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The importance of sex differences in valvular heart disease from an imaging point of view

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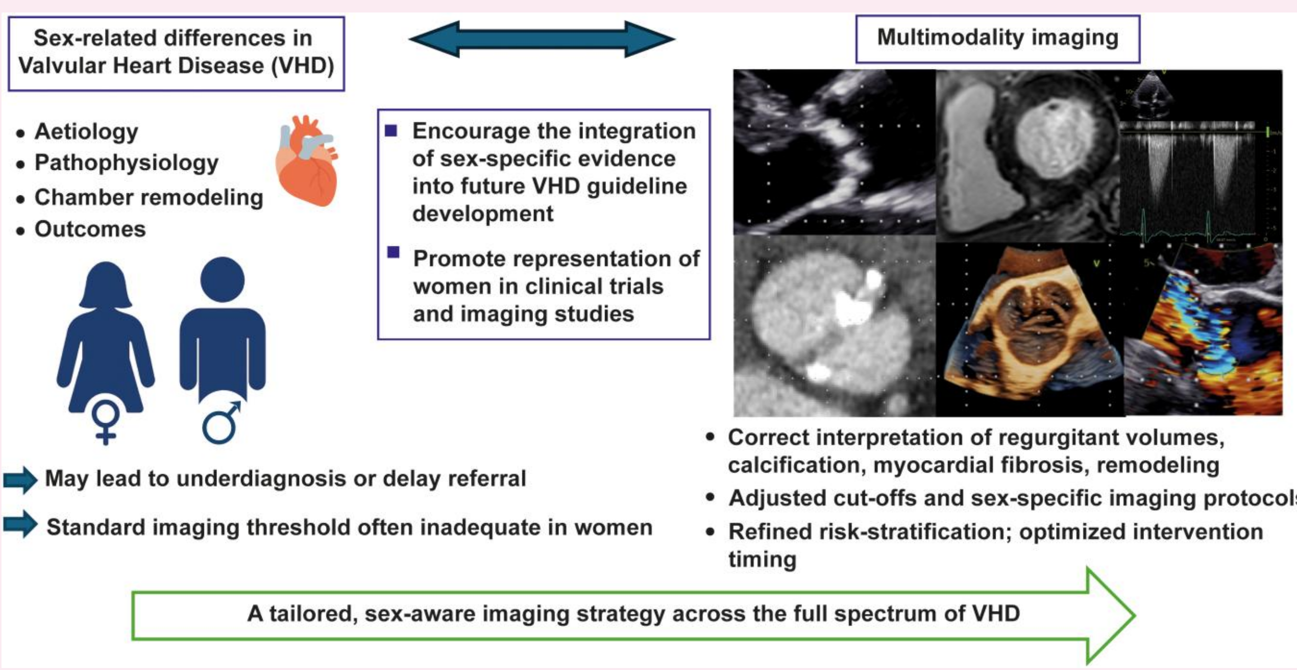
Sex differences in valvular heart disease (VHD) represent an emerging focus in cardiovascular imaging, with implications spanning aetiology, pathophysiology, chamber remodelling, and prognosis. This review aims to illustrate how multimodality imaging can be applied to address sex-specific differences in VHD, with the goal of improving disease grading, staging of extra-valvular cardiac damage, and risk stratification across the whole VHD spectrum.

Graphical Abstract



Sex differences and the role of multimodality imaging. Multimodality imaging plays a pivotal role in addressing sex-related disparities in VHDs by enabling sex-specific interpretation of key diagnostic parameters. Adjusted imaging thresholds and tailored protocols are essential to improve diagnostic accuracy, refine risk stratification, and optimize the timing of intervention.

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Keywords valvular heart diseases • sex-difeferences • aortic valve stenosis • aortic valve regurgitation • mitral valve stensis • mitral valve regurgitation • tricuspid valve regurgitation • pregnancy

Introduction

The prevalence of valvular heart disease (VHD) has shown a rising trend in recent years, primarily driven by the aging of the population and a marked reduction in rheumatic fever sequelae among native populations of high-income countries. This shift has led to a decline in rheumatic and congenital causes and a parallel increase in degenerative aetiologies in high-income countries. However, with ongoing migratory flows, rheumatic valve disease remains present and should not be considered outside the scope of physicians practising in high-income countries.

Sex-related differences in VHD are evident across epidemiology, comorbidities, clinical presentation, and cardiac adaptation, reflecting an intricate framework where the multi-imaging approach plays an important role (*Graphical Abstract*).

Specifically, women are more frequently affected by mitral and tricuspid valve disease, while men more commonly present with aortic valve disease, especially at a younger age.[1] In terms of clinically associated extra-valvular conditions, coronary artery disease is predominantly observed in men, whereas women are more prone to microvascular dysfunction and hypertension. These differences also influence myocardial response: women tend to develop concentric left ventricular (LV) remodelling, with smaller LV cavities and lower stroke volumes, whereas men more often exhibit eccentric remodelling.[2]

In women, a smaller LV size may result in less ventricular dilatation and lower regurgitant volumes (RVol), even in the presence of severe valvular regurgitation. Similarly, low-flow states, more common in women, can lead to reduced transvalvular gradients, potentially masking the severity of valve stenosis.[3] These physiological differences contribute to an underestimation of VHD severity and a higher likelihood of discordant echocardiographic findings in women, which adds complexity to the accurate grading of VHD.[3] As a result, second-line imaging modalities [i.e. computed tomography (CT), cardiac magnetic resonance (CMR), and transoesophageal echocardiography (TEE)] could help evaluate the severity of VHD when echocardiographic findings are inconclusive or conflicting.

Moreover, the studies that formed the basis of current VHD guidelines exhibit significant disparities, being largely based on a male-predominant cohort. As a result, intervention thresholds and cut-off values may be biased in female patients, with most current recommendations lacking sex-specific criteria to guide therapeutic decision-making.[1]

Importantly, women with VHD often present with more subtle or nuanced symptoms compared with men. In this population, exercise echocardiography and cardiopulmonary testing may play an important role in assessing haemodynamic changes during exertion and in unmasking latent symptoms.

Adding further complexity to this framework, sex-related differences in natriuretic peptides have recently gained increasing attention. Women generally display higher brain natriuretic peptide (BNP) as well as its N-terminal pro-peptide (NT-proBNP) levels due to hormonal and physiological factors.[4] In VHD, these biomarkers remain diagnostically valuable, especially if the maximal expected value for age and sex is considered. Large-scale studies proposed the use of the BNP ratio (or NT-proBNP) ratio (i.e. the measured level of the peptide divided by the maximal expected value—i.e. 99th percentile—for age, sex, and assay used) and showed that these ratios were associated with mortality when abnormal.[5,6]

Finally, pregnancy can induce haemodynamic fluctuations in women, posing further challenges in the diagnosis and the severity grading of VHD, and thus merits a dedicated focus in this review.

Therefore, this manuscript aims to highlight sex-specific features of native VHD and their implications for the tailored application of multimodality imaging, based on the most recent body of evidence (*Table 1*).

Sex differences in aortic valve stenosis

Calcific aortic stenosis (AS) is a leading cause of morbidity and mortality in high-income countries, with clear sex-specific variations in presentation, progression, and response to treatment. In women, AS is often characterized by smaller aortic annuli, less valvular calcification than men, extensive valvular fibrosis, concentric LV remodelling with diffuse myocardial fibrosis, and preserved or elevated LV ejection fraction (LVEF) despite impaired diastolic function (*Figure 1*).[7] These features are associated with limited post-replacement LV function recovery and an increased risk of patient–prosthesis mismatch (PPM).[8] Men, on the other hand, more commonly exhibit LV dilatation and impaired LVEF.

In rheumatic AS, calcification and thickening primarily occur at the commissures, leading to commissural fusion and a triangular-shaped valve opening in systole. Calcification is less important than in calcific AS and thus aortic valve calcification measurement by CT could be falsely negative (i.e. severe AS with non-severe calcification). Rheumatic AS often coexists with aortic regurgitation (AR) and mitral stenosis (MS).[9]

In women, conventional echocardiographic measures often underestimate AS severity. Multimodality imaging, particularly cardiac CT and CMR, enhances the detection of aortic valve calcification and LV myocardial fibrosis. Thus, with close attention to AS sex-specific features, multimodality imaging could provide earlier diagnosis, tailored risk assessment, and timely intervention.

Transthoracic echocardiography

Transthoracic echocardiography (TTE) remains the cornerstone imaging modality for the assessment of AS, providing essential information regarding valvular anatomy, disease severity, and a comprehensive evaluation of cardiac chambers, crucial for identifying the presence and extent of extra-valvular cardiac damage.

Valve morphology is key to sex-specific management. Bicuspid aortic valve, the most common congenital valve abnormality, is three times more prevalent in men than women (3:1 ratio). However, its clinical expression differs by sex: in women, the bicuspid aortic valve more frequently leads to stenosis, whereas in men it is more often associated with aortic regurgitation with or without concomitant endocarditis.

Multi-window interrogation enables the optimization of the Doppler beam alignment[10] and represents the first step in avoiding AS severity underestimation. Also, careful measurement of the LV outflow tract must be performed, and in case of doubtful measurement, the dimensionless velocity index could be used instead of the aortic valve area (AVA) (*Table 2*). Nevertheless, even with meticulous technique and exclusion of measurement errors, discordant parameters of severity can persist and are more commonly observed in women.[11]

This clinical scenario typically represents the low-gradient AS, characterized by a severely reduced aortic valvular area despite transvalvular gradients falling within the non-severe range. This phenotype includes several distinct subgroups: (i) classical low-flow low-gradient (CLF-LG), AS with reduced LVEF; (ii) paradoxical low-flow low-gradient (PLF-LG) AS, with preserved LVEF but reduced stroke volume

Table 1 Sex differences in valvular heart disease: an overview from an imaging perspective

