patients with severe MR and preserved LVEF should be followed up every 6 months.[12] Asymptomatic patients with moderate MR and preserved LV function should be followed up 1–2 yearly. Post-intervention follow-up should focus on assessing symptoms, arrhythmias, valve function, and MR recurrence. Serial NT-proBNP may support closer monitoring or earlier referral in borderline cases. Ideally, these patients should be followed up at a heart valve centre.

The South African perspective

Recent studies from Chris Hani Baragwanath Academic Hospital noted MR secondary to RHD as the most common valve lesion in adults with mitral valve disease.[14,22,42] Most patients were African females with comorbidities, such as HIV and arterial hypertension. Myxomatous mitral valve degeneration was noted in a minority of cases. Most patients were late presenters, manifesting in heart failure. Limited surgical resources resulted in delays in mitral valve intervention. Consequently, many patients were treated with anti-remodelling heart failure drugs, serving as a bridge to surgery.[43]

Notably, rheumatic MR is characterised by eccentric jets; therefore, the value of quantitative parameters, such as the proximal isovelocity surface area method, cannot be relied upon solely for MR quantification, and a multiparametric approach must be utilised. If there is doubt regarding MR severity, additional imaging is indicated, such as TOE when available.[44] CMR imaging in rheumatic MR allows severity assessment of the severity and LV fibrosis through tissue characterisation sequences, which can aid in decision-making regarding surgery and prognostication.[45]

In South Africa, advanced echocardiography and CMR are scarce resources with limited expertise. Mitral valve repair generally offers better outcomes, including preservation of the patient's native valve, which can lead to improved haemodynamics and reduced complications related to prosthetic valves (thrombosis or IE), though it carries a higher risk of reoperation.[46] Most patients in South Africa with severe SMR do not currently have access to percutaneous mitral valve repair. Therefore, patients who are not candidates for surgery should be treated according to the existing heart failure guidelines.

Currently, 2 centres in the Western Cape and 1 in Gauteng perform percutaneous mitral valve repair. Patients with inoperable primary MR or those with SMR and ongoing symptoms despite maximally tolerated guideline-directed therapy (including cardiac resynchronisation therapy if indicated) should be referred for assessment for transcatheter mitral edge-to-edge repair.

MITRAL STENOSIS (MS)

Aetiology

RHD is the leading cause of MS.[12] Other aetiologies include degenerative disease, and, less commonly, chest radiation, carcinoid heart disease, and inherited metabolic disorders. In contrast to other aetiologies, the hallmark of rheumatic MS is commissural fusion.

Assessment

Significant MS presents with dyspnoea, haemoptysis, fatigue, and, in advanced cases, peripheral oedema, hoarseness, and embolic events. On auscultation, a low-pitched mid-diastolic rumbling murmur is present at the apex, accompanied by an opening snap; loud S1/features of AF.[47] Transthoracic echocardiography is the first-line modality for MS evaluation.[12] It assesses aetiology, severity, and haemodynamic consequences. A mitral valve area ≤ 1.5 cm^2, a mean transmitral gradient ≥ 10 mmHg, and pulmonary hypertension are considered clinically significant (Table IV).

TOE is indicated before balloon mitral valvuloplasty. It provides detailed information on valve anatomy and excludes left atrial thrombus. Three-dimensional echocardiography with slice rendering is useful for accurate valve planimetry. In patients with equivocal symptoms or borderline MS severity, exercise echocardiography provides objective data on increases in transmitral gradient and SPAP.[48] Proposed mean gradient thresholds for severe MS include values exceeding 15 mmHg during exercise or 18 mmHg during dobutamine infusion.[48]

Management

Intervention on the mitral valve should be reserved for moderate-to-severe MS.[12] Depending on the patient's clinical characteristics and anatomy of the valve and subvalvular structures based on standardised scores (Wilkins or Cormier) and local expertise, MS can be treated with balloon mitral valvuloplasty (Class I, LOE B) or surgery (Class I, LOE C).[12] Balloon mitral valvuloplasty is not indicated in degenerative MS, since it is characterised by mitral annular calcification and not commissural fusion. In highly symptomatic patients, transcatheter valve replacement or surgery may be considered.

TABLE IV: Severity grading of mitral stenosis.

