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Multimodality imaging for myocardial injury in acute myocardial infarction and the assessment of valvular heart disease

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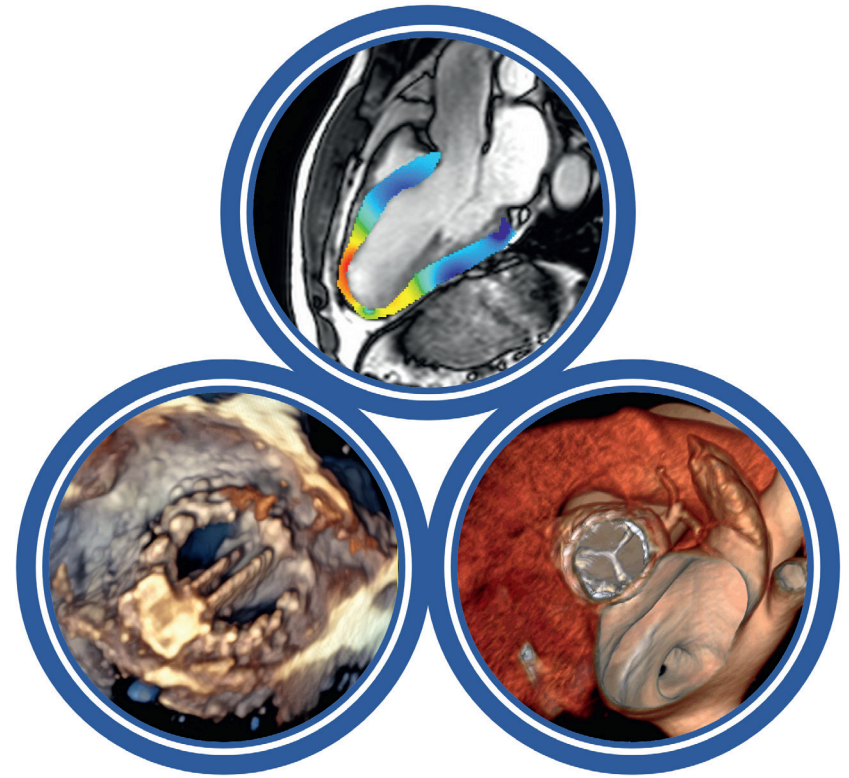
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Part II



**Multimodality Cardiac Imaging
in Valvular Heart Disease**

5

Imaging of valvular heart disease in heart failure

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ABSTRACT

Valvular heart disease (VHD) and heart failure (HF) are major health issues that are steadily increasing in prevalence in Western populations. VHD and HF frequently co-exist, which can complicate the accurate diagnosis of the severity of valve stenosis or regurgitation and affect decisions about therapeutic options. Transthoracic echocardiography is the first-line imaging modality to determine left ventricular (LV) systolic function, to grade valvular stenosis or regurgitation and to characterize the mechanism underlying valvular dysfunction. 3D transesophageal echocardiography, cardiovascular magnetic resonance and cardiac computed tomography are alternative imaging modalities that help in the diagnosis of patients with HF and VHD. The integration of multimodality cardiovascular imaging is important when deciding whether the patient should receive transcatheter valve repair and replacement therapies. In this article, the use of multimodality imaging to diagnose and treat patients with VHD and HF is reviewed.

INTRODUCTION

Heart failure (HF) is a rapidly growing public health problem with an estimated prevalence of more than 26 million people worldwide.¹ In developed countries the prevalence is 1–2% peaking at $\geq 10\%$ among people aged over 70 years.² In the United States, the lifetime risk of developing HF is 20% among individuals aged 40 years old or older.³ Diagnosing the underlying cause of HF is central to the choice of appropriate treatment. Significant valvular heart disease (VHD; moderate and severe) was found in 14% of patients who were referred for echocardiography due to suspected HF.⁴ Among patients with moderate and severe native VHD included in the Euro Heart Survey, 69.8% presented with HF symptoms and the most frequent valvular lesions were aortic stenosis (AS) and mitral regurgitation (MR).⁵