Valvular heart disease	Key sex-specific differences	Impact on Echocardiographic assessment	Imaging strategies in clinical practice
Aortic stenosis (AS)	• Women: More diffuse fibrosis, PLF–LG AS, concentric LV remodelling, smaller LV, preserved EF. • Men: Greater calcific burden, CLF–LG AS, eccentric remodelling, LV dilatation, reduced EF	• Women: Challenges and potential underestimation in small LV/low-flow states • Men: Challenges due to Doppler misalignment especially in bicuspid aortic valve—BAV (asymmetric opening)	• Women: TTE for remodelling/PLF–LG; CT with sex-specific AVC thresholds; CMR for diffuse fibrosis • Men: DSE for CLF–LG; CT (sex-specific AVC thresholds)
Aortic Regurgitation (AR)	• Women: Smaller LV volumes, less dilatation despite severity, later referral, higher RF for same RVol • Men: Larger LV volumes, earlier dilatation, bicuspid AR more common, higher RVol for same RF	• Women: TTE may underestimate severity due to small LV (sex-specific cut-offs may be needed). Volumetric method for avoiding pitfalls • Men: More pronounced LV dilatation. Challenges in eccentric jets (BAV)	• Women: CMR in case of discordant TTE metrics or disproportional LV dilatation/AR severity assessment; 3D TTE for cusp prolapse (anatomy) • Men: CMR for LV remodelling (dilatation); CT for BAV/aortic aneurysm association
Mitral Regurgitation (MR)	• Women: Higher prevalence of bileaflet prolapse, arrhythmic MVP, more LA stiffness (atrial MR), underdiagnosed severe MR • Men: More ventricular MR, greater LV dilatation, better postoperative remodelling	• Women: TTE may underestimate MR due to smaller LV/annulus; thresholds may need adjustment. Volumetric method for avoiding pitfalls • Men: LV enlargement more apparent on echo	• Women: 3D TEE for complex anatomy; CMR for arrhythmic MVP/fibrosis/discrepant metrics; CT for MAC and surgical planning. • Men: CMR especially for ventricular MR and myocardial scar assessment
Mitral Stenosis (MS)	• Women: degenerative MAC-related MS; rheumatic MS in younger women • Men: Less frequent overall; rheumatic and MAC-related MS less common	• Women: Echo may underestimate (discordant phenotypes) • Men: Conventional 2D echo more reliable than women in quantification	• Women: 3D TEE to evaluate MAC extension, commissural fusion in rheumatic MS and planimetric area (discordance) • Men: Standard TTE/2D TEE adequate in most cases
Tricuspid Regurgitation (TR)	• Women: More atrial functional TR, smaller RVs, later referral, underestimation of severity • Men: More ventricular functional TR, larger RVs, earlier referral, more systolic dysfunction	• Women: RV parameters (TAPSE, RV size) may underrepresent severity. • Men: RV dilatation more clearly demonstrated	• Women: 3D TTE/TEE for annular dilatation and atrial TR; CT for annular geometry • Men: CMR and 3D TTE for RV dilatation and systolic dysfunction (ventricular TR)
Infective Endocarditis (IE)	• Women: More mitral involvement, higher rates of culture-negative IE, HF at presentation • Men: Higher prevalence overall, more aortic/tricuspid IE, typical bacterial pathogens	• Women: TTE less sensitive due to smaller anatomy • Men: Vegetations and complications easier to detect	• Women: CT/TEE when TTE is inconclusive, FDG-PET/CT valuable in culture-negative/prosthetic IE • Men: TTE/TEE often sufficient; CT for peri-annular complications

AR, aortic regurgitation; AS, aortic stenosis; AVC, aortic valve calcification; BAV, bicuspid aortic valve; CLF–LG, low-flow low-gradient; CMR, cardiovascular magnetic resonance; CT, computed tomography; DSE, dobutamine stress echocardiography; ECV, extracellular volume fraction; EF, ejection fraction; FDG-PET/CT, fluorodeoxyglucose positron emission tomography/computed tomography; HF, heart failure; IE, infective endocarditis; LA, left atrium/left atrial; LV, left ventricle/left ventricular; MAC, mitral annular calcification; MR, mitral regurgitation; MS, mitral stenosis; MVP, mitral valve prolapse; PLF-LF, paradoxical low-flow low-gradient; RF, regurgitant fraction; RVol, regurgitant volume; RV, right ventricle/right ventricular; sPAP, systolic pulmonary artery pressure; TAPSE, tricuspid annular plane systolic excursion; TEE, transoesophageal echocardiography; TTE, transthoracic echocardiography; TR, tricuspid regurgitation.

index; and (iii) normal-flow, low-gradient (NF-LG) AS, where stroke volume is preserved despite discordant severity indicators, often associated with elevated blood pressure and/or reduced arterial compliance. All these presentations present a diagnostic challenge due to the discordance between aortic valve area and gradients/velocity, complicating severity grading and patient management.[12]

LV remodelling patterns and geometry follow distinct sex-specific patterns, which are particularly relevant when AS severity parameters are discordant. Women typically exhibit smaller LV cavity size, more concentric remodelling, and higher ejection fractions, features commonly associated with PLF-LG AS phenotype. In contrast, men more commonly present with LV dilatation and reduced LVEF, aligning predominantly with the CLF-LG AS group.

Importantly, these sex-specific remodelling patterns may carry sex-specific prognostic implications. For instance, concentric remodelling has been shown to have adverse prognostic value in women.[2] Therapeutic

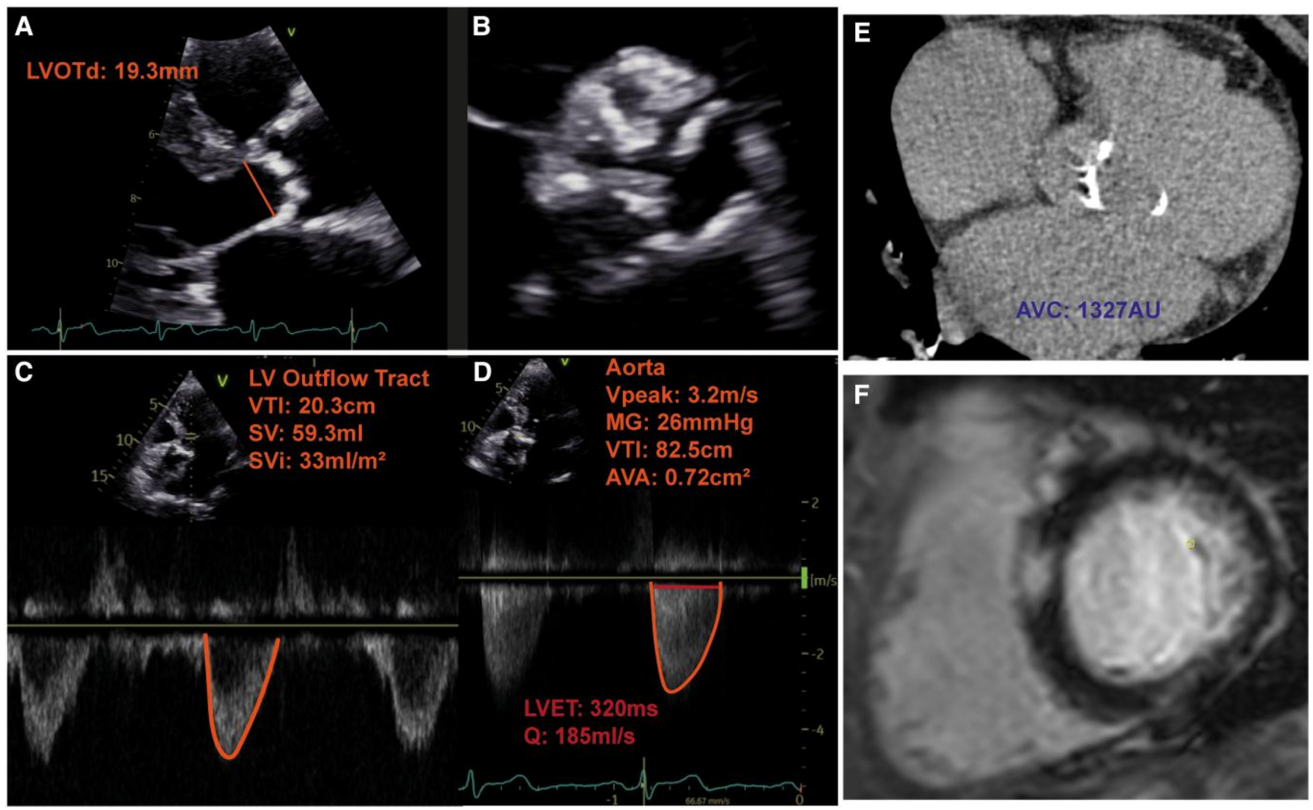

Figure 1 Paradoxical low-flow low-gradient aortic stenosis (PLF-LG AS) in a 72-year-old woman. The figure shows a multimodality imaging snapshot of the main features of the PLF-LG phenotype, which is more frequently observed in women. Transthoracic echocardiography (panels *A*, *B*, *C*, and *D*) illustrates a low-flow state with low transvalvular gradient, despite aortic valve area was severely reduced. CT images show a calcium burden of the aortic valve in the severe range (panel *E*), and finally, CMR underscores the high myocardial fibrotic burden in terms of LGE (panel *F*). AVA, aortic valve area; AVC, aortic valve calcification; LV, left ventricular; LVET, LV ejection time; LVOTd, LV outflow tract diameter; MG, mean gradient; *Q*, flow rate; SV, stroke volume; V_{peak}, peak aortic jet velocity; VTI, velocity-time integral.

Table 2 Parameters used to assess aortic stenosis and flow

Aortic stenosis assessment			Mild AS	Moderate AS	Severe AS
Echocardiography					
Vpeak (m/s)	Measured		2.5–3	3–4	≥4
MG (mmHg)	Simplified Bernoulli equation: $4V^2$		<20	20–40	≥40
AVA (cm^2)	Continuity equation: SV/VTI_{Ao}		>1.5	1.0–1.5	≤1.0
Indexed AVA (cm^2/m^2)	AVA/BSA		>0.85	0.60–0.85	≤0.6
DVI	VTI_{LVOT}/VTI_{Ao}		>0.5	0.25–0.5	≤0.25
Computed tomography					
AVC (AU)	Measured	Female	< 360	360–1200	≥1200
		Male	<1030	1030–200	≥2000
AVC density (AU/cm^2)	$\frac{AVC}{LVOT_{Area^a}}$	Female	—	—	≥300
		Male	—	—	≥500
Flow assessment			**Low flow**	**Grey zone**	**Normal flow**
SVi (mL/m^2)	$\frac{LVOT_{Area} \times VTI_{LVOT}}{BSA}$		≤35	—	>35
		Female	< 32	32–35	>35
		Male	<35	35–40	>40
Flow rate (mL/s)	$\frac{SV}{LVET}$		<210	210–250	>250
		Female	< 179	—	>179
		Male	< 209	—	>209

AVA, Aortic valve area; AVC, aortic valve calcification; BSA, body surface area; DVI, Doppler velocity index; LVOT, left ventricular outflow tract; MG, mean gradient; SV, stroke volume; SVi, Stroke volume index; *V*, velocity; *V*peak, peak aortic jet velocity; VTI_{Ao}, velocity-time integral in the aorta; VTI_{LVOT}, velocity-time integral in the LVOT.
[a]For AVC density calculation, the use of measured $LVOT_{area}$ by 3D-imaging modality is preferable. Calculation at echocardiography could be used: $LVOT_{Area} = \pi \times \left(\frac{LVOT_{diameter}}{2}\right)^2$.

strategies aimed at modulating LV remodelling—such as angiotensin receptor blockers—could possibly slow down AS progression by attenuating valvular fibrosis and may be especially beneficial in women.[13,14]

Defining the baseline flow state in AS is essential not only for clarifying discordant AS grading, but also in its own right, as it serves as an independent predictor of prognosis.[15] Stroke volume index (SVi) is a key prognostic parameter, with sex-specific thresholds below 32 mL/m^2 for women and 40 mL/m^2 for men.[16] Correspondingly, optimal cut-off values for flow-rate have been established at 179 mL/s for women and 209 mL/s for men[17] (*Table 2*), further underscoring the need for sex-specific AS evaluation.