	Mild	Moderate	Severe
Valve area (cm^2)	> 1.5	1–1.5	≤ 1.5
Mean gradient (mmHg)	< 5	5–10	> 10
Pulmonary artery pressure (mmHg)	< 20	30–50	> 50

The entity of LFLG MS is also noteworthy.[49] This is defined as a mean mitral valve area < 1.5 cm^2, measured on planimetry, a mean gradient < 10 mmHg, and a transmitral flow < 35 ml/m^2. Recent evidence suggests that these patients are older, more ill, with AF, and more subvalvular disease. After valvotomy, they have a lesser reduction in left atrial pressure, and, most importantly, a suboptimal symptomatic response. This may be related to independent ventricular-vascular uncoupling, decreased LV compliance, and a high prevalence of AF in addition to intrinsic MS.

Medical management aims to control heart failure symptoms, achieve rate or rhythm control, and prevent thrombus and systemic embolism.[12] In the absence of contraindications, beta blockers are the mainstay of treatment for AF rate control.[12] Alternative agents for rate control include digoxin and non-dihydropyridine calcium-channel blockers.[12] Amiodarone is effective for maintaining sinus rhythm after cardioversion.[12] Cardioversion and pulmonary vein isolation are not indicated in patients with severe, untreated MS. Cardioversion can be considered in recent-onset AF with a moderately enlarged left atrium and less severe MS.

Oral anticoagulation with a VKA is indicated in AF. The INVICTUS study found that VKAs were associated with a lower rate of a composite of cardiovascular events and death than rivaroxaban, without a higher bleeding rate.[19] In patients in sinus rhythm, oral anticoagulation in MS is indicated in the presence of dense, spontaneous echocardiographic contrast, a history of thromboembolism, and a left atrial diameter > 50 mm or volume > 60 ml/m^2.[12]

The South African perspective

In a recent South African study conducted at a referral centre, isolated rheumatic MS was documented in 23% of patients.[14] Females were predominantly affected, which aligns with data from other LMICs. None of the patients in this study had degenerative (calcific) MS; a likely reflection of the study patients' younger age compared with those in higher-income countries.

In the local setting, where most patients with MS are still young and surgical resources are scarce, balloon mitral valvuloplasty should be the first line of treatment when feasible.[50] In patients with contraindications to balloon mitral valvuloplasty, stabilisation with medical therapy is a reasonable option while awaiting definitive surgical intervention.[14] Zühlke, et al. reported suboptimal use of oral anticoagulation in patients with RHD.[10] Close attention to anticoagulation is mandatory, and an international normalised ratio in the therapeutic range (2–3) should be targeted to prevent stroke.

TRICUSPID REGURGITATION (TR)

Aetiology

Most TR (> 90%) is ventricular secondary (i.e. due to leaflet tethering caused by right ventricular or annular dilatation).[51,52] Primary aetiologies (i.e. intrinsic valve disease) are uncommon (e.g. IE, cardiac implantable electronic devices, congenital abnormalities of the tricuspid valve, and RHD). Atrial secondary TR is recognised as another aetiological group, in which right atrial and tricuspid annular dilatation lead to non-coaptation of the valve leaflets.[53]

Assessment

Multiparametric, transthoracic echocardiography should be used to determine the mechanism and severity of TR (Table V).[54]

Management

TR intervention comprises surgical valve repair, replacement, or transcatheter valve repair.[55] Treatment is indicated for symptomatic patients with severe primary TR, and in asymptomatic or mildly symptomatic individuals with right ventricular dilatation or declining right ventricular function. Although the survival benefit of tricuspid valve intervention for severe, primary TR is not well established, it can be performed safely in selected patients without severe right ventricular or LV dysfunction and without severe, pre-capillary pulmonary hypertension.

The mortality risk of surgical intervention for isolated TR (i.e. in the absence of concomitant valve disease) is in excess of 10%.[2] Tricuspid valve repair should be performed in patients with severe secondary TR who are undergoing left-sided valve surgery, as well as in those with mild or moderate TR who have dilated tricuspid annuli (a predictor of progressive TR worsening in this population).[56]

Since adding tricuspid valve repair to left-sided valve surgery does not increase operative mortality compared with the very

TABLE V: Severity grading of tricuspid regurgitation and stenosis.