Cardiac imaging plays a central role in determining the mechanism and the severity of VHD as well as the degree of accompanying left ventricular (LV) remodeling and systolic dysfunction. The primary dilemma in patients with VHD and HF is to determine whether the LV dysfunction is due to the disease of the valve or the ventricle. In patients with AS and HF symptoms, LV systolic dysfunction is usually secondary to the valve disease, while in patients with HF and functional MR, LV systolic dysfunction and remodeling are primary and are responsible for mitral valve malcoaptation. Furthermore, LV dimensions and ejection fraction (LVEF) are key parameters to indicate the need for valve surgery.^{6–8} With advances in percutaneous valve interventions – transcatheter aortic valve replacement (TAVR) and percutaneous transcatheter mitral valve repair, several other imaging parameters need to be evaluated to assess feasibility and predict therapeutic success. Echocardiography is the primary imaging modality and may be complemented by cardiac computed tomography (CT) and cardiovascular magnetic resonance (CMR) when additional anatomical or functional information is needed. This review article focuses on the use multimodality imaging to evaluate patients with HF and most frequent VHD – MR and AS – and how to decide the optimal intervention.

MITRAL REGURGITATION IN HEART FAILURE

Significant (moderate and severe) MR is among the most common VHD, with an estimated prevalence of 1.7% in the United States peaking at 9.3% in people older than 75 years of age.⁹ In a study involving 70,043 patients with suspected HF referred for echocardiography, MR of any severity was found in 12.5% and moderate or severe MR in 3.1% of patients.⁴ MR is classified as primary (organic) if there is primary structural abnormality of any component of the

mitral valve apparatus (leaflets, chordae tendineae, papillary muscles or mitral annulus). The most common etiologies include degenerative disease, rheumatic disease and endocarditis.^{10,11} In contrast, secondary (functional) MR results from LV dilation and dysfunction whereas the components of the mitral valve were originally normal. The main causes of secondary MR are ischemic heart disease and dilated cardiomyopathy.^{10,11}

Patients with severe primary MR commonly present with no or minimal symptoms.¹² In contrast, HF is always present in secondary MR.¹³ In a large retrospective study including 1,256 patients with ischemic and non-ischemic cardiomyopathy, any grade of secondary MR was present in 73% and 24% had severe MR.¹³

Patients with HF and significant MR are usually evaluated using transthoracic and transesophageal echocardiography. The underlying mechanism (primary versus secondary) and the severity of MR are systematically analyzed. Grading of MR is based on a multiparametric approach which includes qualitative, semiquantitative and quantitative parameters (Table 1).^{6,10} It is important to note that the evaluation of MR severity is significantly influenced by the LV loading conditions and the systemic blood pressure.¹⁴ In patients with HF, decreased transmitral pressure gradients – due to lower systemic blood pressure and high left atrial (LA) pressures – result in lower velocity regurgitant jets, which appear small on Doppler color flow images. Furthermore, vena contracta and flow convergence assume circular geometry at the regurgitant jet orifice. In secondary MR, the regurgitant orifice is frequently crescent in shape, and vena contracta, regurgitant volume and effective regurgitant orifice area (EROA) calculated using the proximal isovelocity surface area (PISA) method may therefore significantly underestimate the severity of MR.^{10,11}

Table 1: Echocardiographic criteria for the definition of severe mitral regurgitation.