The presence of a small aortic root could also increase the conundrum of grading aortic stenosis, but not with regard to discordance between AVA and gradient. Indeed, in patients with small aortas, a part of the pressure energy transformed into kinetic energy through the valve is retransformed in pressure energy after the valve instead of being totally dissipated: this is the pressure recovery phenomenon. Thus, as the aortic valve area (calculated by Doppler-echocardiography) does not take into account pressure recovery either, pressure recovery cannot be a reason for discordance between aortic valve area and mean gradient at Doppler-echocardiography. However, pressure recovery is important to explain differences between gradients measured at Doppler-echocardiography and by catheter, as well as the mismatch between AS severity and symptoms or LV remodelling. Indeed, the haemodynamic load actually experienced by the ventricle and thus by the patients is better represented by the recovered gradient/aortic valve area that are less severe. To approximate the pressure recovery phenomenon, the energy loss coefficient could be calculated by the following equation: (aortic valve area × aortic area)/(aortic area—aortic valve area).[18] This coefficient modifies the AVA to consider the pressure recovery phenomenon and reflect the trough AS severity felt by the patient.

Myocardial deformation imaging by speckle-tracking echocardiography provides incremental prognostic value beyond conventional echocardiography, especially in the early stages of myocardial damage. In this context, an impairment of LV global longitudinal strain may reveal subtle myocardial dysfunction that can be masked by normal or even supernormal LVEF.[19] Additionally, a comprehensive assessment of the longitudinal deformation of the left atrium (LA)[20] and the right ventricle emerged as important additional risk-stratification parameters in this setting.[21] Further research is needed to determine how best to integrate these parameters into a sex-specific framework for staging myocardial damage.

TTE plays an important role not only in diagnosis, but also in the follow-up of AS in a sex-specific key. It has been previously demonstrated that men are progressing faster than women regarding transvalvular gradients and velocities;[22] however, these parameters may not fully capture the degenerative process of the AS, being also importantly influenced by concomitant sex-specific SVi trajectories.[23] Specifically, in women with AS, reduced SVi reserve due to LV concentric remodelling leads to lower progression in velocities and gradients. Since these metrics are highly flow-dependent, longitudinal assessment should incorporate SVi trends to avoid underestimating disease progression.[23]

Cardiac computed tomography and dobutamine stress echocardiography

Cardiac CT and dobutamine stress echocardiography represent valuable diagnostic tools, especially when TTE yields discordant parameters of AS severity.[12] Specifically, CT plays an important role in patients with PLF-LG, CLF-LG, and NF-LG AS to assess with high accuracy the AS severity through calcium score assessment for aortic valve calcification (AVC).[24] Interestingly, women present with less aortic valve calcification and more aortic valve fibrosis than men, for the same AS severity. Thus, AVC has sex-specific thresholds indicating AS severity: an absolute AVC above 1200 AU in women and 2000AU in men is indicative of severe AS.[24] Similarly, calcium density thresholds (derived by dividing the total AVC by the aortic annulus area) are set above 300 AU/cm^2 for women and 500 AU/cm^2 for men[25] (*Table 2*). These thresholds have been validated in many different cohorts, especially in women and in patients with discordant grading with and without preserved ejection fraction.[24,26–29]

Although positron emission tomography (PET) scans can detect early AVC, their clinical applicability in AS remains limited. Indeed, CT offers comparable prognostic insights at a lower cost and with reduced radiation exposure.

These sex-specific thresholds are based on the observation that women tend to develop more valvular fibrosis than men during the degenerative AS process. However, despite accounting for sex differences, certain limitations of AVC must be acknowledged. Notably, these thresholds may not be applicable in patients with bicuspid aortic valves, especially in younger patients (*Figure 2*), or in those with cardiac amyloidosis. Contrast-enhanced CT further enhances anatomical assessment of AS severity, especially when non-calcified tissue contributes substantially to valve obstruction.[30] Further studies are needed to refine this imaging strategy and validate robust clinical thresholds.

Contrast-enhanced cardiac CT is further crucial for pre-procedural transcatheter intervention planning, particularly in women, due to their higher risk of iliofemoral complications and access challenges, and smaller aortic root. More recently, cardiac CT has also emerged as an important tool for detecting diffuse myocardial fibrosis through extracellular volume (ECV) assessment.[31]

Dobutamine stress echocardiography is a valuable tool in patients with CLF-LG AS and especially those with relevant systolic dysfunction (LVEF below 35%).[32] In low-flow, low-gradient aortic stenosis, the role of dobutamine stress echocardiography may be less prominent in women, as the PLF-LG AS is more typical of women.

Cardiac magnetic resonance

CMR allows myocardial characterization in patients with AS, highlighting distinct sex-specific myocardial responses to pressure overload. Women with AS have greater diffuse myocardial fibrosis (assessed by CMR ECV and T1 mapping—*Figure 1*[33]) and less or comparable non-ischaemic focal fibrosis (assessed by late gadolinium enhancement, LGE),[34] despite having fewer risk factors and smaller LV mass.[35] In patients with low-gradient AS, the CMR markers (GLS, ECV, and LGE) resulted independently associated with adverse outcome, underscoring their additive prognostic value beyond echocardiography.[36] Interesting sex differences regarding LV myocardial response have been detected by CMR studies, with men showing more favourable interventricular septal remodelling after aortic valve replacement than women.[37]

Sex differences in aortic valve regurgitation

Aortic regurgitation (AR) is characterized by combined LV volume and pressure overload, leading to progressive LV negative remodelling with dilatation and dysfunction in later stages.[38] AR is mostly due to chronic valve degeneration, with nearly half of the cases linked to congenital anomalies, especially bicuspid aortic valves. Patients with AR secondary to bicuspid valve disease tend to be approximately 20 years younger, are predominantly male, and often present with concomitant dilatation of the ascending aorta.[39]

Mechanistically, AR results from inadequate cusp coaptation due to primary leaflet pathology (e.g. bicuspid degeneration, myxomatous disease, endocarditis) or secondary aortic root dilatation.

Rheumatic AR typically exceeds stenosis in severity, caused by leaflet fibrosis and retraction with commissural fusion.[40] It frequently accompanies rheumatic MV involvement and progresses to mixed valvular disease,[9] with haemodynamic severity underestimated if AR coexists with AS.

A global expert panel emphasized echocardiography as the primary tool for AR assessment, with CMR complementing certain aspects. Key insights included the importance of LV size and function, potential revision of current intervention thresholds, potential value of LV end-systolic volume index, and interest in emerging markers, such as LV global longitudinal strain and regurgitant fraction (RF).[39] Women have smaller LV volumes and may show less dilatation in response to AR than men, despite similar disease severity.[41] Women are therefore referred later than men for intervention, since the current guidelines do not account for sex-specific LV remodelling.[42] Standard intervention thresholds based on LV size may therefore underestimate risk in women, highlighting the need for sex-specific criteria.[43]

Transthoracic and transoesophageal echocardiography

TTE is the first-line tool for evaluating AR, providing insights not only regarding valve anatomy, mechanism, and haemodynamic impact but also heart chamber assessment. When TTE images are suboptimal, TEE offers improved visualization of valve morphology, mechanism, and severity (*Figure 3*). Three-dimensional echocardiography or CMR with volumetric assessment yields important insight in quantification in case of eccentric jets not clearly defined by the proximal isovelocity surface area (PISA) method (*Figure 4*). In severe AR, women and older adults present with smaller LV dimensions than men and younger patients, yet adverse outcomes occur at lower LV end-systolic volume index (LVESVi) thresholds. Notably, body size alone does not account for these differences. In a large cohort, Akintoye *et al*. showed that adverse events occurred at LVESVi cut-offs of 50 mL/m^2 in younger men, 35 mL/m^2 in older men, and 27 mL/m^2 in women. These findings indicate that LV dilatation is not always a reliable marker of disease severity—particularly in women and older patients—and that reliance on conventional cut-offs may underestimate AR severity and delay intervention in these subgroups.[43] In contrast, recent evidence shows that LA remodelling progresses similarly across sex and age groups and may provide more uniform and reliable criteria for guiding intervention timing in AR, with thresholds of LA reservoir strain $\leq$35% and LA volume index $\geq$37 mL/m^2 associated with adverse outcomes.[44]

Cardiac magnetic resonance and cardiac computed tomography

Age- and sex-specific CMR-based parameters may improve accuracy in assessing AR severity through precise quantification, thereby potentially guiding intervention trigger.[45] CMR is particularly valuable in the presence of eccentric regurgitant jets, discordant echocardiographic measurements, or when there is a discrepancy between the degree of LV dilatation and the severity of AR. Beyond volumetric quantification, CMR also refines myocardial characterization and provides a robust reference to validate echocardiographic findings.