Severe tricuspid regurgitation	
Tricuspid valve morphology	Abnormal/flail
Colour flow regurgitant jet	Large central jet or eccentric jet impinging on wall at a Nyquist limit of 50–60 cm/s
Continuous wave signal of regurgitant jet	Dense or triangular with early peak
Vena contracta	> 7 mm at a Nyquist limit of 50–60 cm/s
Proximal isovelocity surface area radius	> 9 mm at a Nyquist limit shift of ≈ 30 cm/s
Hepatic vein flow	Systolic flow reversal
Tricuspid inflow	Dominant E wave ≥ 1 m/s in the absence of other causes of an elevated right atrial pressure
Effective regurgitant orifice area	≥ 40 mm^2
Regurgitant volume	≥ 45 ml/beat
Enlargement of cardiac chambers	Right ventricle, atrium, or inferior vena cava
Severe tricuspid stenosis	
Mean transvalvular gradient	> 5 mmHg

significant risk (> 10%) of late repair of isolated TR, it should be used liberally.[56] Valve replacement is performed when valve repair is not technically feasible or carries a high risk of TR recurrence. Transcatheter valve repair technologies appear promising, although randomised data remain limited.[57]

The South African perspective

In a contemporary South African cohort of patients with moderate or severe rheumatic MR, moderate or severe TR was documented in 31%.[22] This aligns closely with the prevalence of TR reported in studies of rheumatic MR from Israel and Japan.[58,59] Nyaope (an intravenous mixture of heroin, cocaine, and antiretroviral drugs) abuse is an emerging cause of IE affecting the tricuspid valve.[17] In a recent local study, 60% of patients with nyaope-associated IE had tricuspid valve involvement. Transcatheter valve repair technologies are not commercially available in South Africa and are not currently offered to patients. Loop diuretics and use of c (MRAs) are the cornerstone of the medical therapy of tricuspid incompetence.

TRICUSPID STENOSIS (TS)

Aetiology

The most common aetiology of TS is RHD. Other causes are infrequently seen (e.g. congenital heart disease and carcinoid heart disease).

Assessment

Valve morphology should be carefully assessed on transthoracic echocardiography to determine the aetiology and the suitability for surgical intervention.[60] A mean transvalvular gradient > 5 mmHg indicates significant stenosis (Table V).[12]

Management

While diuretic therapy may benefit patients symptomatically, durable treatment requires mechanical relief of severe stenosis. Percutaneous balloon valvuloplasty may be considered in cases of isolated TS or when concomitant mitral balloon valvuloplasty is performed.[61] Surgical repair is possible in some patients, but most often valve replacement is required. Implantation of a bioprosthesis is preferred due to the higher risk of mechanical valve thrombosis in the tricuspid position.[12]

The South African perspective

Sparse local data exist on the prevalence or aetiology of TS.

MIXED AND MULTIPLE VALVE DISEASES

Mixed disease refers to both a stenotic and regurgitant lesion within the same valve. Multiple valve disease refers to lesions involving > 1 valve, with each lesion at least moderate in severity. The EuroHeart survey showed a 20% prevalence of multiple valve disease in patients with native valves; however, data on multiple valve lesions remain scarce.[62]

Aetiology

RHD accounts for 8% of clinical heart failure in an urban, South African, black population, with the mitral valve being affected most frequently.[63] A contemporary study by Banderker, et al. found combined disease (MS/MR) and multiple valve disease in 38% and 29% of patients, respectively, mostly due to rheumatic origin.[14] The REMEDY study, which enrolled 3 343 patients from 12 African countries, India, and Yemen, showed that children in the first decade of life presented mainly with isolated MR, while mixed mitral and mixed aortic diseases dominated in the second decade of life.[10]

Another South African study revealed that concomitant primary rheumatic tricuspid valve disease was present in 29% of patients, with rheumatic moderate or severe MR.[22] Of these, 31% had moderate or severe TR with attendant tricuspid valve annular dilation (38 ± 7.2 mm).[22] Assessment for tricuspid disease is important in patients with mitral valve disease, considering the increased morbidity and mortality associated with untreated TR.[64] Multivalve involvement is not uncommonly seen in patients with IE.[14,65,66]

Principles of assessment

The initial assessment of multivalve pathology is difficult. Many Doppler-derived severity parameters are validated for single-valve pathology only. Nevertheless, it is recommended to assess each valve individually against severity criteria and, subsequently, consider the combined haemodynamic interplay between the valve lesions to determine which severity parameters are useful, erroneous, or redundant.