	Signs of severe MR		Strengths	Limitations
	Primary	Secondary		
QUALITATIVE				
Valve morphology	Flail leaflet, ruptured papillary muscle, severe retraction, large perforation	Severe tenting, poor leaflet coaptation	• 3D echocardiography provides detailed views of the MV, including surgical view	• Absence of specific signs does not exclude severe MR
LV and LA size	Dilated		• Normal size almost excludes severe chronic primary MR	• Nonspecific in secondary MR • Can be within the normal range in acute severe MR or in smaller people
Color flow regurgitant jet*	Large central jet or eccentric wall-impinging jet of variable size		• Rapid qualitative assessment • Good for screening for MR • Evaluates the spatial orientation of the regurgitant jet	• Dependent on hemodynamic and technical variables • May underestimate the severity in eccentric jets
Continuous wave Doppler signal of regurgitant jet	Holosystolic, dense, triangular		• Easy to use	• Triangular signal is insensitive • Signal density is gain dependent
Flow convergence	Large throughout systole (≥ 1 cm at a Nyquist limit of 30-40 cm/sec)		• Rapid qualitative assessment • Can be used in eccentric jets • Absence of PISA is usually a sign of mild MR	• PISA size is affected by • Multiple jets • Non-circular regurgitant orifices (common in secondary MR) • non-holosystolic MR
SEMIQUANTITATIVE				
Vena contracta width (mm)*	≥ 7 (>8 for average between apical two- and four-chamber views)		• Less dependent on hemodynamic and technical factors (e.g. pulse repetition frequency) • Can be applied in eccentric jets	• Challenging in • Multiple jets • Non-circular regurgitant orifices (common in secondary MR) • Non-holosystolic MR
Pulmonary vein flow	Minimal to no systolic flow/systolic flow reversal		• Systolic flow reversal in ≥ 1 pulmonary vein is specific for severe MR	• Insensitive • Not accurate if MR jet is directed into the sampled vein • Blunting of the systolic wave in AF, elevated LA pressure
Mitral inflow	E-wave dominant (≥ 1.5 m/s ⁶ ; ≥ 1.2 m/s ¹⁰)		• Easy to use • Dominant A-wave inflow pattern virtually excludes severe MR	• Non-specific (high E waves in secondary MR, AF and MS)
QUANTITATIVE				
2D EROA (mm ²)†	≥ 40	$\geq 20^6$	• PISA method • Main method of MR quantification • Practical calculation • Can be used in eccentric jets • Volumetric method • Valid with multiple and eccentric jets • Valid in non-holosystolic MR	• PISA method • PISA size affected by several factors (see flow convergence) • Error in PISA radius is squared • Volumetric method • Not valid for in concomitant AR • Cumbersome, training needed • Errors in measurements can combine in the final results
Regurgitant volume (mL)‡	≥ 60	$\geq 30^6$		
Regurgitant fraction (%) ¹⁰	≥ 50		• Accounts for low-flow conditions (common in secondary MR)	• Errors in measurements of each parameter (regurgitant volume, LV end-diastolic volume) can magnify in the final results

2D = 2-dimensional; 3D = 3-dimensional; AF = atrial fibrillation; AR = aortic regurgitation; CW = continuous wave; EROA = effective regurgitant orifice area; LA = left atrium; LV = left ventricle; MR = mitral stenosis; MR = mitral regurgitation; MV = mitral valve; PISA = proximal isovelocity surface area.

*At a Nyquist limit 50-70 cm/sec.

†European guidelines recommend lower thresholds values for severe secondary MR compared with the American guidelines.

Source: Baumgartner *et al.*⁶; Zoghbi *et al.*¹⁰

With the development of 3-dimensional (3D) echocardiography, the vena contracta area can be directly visualized using multiplanar reformation planes across the regurgitant orifice and measured by planimetry (Figure 1). Zeng *et al.*¹⁵ proposed definition of severe MR to have

a cut-off value of 3D vena contracta area $\geq 0.41 \text{ cm}^2$. In patients with functional MR, the 3D vena contracta area has been shown to be significantly larger than the 2-dimensional PISA-derived EROA ($0.39 \pm 0.17 \text{ cm}^2$ versus $0.27 \pm 0.11 \text{ cm}^2$, respectively; $P < 0.001$), resulting in an average 27% underestimation of the EROA by the PISA method compared with the 3D vena contracta area.¹⁵