Recent CMR data suggest that women exhibit a steeper RF–RVol relationship, meaning they tend to have higher RF for the same RVol, likely due to lower stroke volume. Consequently, the optimal RVol CMR-derived cut-off for severe AR was lower in women (39 mL) than in men (59 mL).[45] These findings suggest that RF may be a more reliable metric than RVol for assessing AR severity, especially in women. Finally, CMR also revealed sex-specific differences in myocardial tissue

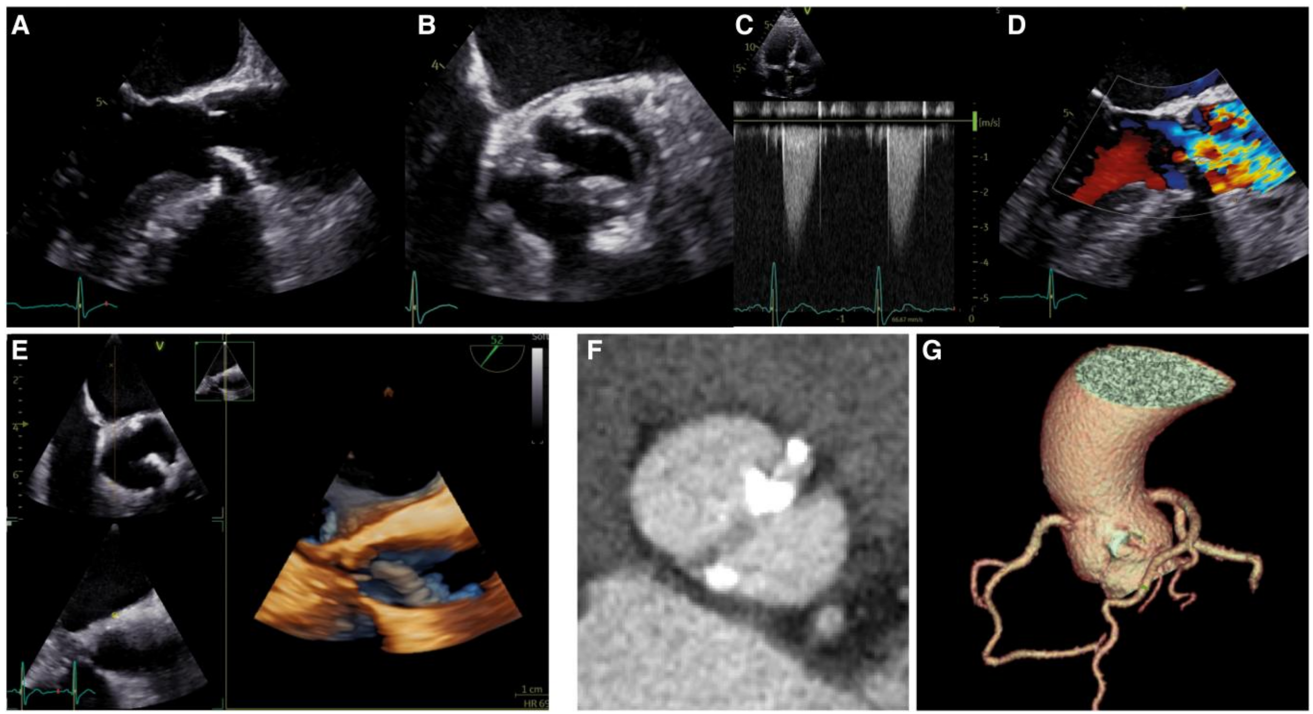

Figure 2 Bicuspid aortic valve (BAV) in a 63-year-old man. Transoesophageal echocardiography (2D and 3D; panels *A* to *E*) demonstrates a BAV with a two-sinus anatomy, which was confirmed by computed tomography (CT; panels *F* and *G*), a feature that is more commonly encountered in men. Interestingly, 3D transoesophageal echocardiography identified a long, calcific longitudinal band located just above the aortic valve, within the aortic root. CT imaging further delineated the anatomy of the aortic root and ascending aorta.

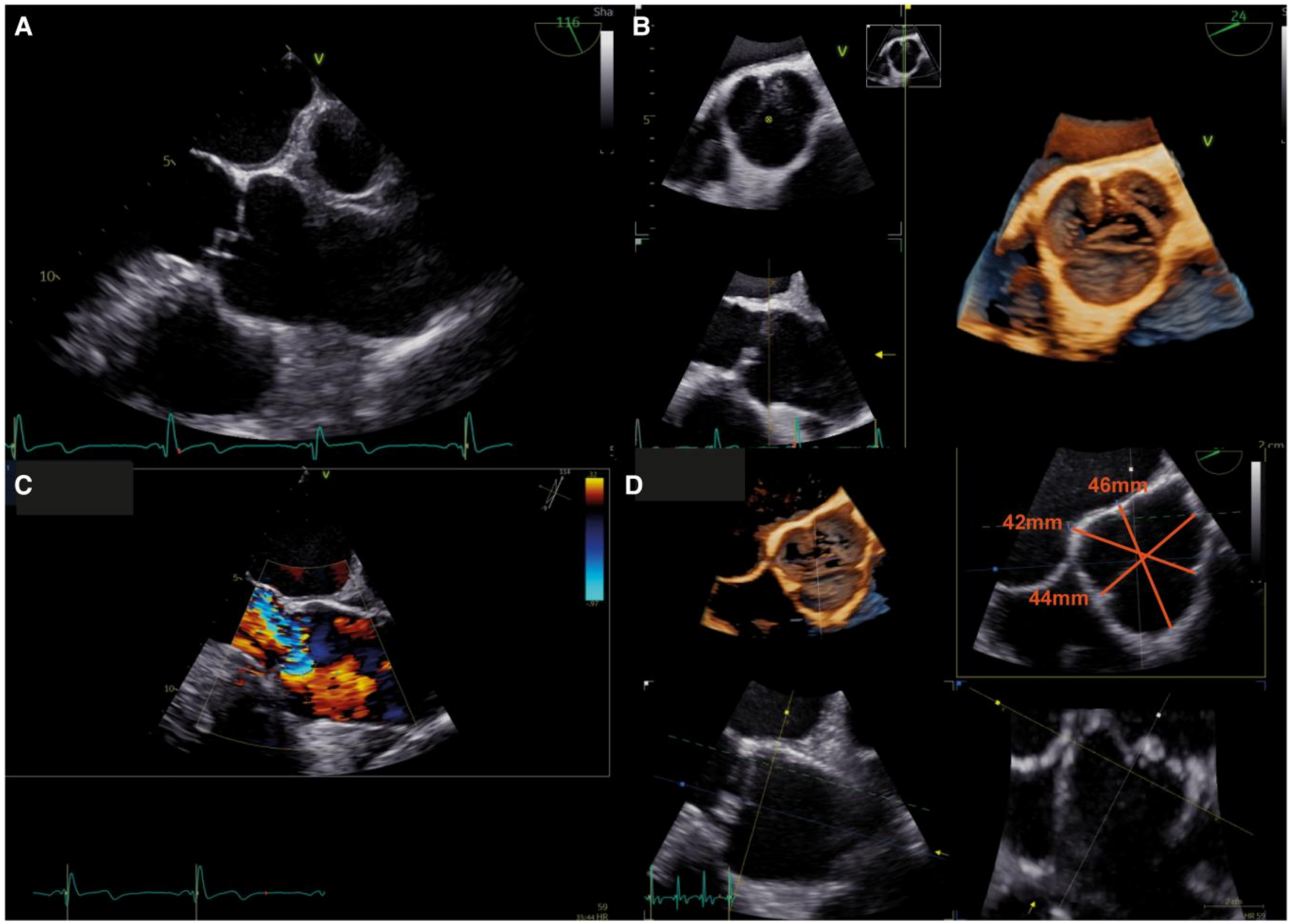

Figure 3 Primary aortic regurgitation in a 71-year-old man. Two- and 3-dimensional transoesophageal echocardiography revealed a 'transverse fold' in the right coronary cusp (panels *A* and *B*), suggestive of cusp prolapse (more frequently observed in men). Colour Doppler imaging demonstrated a markedly eccentric, severe regurgitant jet (panel *C*). By 3D transoesophageal imaging, the aortic root appeared dilated (panel *D*).

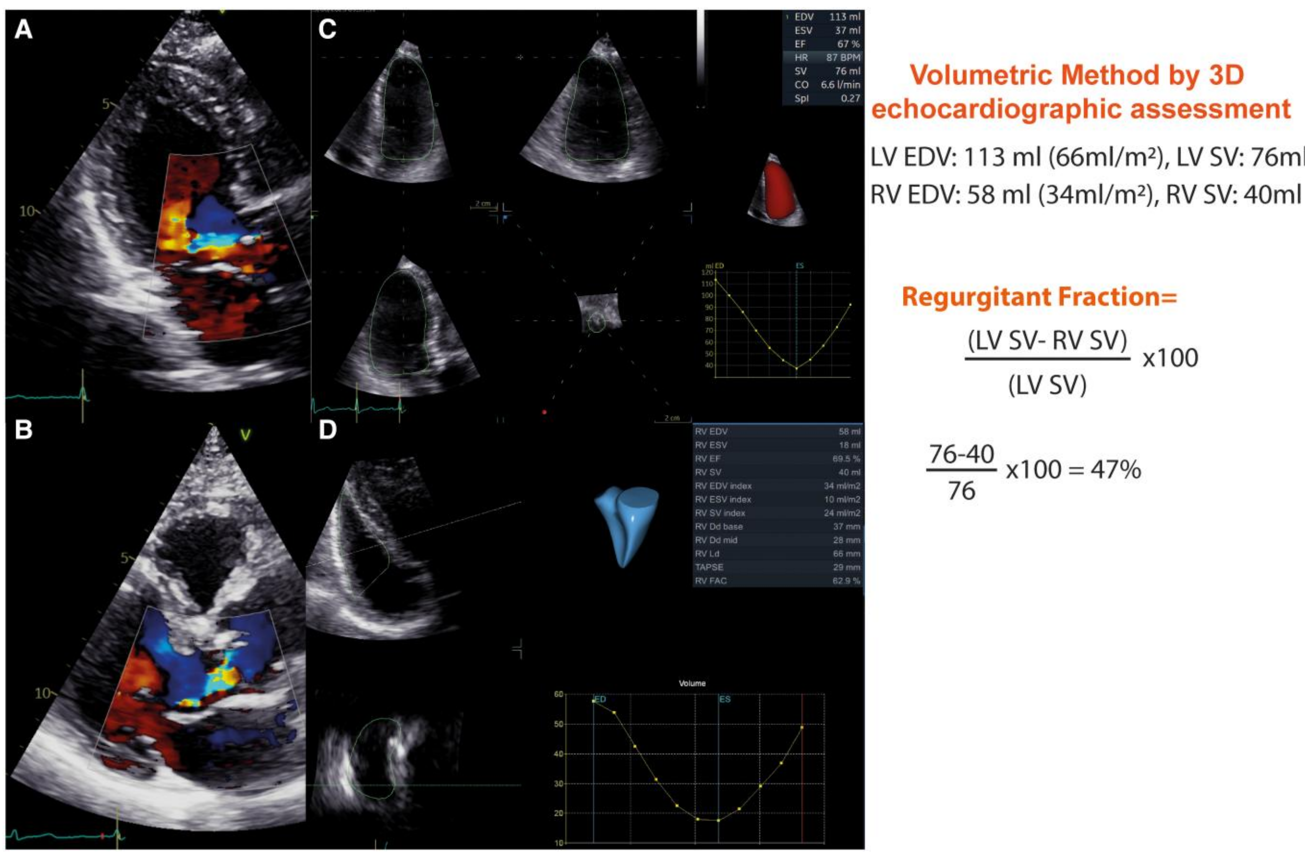

Figure 4 Example of a 58-year-old woman with isolated aortic regurgitation (AR). Due to an eccentric regurgitant jet (panels *A* and *B*), quantification by the conventional PISA method was not feasible. Three-dimensional volumetric assessment (panels *C* and *D*) demonstrated a left ventricular end-diastolic volume (LVEDV) of 113 mL (66 mL/m^2) with a stroke volume (SV) of 76 mL, and a right ventricular end-diastolic volume (RVEDV) of 58 mL (34 mL/m^2) with an SV of 40 mL. The calculated regurgitant fraction was 47%, confirming severe AR (>35%).