The clinical presentation and signs, as well as haemodynamic impact, are most frequently determined by the most severe or dominant lesion.[67,68] In patients with balanced involvement of different valves, the pathophysiology and clinical features often reflect the proximal lesion, thereby masking the manifestations of the distal lesion.[67,69] In general, fewer load-dependent parameters should be employed.[69,70] An example is significant AR, which may not be apparent in a patient with severe MS.

Transthoracic echocardiography remains the first-line imaging modality, though more advanced imaging (TOE, CT, and CMR) is frequently required. NT-proBNP, exercise echocardiography, and cardiac catheterisation may also be used, especially in the setting of disproportionate symptoms.[69] A few common valve-specific echocardiography interactions and pitfalls include:[69,70]

- AS and AR: AR pressure half-time is unreliable; the simplified Bernoulli equation for AS gradient determination might not be applicable if the LV outflow tract velocity is elevated.
- AS and MS: The MS pressure half-time method for mitral valve area is unreliable. LFLG MS can occur (three-dimensional echocardiography for mitral valve planimetry is superior).

LFLG AS is common:

- AS and MR: The presence of AS can increase the MR volume. AS and MR jets may be confused on Doppler (look for aortic valve closure; the AS trace will not extend into the isovolumic relaxation time as in MR).

- AR and MS: An AR jet can be mistaken for a MS jet (if the end-diastolic velocity is > 3 m/s, it is an AR jet). The continuity equation is unreliable when aortic valve flow is used as the reference flow. MS pressure half-time is unreliable for assessing mitral valve area. MS can blunt the increased pulse pressure and LV dilatation of severe AR.
- AR and MR: Doppler volumetric method using left-sided assessment of net forward flow is invalid. AR pressure half-time invalid. This combination is poorly tolerated and more likely to result in residual LV dysfunction, even post-operatively.
- MS and MR: Doppler mitral gradient reflects the severity of both MS and MR.

Management: General principles and surgical considerations

Data on indications for intervention in mixed valve and multiple valve diseases are limited. Decisions are individually tailored to patients. In those with both regurgitation and stenosis of the same valve, management usually follows the guideline recommendations for the dominant lesion. In balanced disease, greater emphasis is placed on symptoms rather than solely on severity criteria. Generally, the decision to intervene in patients with symptomatic disease and 2 severe lesions is straightforward. In the case of 2 non-severe lesions, symptoms and the degree of LV impairment take precedence.

Age and comorbidities are crucial considerations, and risk stratification based on the combined procedure risk is also important. Both the EuroSCORE II and STS scores underestimate risk in patients with ≥ 2 valves requiring surgery; this is a research gap that requires more study. The risk of surgery is weighed against the risk of the natural history if the diseased valve is left untreated. The presence of concomitant CAD further complicates the decision process. Given the complexity of these decisions, collaboration between cardiologists and cardiac surgeons is paramount.

Surgical management

VHD treatment may be percutaneous or via open-heart surgery, and may comprise valve repair or replacement. Mitral valve repair is rarely indicated in RHD.[67] In patients with AR/MR, chronicity may impact LV function (which may also persist post-operatively), necessitating early intervention.[71] Combined, severe MR and AR portend a high risk when surgical treatment of both valves is necessary.[71] Even when treated surgically, post-operative outcomes (persistent symptoms, LV dysfunction, and survival) are worse compared with isolated valve disease.[67] Combined MR and AR have a high risk for LV dysfunction in the young after surgery for RHD.[71] The indication for intervention should be based on LV size (dimensions and volumes) and surgical indications for MR, rather than on the higher threshold of LV size for isolated AR.[71]

Percutaneous treatment options for RHD AS are rarely employed, since isolated RHD AS is relatively rare. Before the era of TAVI, percutaneous aortic valvuloplasty was fraught with high complication rates of up to 25%.[67] In a study by Rifaie, et al., 100% success was achieved for RHD AS, though the sample size was small (*n* = 9).[72] Transcatheter treatment for RHD AR is an active area of research, which may prove viable in the future.[73,74] In the presence of moderate or severe MS and moderate aortic valve disease, percutaneous treatment (percutaneous mitral commissurotomy) may have a role to buy time for subsequent surgical treatment of both valves; however, surgery is preferred in the presence of severe MS/severe aortic valve disease.

The South African perspective

As highlighted by recent South African studies, multiple valve lesions are common in patients with RHD. However, outcome data remain sparse.

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