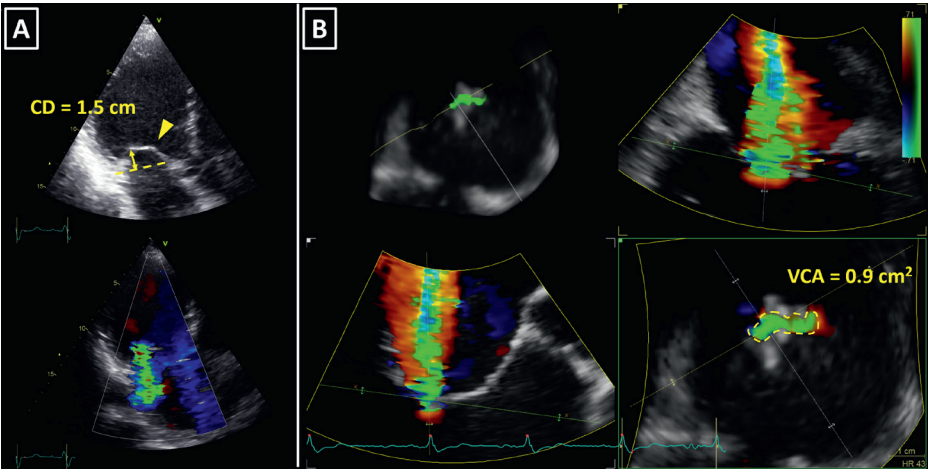


Figure 1: 3-dimensional vena contracta area in secondary mitral regurgitation. (A) Apical left ventricular long axis view, showing restriction and severe tenting of both mitral valve leaflets (upper image); the coaptation depth (CD, yellow arrow) was 1.5 cm and the bend in the body of the anterior mitral leaflet (yellow arrowhead) demonstrated tethering by the secondary chordae (known as the “seagull” or “hockey stick” sign). Bottom image shows prominent color flow Doppler regurgitant jet. (B) Multi-planar reconstruction of the 3-dimensional color flow Doppler dataset across the regurgitant orifice. Note the highly crescentic shape of the vena contracta (bottom right image), which involved the whole coaptation line from the anterolateral to the posteromedial mitral valve commissure. 3-dimensional vena contracta area (VCA) of 0.9 cm^2 (yellow dotted line) was in the range of severe mitral regurgitation.¹⁵

The assessment of the severity of MR with color flow Doppler echocardiography is based on instantaneous peak flow rates and is therefore reliable only when there is little temporal variation of MR during the cardiac cycle. However, secondary MR is often dynamic, peaking in early and late systole and improves during mid systole when LV pressures are at their maximum.¹⁶ In such circumstances, MR should be quantified with volumetric methods, which account for the whole systole. In the absence of aortic regurgitation or intracardiac shunt, the difference between stroke volume measured at the mitral annulus (LV inflow) and the LV outflow tract (LV outflow) equals MR volume. Volumetric method is frequently used with CMR.^{6,7} The preferred method to quantify MR with CMR is to use phase contrast CMR to subtract the aortic forward flow from the LV stroke volume, assessed by planimetry of the LV short-axis cine images (Figure 2).¹⁰