characterization: women showed higher native T1 and ECV values, indicative of more diffuse myocardial fibrosis compared to men.[45]

Both CMR and CT improve the assessment of the aortic root and ascending aorta, allowing for personalized surveillance in cases of coexistent aortic dilatation as a possible mechanism underlying AR. Women with ascending aortic aneurysms are typically older at diagnosis, more frequently show tubular involvement, and exhibit faster growth in that segment, whereas men more often have root involvement with more rapid root dilatation over time.[46] Once again, despite these sex-specific differences in anatomy and progression, no sex-specific thresholds have been proposed in the current guidelines, and consequently, the current definition of disease severity may underestimate risk in women.[47]

Sex differences in mitral valve stenosis

Mitral valve diseases, including mitral regurgitation (MR) and MS, are highly prevalent conditions, with significant sex-specific variation in pathophysiology, clinical presentation, and imaging expression. These differences often necessitate a tailored imaging approach, particularly in women, in whom current echocardiography thresholds may underestimate disease severity.[48]

Aetiologies and mechanisms

Nonrheumatic MS, usually caused by mitral annular calcification (MAC) extending into the leaflets, is more common in elderly women and carries a high burden of comorbidities, serving as a marker of increased cardiovascular risk.[49]

Rheumatic MS, by contrast, predominantly affects young women in developing countries (*Figure 5*).[50] Despite favourable outcomes with balloon valvuloplasty, access remains limited in low-income countries.

It results from inflammatory injury during rheumatic carditis, leading to leaflet thickening, commissural fusion, and calcification that progressively obstruct mitral inflow. Chronic pressure overload on the left atrium promotes atrial fibrillation, pulmonary hypertension, and ultimately right heart dysfunction. The female predominance in rheumatic MS is thought to reflect heightened autoimmune susceptibility, which accelerate the onset of symptoms.[51]

Transthoracic and transoesophageal echocardiography

MS quantification may be affected by sex differences. Current guidelines emphasize mitral valvular area planimetry as the reference method for severity assessment in MS,[52] particularly to overcome underestimation in low-gradient forms.

Women are more likely to present with discordant severity parameters, such as low mean transmitral gradients (below 10 mmHg) despite a severely reduced mitral valve area ($\leq$1.5 cm^2, or $\leq$1.0 cm^2 in very severe cases).[53] This discrepancy may be explained by their smaller body size, lower stroke volume, and lower transvalvular flow, which can lead to underestimation of haemodynamic severity when relying solely on gradient-based assessment.

A recent study by Cho *et al*. further highlighted the prognostic value of LA strain in this predominantly female phenotype. However, additional data addressing sex-specific differences and thresholds are still needed.[54]

TEE and 3D echocardiography are key for mitral stenosis assessment, providing superior visualization of commissural fusion, leaflet thickening, and restricted motion. 3D multiplanar reconstruction refines valve area planimetry, while TEE offers higher spatial and temporal resolution for evaluating MAC, including caseous degeneration, and for procedural planning. As MAC-related MS is often more extensive in women, these modalities are critical for accurate characterization and management.

Cardiac magnetic resonance and cardiac computed tomography

CT is critical in assessing the severity and extent of MAC-related MS. Women tend to show more extensive MAC phenotypes (partial/horseshoe) that influence decisions between surgical replacement, repair, or transcatheter interventions.[55]

CMR has limited direct utility in MS quantification but provides valuable information on atrial remodelling, fibrosis, and pulmonary pressures.

Sex differences in mitral valve regurgitation

Aetiologies and general mechanisms

The leading cause of primary MR is leaflet prolapse, with a higher prevalence in women (*Figure 6*).[56]

Primary MR most often results from myxomatous degeneration, causing chordal elongation or rupture and leaflet flail, whereas secondary MR arises from LV or LA remodelling that impairs leaflet coaptation. Sex influences these mechanisms: women with prolapse typically show diffuse, thickened bileaflet disease, while men more often present with isolated posterior prolapse and flail.[1] Women with mitral prolapse progress to severe regurgitation less frequently than men, and calcification patterns diverge, with posterior leaflet calcification more common in men and MAC in women.[1]

Recently, arrhythmogenic mitral valve prolapse has gained attention. It is more commonly observed in young women and is associated with mitral annular disjunction and papillary muscle/infero-basal LV fibrosis. These structural abnormalities may serve as the substrate for sudden cardiac death, even in the absence of significant MR.[57]

Secondary MR arises from LV remodelling due to ischaemic or non-ischaemic causes, or from LA and annular remodelling. Men are nearly twice as likely as women to develop heart failure with reduced ejection fraction (HFrEF) and the ventricular MR phenotype,[58] while women more commonly present with heart failure with preserved EF (HFpEF) and the secondary atrial MR phenotype.[59]

Transthoracic and transoesophageal echocardiography

TTE is the first-line tool for MR evaluation. However, sex-neutral thresholds for effective regurgitant orifice area (EROA) and regurgitant volume (RVol) may underestimate MR severity in women due to smaller LV volumes.[48] Regurgitant fraction (RF) may therefore be the preferred metric in women, derived by 3D echocardiography or CMR (*Figure 7*).

Non-holosystolic or eccentric jets, more frequent in women with bileaflet prolapse or annular calcification, complicate quantification, contributing to diagnostic delays and reduced surgical referral rates despite equal or greater symptom burden.

Surgical timing is also challenging: thresholds based on LV end-systolic diameter (LVESD) and LVEF neglect sex-specific remodelling patterns, especially when LV dimensions are not indexed to body size. In a large US cohort, mortality risk in women increased at a lower indexed LVESD (1.8 cm/m^2 vs. 2.1 cm/m^2 in men). Both sexes had an increased risk when LVEF dropped below 58%, but women showed a steeper increase.[60] This supports adopting sex-specific thresholds using indexed dimensions and LV volumes.

In primary MR, assessment of LA size and function is particularly important in women, who often present with marked LA dilatation despite normal or only mildly enlarged LV dimensions. In this context, the use of atrial-dedicated echocardiographic views is recommended to ensure accurate measurement and to avoid underestimation of LA size, especially in elderly women.

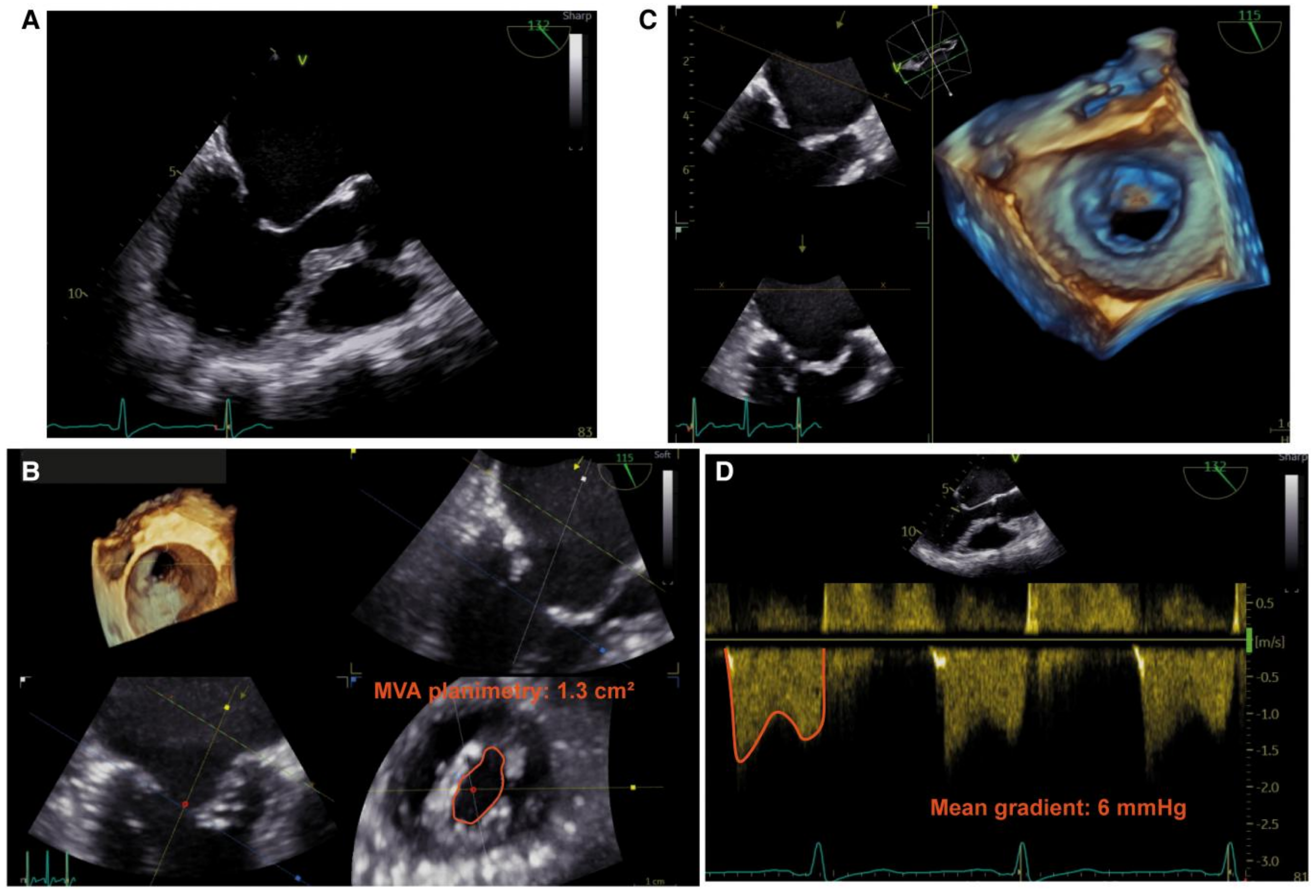

Figure 5 Rheumatic mitral stenosis (MS) in a 52-year-old woman. Rheumatic MS is more commonly observed in women. In this case, 3D transoesophageal echocardiography (panels *A* and *C*) demonstrated commissural fusion and diastolic doming of the anterior leaflet, with a markedly reduced mitral valve area (1.3 cm^2), despite mean transmitral gradients in the non-severe range (6 mmHg; panel *D*). This pattern is frequently encountered in women, who often present with reduced anterograde flow and lower transmitral gradients. MVA, Mitral valve area (measured by planimetry).

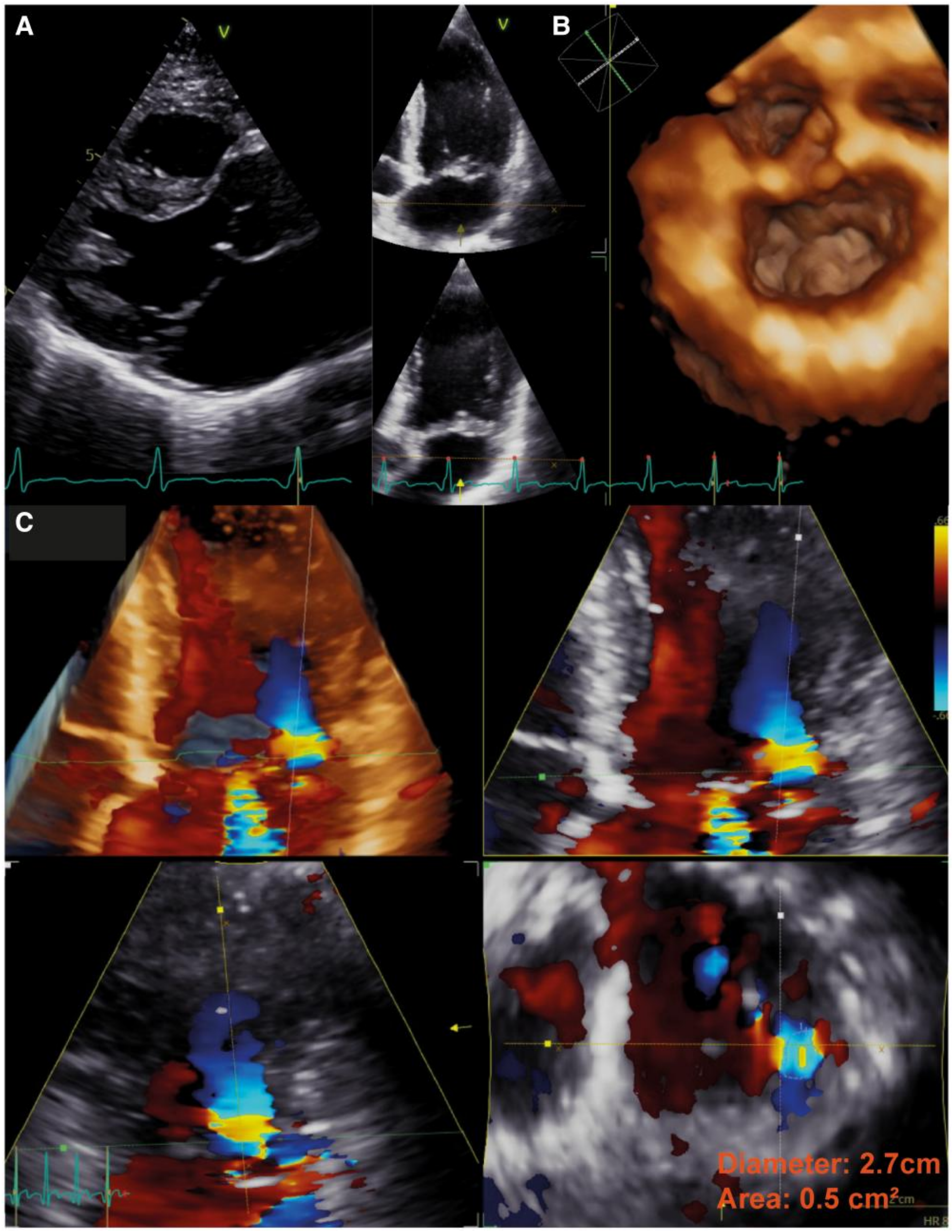

Figure 6 Primary mitral regurgitation (MR) in a 55-year-old woman. In women, mitral valve prolapse often presents with more complex anatomy and frequent bi-leaflet involvement. In this case, significant prolapse of the A2 and P2 scallops—more pronounced in P2—(panels *A* and *B*) resulted in severe MR with an eccentric regurgitant jet. The measurement of the 3D vena contract was performed using 3D transthoracic echocardiography (panel *C*).

Emerging evidence suggests that sex-specific cut-offs may be needed for myocardial deformation indices. Women demonstrated lower LA reservoir strain (22.2% vs. 25.0%) and higher stiffness (0.56 vs. 0.44) than men, even with smaller MR volumes. Female sex independently predicted higher LA stiffness, highlighting sex differences in atrial remodelling.[61]

Women more frequently present with anatomically complex primary MR. Distinct morphologies include bi-leaflet or anterior leaflet prolapse, generalized myxomatous degeneration, severe MAC, and rheumatic involvement with commissural fusion/restricted motion (*Figure 8*).[50]

MAC distribution also varies by sex: men more often show posterior leaflet involvement, while women more often have MAC confined to the annulus.[1]

3D Echo provides superior anatomical definition, especially critical in women, where subtle or multifocal prolapse may be missed in 2D and MAC severity underestimated. It is essential for preprocedural planning in both surgery and transcatheter interventions.[62]

Cardiac magnetic resonance and cardiac computed tomography

CMR is particularly valuable in women with complex MR (late systolic or multiple jets) where echo-CMR concordance is low. CMR-derived RVol better predicts mortality and surgery than echo.[63]

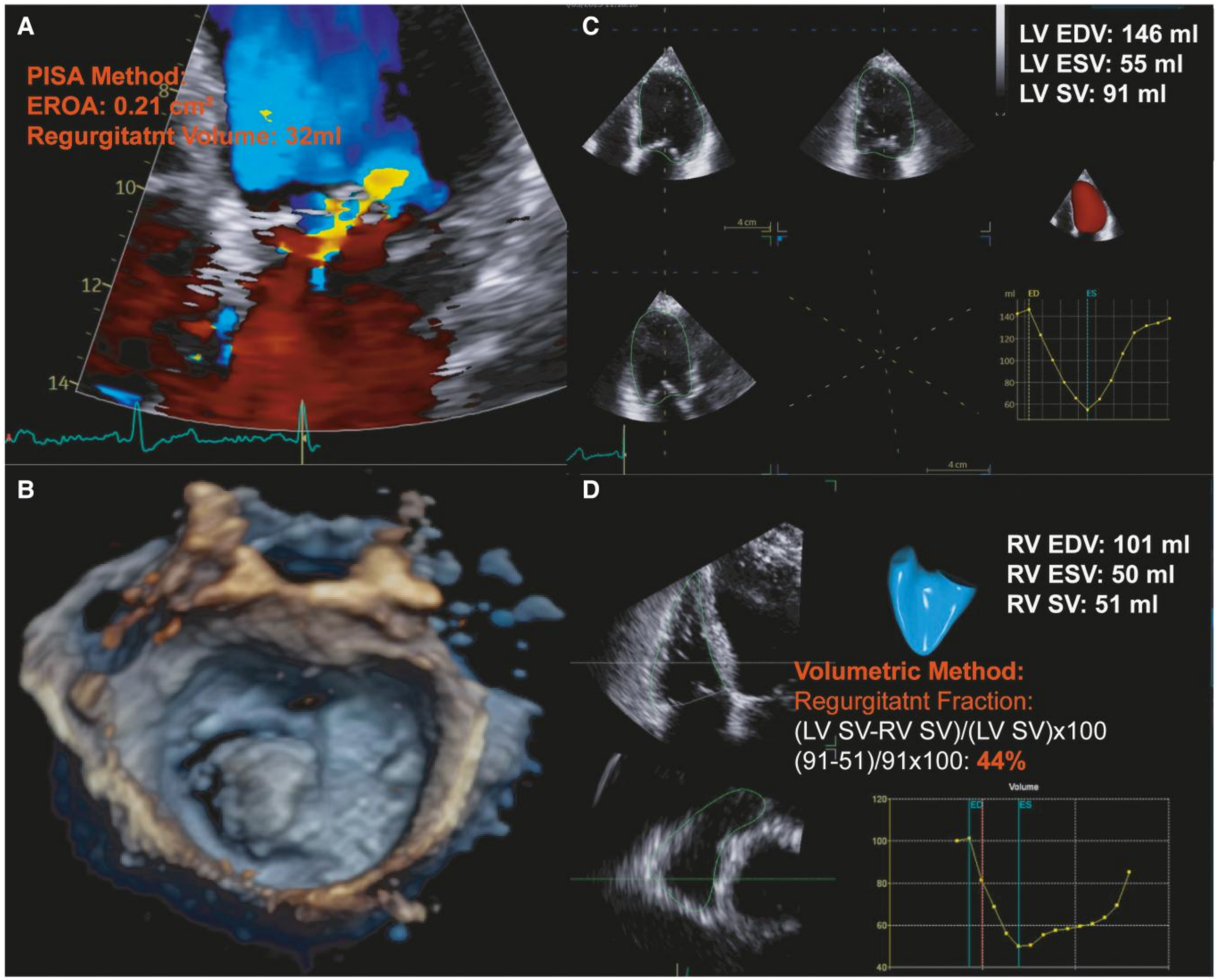

Figure 7 Example of a 65-year-old woman with mitral valve prolapse of the P2 scallop (panels *A* and *B*). Quantification by the PISA method yielded an EROA of 0.21 cm^2 and regurgitant volume of 32 mL, underestimating the severity of mitral regurgitation (MR). Three-dimensional volumetric assessment (panels C and *D*) demonstrated a left ventricular end-diastolic volume (LVEDV) of 146 mL (75 mL/m^2) with a stroke volume (SV) of 91 mL, and a right ventricular end-diastolic volume (RVEDV) of 101 mL (52 mL/m^2) with an SV of 51 mL. The calculated regurgitant fraction was 44%, consistent with severe MR (>40%).

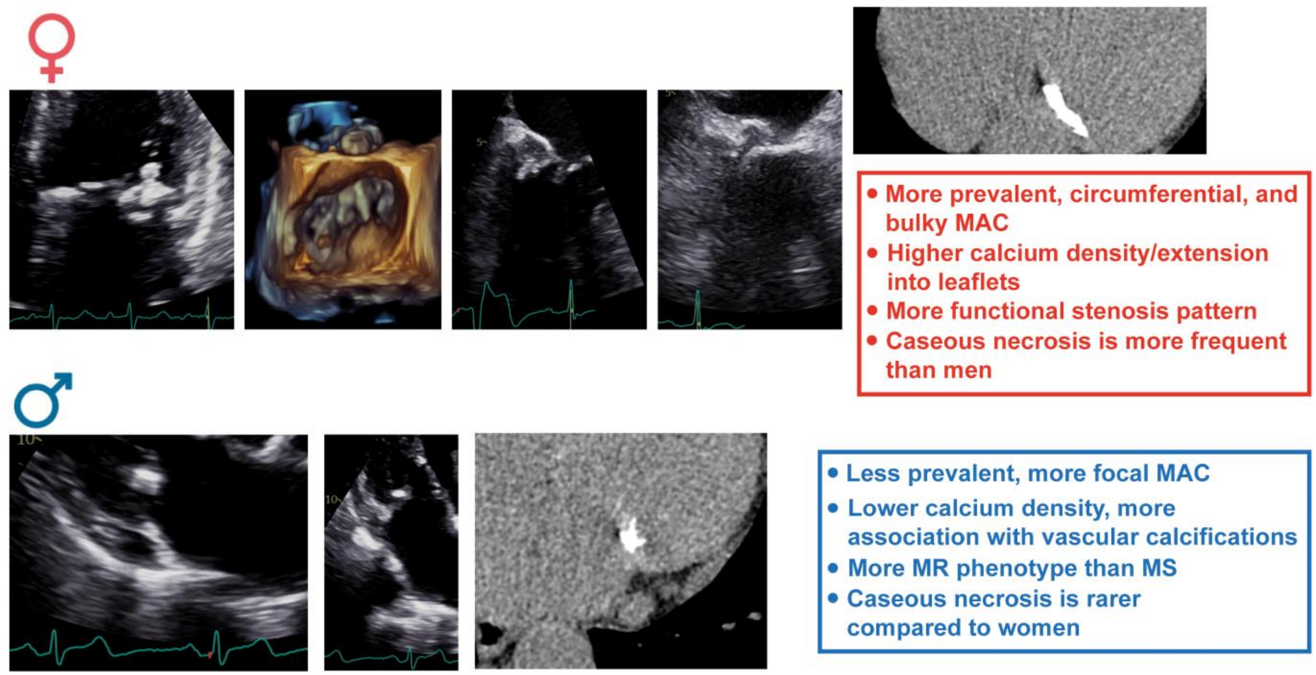

Figure 8 Sex-related differences in mitral annular calcification (MAC) and caseous necrosis. Representative echocardiographic (2D, 3D) and CT images of MAC in women (top panel) and men (bottom panel). Legend: MAC, mitral annular calcification.

In arrhythmic mitral valve prolapse, CMR detects high-risk features (mitral annular disjunction, papillary muscle LGE), linked to malignant ventricular arrhythmias.[64] Interstitial fibrosis (ECV fraction) is also associated with arrhythmic phenotypes, especially in women, suggesting a primary myocardial substrate contributing to female predominance in arrhythmic prolapse.[65]

CT is useful in evaluating MAC, which is more extensive in women despite fewer traditional risk factors.[66] Women with MR often present with more extensive MAC, smaller annuli, steeper mitro-aortic angles, and higher left ventricular outflow tract (LVOT) obstruction risk, making CT critical for individualized procedural planning.[55]

A recent prospective CMR-based study found no sex-based differences in LV remodelling or outcomes when MR was quantified volumetrically. MR volume and fraction, not sex, were the key prognostic predictors.[67] This challenges echo-derived findings relying on linear dimensions and highlights the need for accurate volumetric assessments.

Sex differences in tricuspid valve regurgitation

Overall, tricuspid regurgitation (TR) is more frequently observed in women, particularly in the setting of functional aetiologies. Atrial secondary TR, often associated with atrial fibrillation and HFpEF, is encountered more commonly in women. Additionally, ventricular secondary TR, often linked to left-sided cardiac disease, is also seen more commonly in women. However, men with TR more frequently present with coexisting LV systolic dysfunction (*Figure 9*).[68]

Most TR is secondary, arising from right atrial or ventricular dilatation that stretches the annulus and impairs leaflet coaptation, often in the context of atrial fibrillation or pulmonary hypertension. Anatomical variability of the tricuspid valve, including four-leaflet morphology in many patients, may further influence coaptation.[69]

Women tend to be referred later for surgery or intervention,[70] a delay that may be partially attributed to the use of absolute right ventricle (RV) size and annular dimension thresholds,[71] which may potentially underestimate disease severity and cardiac damage in smaller hearts of women.

Cardiac implantable electronic device–related and primary TR represent a minority of TR cases, accounting for approximately 10–15% and 5–10%, respectively. Primary TR stems from varied causes (i.e. trauma, congenital diseases, drugs, endocarditis, radiation exposure, rheumatic disease, and carcinoid syndrome) and typically involves structural damage, such as leaflet restriction or perforation. Endocarditis- and carcinoid-related TR are more common in men, while rheumatic TR predominates in women.[72,73] Rheumatic tricuspid involvement occurs rarely isolated, almost frequently with rheumatic MS or AR.[9] Diastolic doming of the leaflets and commissural fusion represent the hallmarks.

Sex-specific data for Cardiac implantable electronic device–related TR are currently lacking.

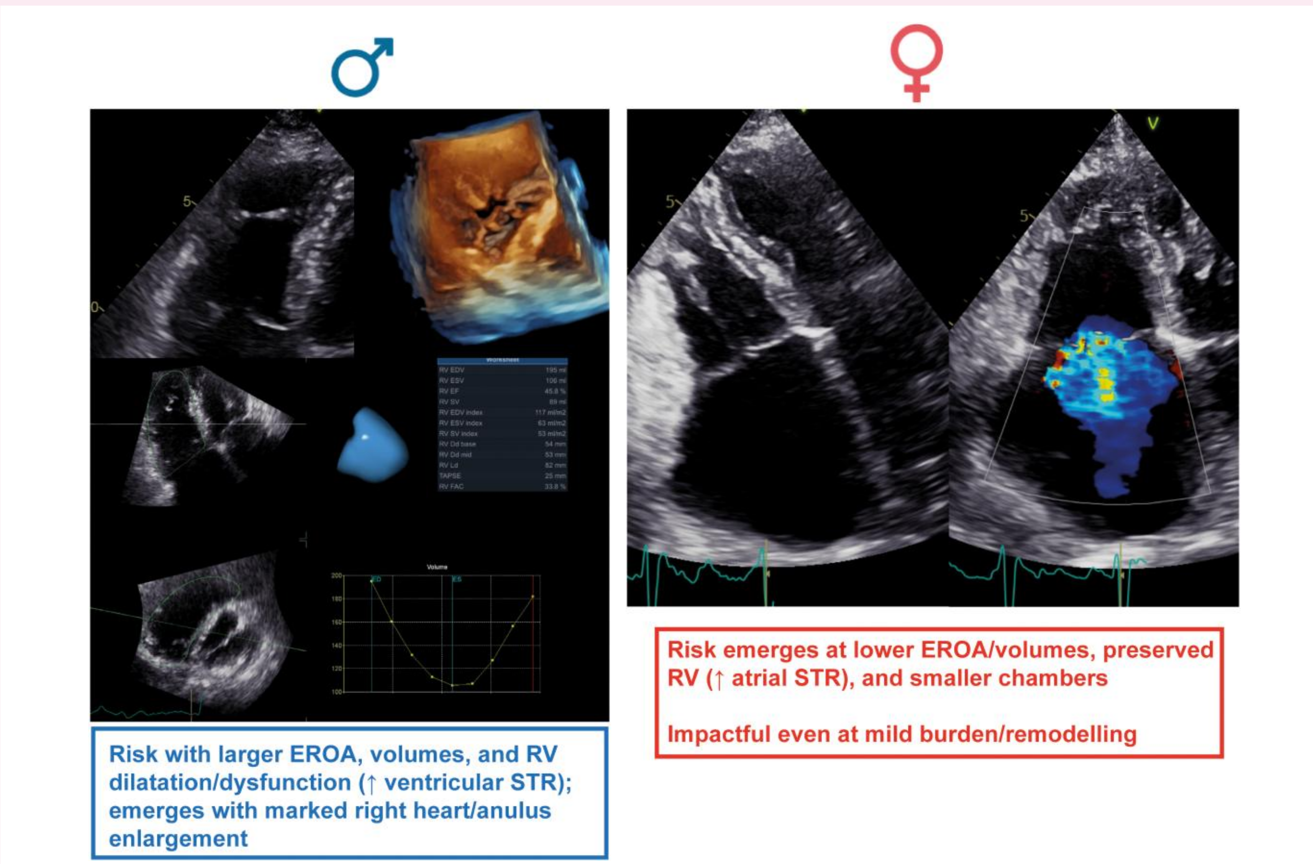

Figure 9 Sex differences in secondary tricuspid regurgitation (TR). In men, secondary TR is associated with a larger effective orifice area (EROA), regurgitant volumes (RVol), and a more common ventricular phenotype characterized by significant dilatation or dysfunction of the right ventricle. In women, risk occurs at lower EROA and RVol, with a more common atrial phenotype, characterized by a dilated right atrium and tricuspid annulus, smaller right ventricular size, with preserved systolic function.

Transthoracic and transoesophageal echocardiography

TTE remains essential for grading and evaluating tricuspid leaflet anatomy and RV function in the context of primary and secondary TR. Current TR grading applies uniform thresholds for EROA and RVol, which do not account for the obvious anatomical and physiological differences between sexes. Women often have smaller RVs and a more atrial secondary TR phenotype,[74] leading to lower RVol despite similar symptom burden. These sex-neutral cut-offs may potentially lead to underdiagnosis and treatment delays in women.

TTE also enables reliable assessment of RV–pulmonary arterial coupling through the TAPSE/mPAP ratio, which has emerged as an independent predictor of mortality in the specific setting of TR. Importantly, sex-specific thresholds have been identified: a TAPSE/mPAP ratio below 0.434 mm/mmHg in men and 0.612 mm/mmHg in women indicates increased mortality risk, underscoring the need for sex-adjusted risk stratification.[75]

TTE further identifies sex-specific predictors of secondary TR: atrial fibrillation and annulus dilatation are more strongly associated with TR in women, while tenting height is more relevant in men.[76] These differences likely reflect intrinsic structural variations, such as reduced annular elasticity in women. Standard 2D four-chamber displaying septal-to-lateral annular dimension may miss identifying posterior annular remodelling associated with atrial fibrillation, highlighting the need for a second-line, 3D-based, sex-specific assessment of tricuspid annulus.

3D TTE echocardiography is the cornerstone for a comprehensive assessment of RV geometry and function, especially in the ventricular secondary TR phenotype more commonly encountered in men. It allows more precise quantification and grading of the RV dysfunction, refining risk stratification.[77] Notably, women experience adverse outcomes at lower RV volumes and higher RV ejection fractions, highlighting the need for sex-specific thresholds in TR evaluation.[71]

Finally, 3D TEE and TTE are valuable tools for en-face visualization of the tricuspid leaflets, allowing for clear assessment of leaflet anatomy and prolapse (more common in women),[78] tricuspid annulus dimension, coaptation gaps, and jet direction, all of which are necessary for planning the interventional strategy.[79]

Cardiac magnetic resonance and cardiac computed tomography

Besides, allowing precise measurement of annular dimensions and remodelling, CMR provides accurate and precise evaluation of TR and right heart structure and function, offering clear advantages over echocardiography, despite limitations due to costs and accessibility. It provides accurate measurements of RV and RA volumes, mass, and function, using reproducible techniques that are unaffected by body habitus.[80] Importantly, CMR reference values for RV and RA size and mass are consistently higher in men than in women,[81] even after indexation for body surface area, highlighting the need for sex-specific thresholds when interpreting TR severity and RV remodelling.

CMR allows for the visualization of subtle regional wall motion abnormalities, quantifies regurgitant flow, RVol, and RF,[81–85] and assesses tissue characteristics, providing critical insights into sex-related differences in disease expression and progression. In surgical candidates, CMR-derived parameters, such as RV end-systolic volume index and ejection fraction, predict outcomes and may help tailor the timing of intervention differently in men and women. Further research is required for sex-specific CMR features guiding risk stratification and intervention referral.

CT is an important tool to precisely assess the tricuspid annulus and leaflet geometry, potentially revealing sex-differences. Notably, annular remodelling follows different patterns by sex: men show predominant septo-lateral dilatation, while women exhibit more diffuse annular enlargement, suggesting sex-specific pathways of TR progression. This feature may be due to different annular anatomies: men typically show the presence of myocardial fibres, which are consistently absent in the tricuspid annuli of women.[69,71–74]

In a predominantly female cohort (65%) with atrial fibrillation, CT imaging highlighted the association between larger anterior and posterior leaflet angles, increased annular dimensions, and massive/torrential TR. These leaflet angles independently predicted severe TR and were associated with non-central jet locations and greater annular ellipticity.[83]

A tailored triphasic contrast-enhanced CT protocol enabled optimal right heart opacification and accurate 3D assessment of tricuspid valve geometry across the cardiac cycle. Scanning should be ECG-gated and with multiphasic acquisition in order to allow precise measurements. This approach showed high reproducibility and revealed progressive annular dilatation and reduced non-planarity with increasing TR severity.

Multiple and mixed-valvular heart diseases

Multiple and mixed VHD (MMVD), defined as either involvement of more than two valves with stenotic or regurgitant lesions, or combined stenosis and regurgitation of the same valve, carries a particularly poor prognosis, making accurate imaging essential for risk stratification.[84]

In the VHD II survey, women with MMVD were generally older, more symptomatic, and carried higher EuroSCORE II values, yet they were less often referred for intervention, even when presenting with multiple left-sided valve lesions and clear guideline-based indications.[85]

Combined AS and AR is associated with adverse outcomes, especially in the setting of LV dysfunction or ischaemic cardiomyopathy, without evidence of sex-related differences in outcomes in a small retrospective cohort. Echocardiography and CMR remain essential for quantifying LV remodelling and systolic performance, though sex-related differences in chamber size, geometry, and flow patterns complicate interpretation.

Paradoxical low-flow, low-gradient AS, more prevalent in women, is further exacerbated by concomitant MR and/or TR, which reduce forward stroke volume and raise pulmonary pressures.[86] Similarly, in AR, women are disproportionately burdened by secondary MR, reflecting advanced LV and LA remodelling, AF, and pulmonary hypertension. Patients with combined AR and functional MR, typically older and more often female, present with the most adverse profile: the largest LV volumes, lowest LVEF, and the highest prevalence of right-sided pressure overload, tricuspid regurgitation, and AF. Within this subgroup, AF and severe LA enlargement independently predict mortality, defining a particularly high-risk phenotype.[87]

These observations highlight how sex-related differences in ventricular and atrial adaptation, as revealed by advanced imaging, decisively shape the natural history and therapeutic response of MVD. Yet, current evidence is largely derived from small, single-center studies with limited statistical power. Large, ongoing registries such as European Association of Cardiovascular Imaging-MMVD and MULTIVALVE, which integrate multimodality imaging endpoints, are anticipated to yield more granular sex-specific insights and ultimately support the development of personalized, imaging-guided strategies in the management of MVD.[84]

Infective endocarditis

Infective endocarditis (IE) exhibits distinct sex-based differences that are increasingly recognized through multimodality imaging. IE is more common in men, who often present with native aortic valve involvement, while women are more likely to have mitral valve involvement,

Table 3 Valvular heart disease and pregnancy: physiological echocardiographic considerations and high-risk features

Valvular disease	Echocardiographic changes with pregnancy physiology	Specific high-risk features (maternal/foetal risk)
Aortic stenosis (AS)	↑ cardiac output → higher transvalvular gradients; small annulus exaggerates afterload	Severe symptomatic AS (contraindication to pregnancy); bicuspid valve with aorta >50 mm; rapid gradient progression
Aortic regurgitation (AR)	↓ systemic vascular resistance → lower regurgitant fraction; LV dilatation may lag	Severe AR with LV dysfunction (LVEF <50%) or NYHA III–IV symptoms
Mitral regurgitation (MR)	↑ preload → larger regurgitant volume; eccentric/multiple jets harder to quantify	Severe MR with LV dysfunction or pulmonary hypertension
Mitral stenosis (MS)	↑ heart rate → shorter diastolic filling, higher mean gradients	Severe symptomatic MS; pulmonary hypertension; RV failure risk
Tricuspid regurgitation (TR)	↑ plasma volume → more annular dilatation; altered TAPSE/mPAP ratio	Severe functional TR with RV dysfunction or pulmonary hypertension

AR, aortic regurgitation; AS, aortic stenosis; AV, aortic valve; CMR, cardiac magnetic resonance; EROA, effective regurgitant orifice area; LVEF, left ventricular ejection fraction; LV, left ventricle; LVESD, left ventricular end-systolic diameter; LVESDi, left ventricular end-systolic diameter indexed; MR, mitral regurgitation; MS, mitral stenosis; mWHO, modified World Health Organization; NYHA, New York Heart Association; PA, pulmonary artery; PET, positron emission tomography; PS, pulmonic stenosis; RV, right ventricle; STR, secondary tricuspid regurgitation; SVR, systemic vascular resistance; TAPSE, tricuspid annular plane systolic excursion; TEE, transoesophageal echocardiography; TTE, transthoracic echocardiography; TR, tricuspid regurgitation.

underlying immunosuppressive condition, and heart failure at presentation.[88] Vegetations in women tend to localize more often on the mitral and aortic valves, while in men, they are more frequently found on the tricuspid valve.[88] Women are more likely to present with culture-negative IE, potentially leading to misrecognition.[88] Multimodality imaging with TEE, cardiac CT, and 18F-FDG/position emission tomography-CT plays a critical role in improving detection, particularly in women, where TTE may have lower sensitivity due to smaller cardiac structures and breast tissue attenuation. Recognizing these sex-based disparities can enhance diagnostic precision and optimize individualized care pathways.

Valvular heart disease and pregnancy

Pregnancy induces profound haemodynamic changes, including increased cardiac output and reduced systemic vascular resistance, that can unmask or exacerbate underlying VHD.[89] As such, imaging plays a central role in preconception assessment, risk stratification, and serial monitoring during pregnancy and postpartum[89] (*Table 3*). TTE is the first-line tool for assessing valve anatomy, lesion severity, ventricular function, and haemodynamics. In asymptomatic women with suspected significant stenosis, exercise echocardiography provides valuable insights in the preconception phase. TEE or non-contrast CMR may be indicated when TTE is limited or when precise aortic measurements are required.

In bicuspid AS, imaging identifies women at high risk during late pregnancy and delivery. Severe symptomatic AS contraindicates pregnancy, while asymptomatic women with preserved LV function may be managed medically with close imaging follow-up.[1]

Regurgitant lesions including AR or MR are generally better tolerated during pregnancy but warrant regular imaging surveillance to monitor for ventricular dilatation or dysfunction. In AR, serial echocardiographic tracking of LV size, function, and RVol is essential, along with the ascending aorta measurement. In MR, imaging informs the timing of surgery if symptoms or reduced LVEF are present. Well-compensated MR with normal LV and pulmonary pressures is often tolerated.[1]

Mitral and pulmonic stenosis are less common but can lead to pulmonary hypertension or RV failure. Severe symptomatic MS is also considered a contraindication to pregnancy. In pulmonic regurgitation, RV size and function should be closely monitored, especially in women with prior congenital repairs.

A proactive, imaging-guided approach, embedded in a multidisciplinary team, is essential to individualize care and optimize maternal and foetal outcomes in VHD.[1]

Conclusions

Sex-related differences in native VHD span aetiology, pathophysiology, cardiac remodelling, and clinical outcomes (*Graphical Abstract*). These differences influence disease expression and contribute to underdiagnosis, delayed referral, and potential undertreatment, particularly in women. Standard echocardiographic thresholds, largely derived from male-predominant cohorts, often fail to account for sex-specific variations in anatomy and physiology. Multimodality imaging is, therefore, central to overcoming these limitations. Tailored interpretation of regurgitant volumes, calcification burden, myocardial fibrosis, and ventricular remodelling is essential for accurate grading, staging of cardiac damage, and timely referral to intervention.

In addition to quantitative indices, careful attention should be given to chamber dimensions, changes in LV and LA size over time, markers of early dysfunction such as myocardial deformation imaging/biomarkers, and haemodynamic consequences including pulmonary pressures. Caution should be applied when assessing women with 'moderate-to-severe' lesions, as these patients may in fact harbour clinically significant disease that justifies earlier intervention or, at a minimum, intensified surveillance. Where standard measurements appear discordant with symptoms or remodelling, advanced imaging modalities such as 3D echocardiography or cardiac magnetic resonance can refine quantification.

Looking ahead, the incorporation of sex-specific evidence into practice guidelines is imperative to ensure equity and optimize outcomes. Greater representation of women in imaging registries, prospective cohorts, and randomized trials will be fundamental to building robust evidences. Key priorities for future research include the validation of sex-adjusted thresholds for flow indices, LV and RV dimensions, and myocardial deformation parameters; the integration of emerging imaging biomarkers such as CT-derived extracellular volume, PET tracers for valvular inflammation/calcification, and advanced CMR tissue characterization; and the development of sex-stratified risk models to refine intervention triggers.

A sex-aware, multimodality imaging strategy is thus both a present clinical necessity and a major research frontier. Closing these evidence gaps will allow earlier recognition of subtle disease phenotypes, better alignment of therapeutic timing, and ultimately, improved outcomes for women and men across the full spectrum of valvular heart disease.

Author contributions

Paolo Springhetti (MD (Writing—original draft [lead])), Ana G. Almeida (MD PhD (Writing—review & editing [supporting])), Denisa Muraru (MD PhD (Writing—review & editing [supporting])), and Marie-Annick Clavel (DVM PhD (Writing—review & editing [lead]))

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Data availability

No new data were generated or analysed in support of this manuscript.

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