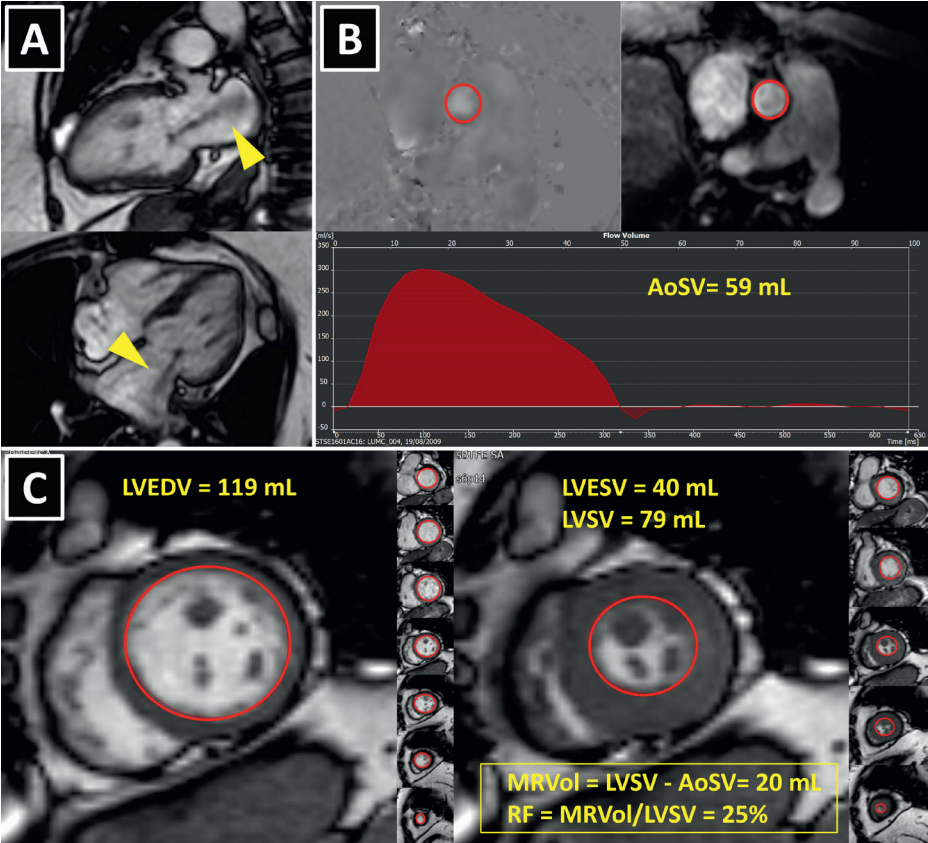


Figure 2: Cardiovascular magnetic resonance to quantify mitral regurgitation. A 74-year-old patient with heart failure symptoms had inconsistent grading of the severity of mitral regurgitation (MR) with echocardiography and was referred for cardiovascular magnetic resonance (CMR). (A) Left ventricular systolic cine images show prominent MR jet (yellow arrowheads). MR was caused by mitral annular dilatation, secondary to severe left atrial dilatation. The patient had a long-lasting history of paroxysmal atrial fibrillation. (B) Left ventricular forward stroke volume (AoSV) was measured with phase contrast CMR in the ascending aorta, just above the aortic valve. (C) Total left ventricular stroke volume (LVSV) was obtained using planimetry of the short-axis cine images as the difference between left ventricular end-diastolic volume (LVEDV; left image) and left ventricular end-systolic volume (LVESV; right image). Since the patient had no aortic regurgitation the difference between the LVSV and AoSV was equal to mitral regurgitant volume (MRVol). The regurgitant fraction (RF) was calculated by dividing MRvol by LVSV. The results (MRVol 20 mL, RF 25%) clearly ruled out severe MR, which was further supported by normal left ventricular volumes.

SELECTING INTERVENTIONS FOR MITRAL REGURGITATION

After establishing the diagnosis of symptomatic severe secondary MR, the type of valve intervention is based upon the degree of LV functional impairment, evidence of myocardial

viability and the ability to perform revascularization. When revascularization is indicated, surgical intervention should be considered.^{6,8} However, the preferred type of surgical treatment, i.e. mitral valve repair by means of restrictive annuloplasty or chordal-sparing valve replacement, is not agreed upon. European guidelines recommend mitral valve repair as the preferred method, while mitral valve replacement may be considered in patients with echocardiographic risk factors for residual or recurrent MR (Table 2).^{6,17} In contrast, American guidelines recommend chordal-sparing mitral valve replacement for severely symptomatic patients (New York Heart Association Class III to IV) with chronic severe ischemic MR.⁸ This recommendation is based on the results of a randomized control trial that showed a higher rate of moderate or severe MR recurrence at 2 years follow-up in patients who underwent mitral valve repair compared with patients who underwent chordal-sparing mitral valve replacement (58.8% versus 3.8%, $P<0.001$), leading to higher incidence of HF and repeat hospitalizations in the mitral valve repair group.¹⁸ When revascularization is not indicated, the decision between surgery and percutaneous edge-to-edge repair is made based on the degree of LV dysfunction and the surgical risk. When the surgical risk is low and LVEF $>30\%$, surgery may be considered, while percutaneous edge-to-edge repair is preferred for patients presenting with high surgical risk or LVEF $<30\%$ despite optimal medical management (including pharmacological treatment and cardiac resynchronization therapy).⁶ In the United States, percutaneous edge-to-edge repair is currently not approved for clinical use in secondary MR.⁸

For successful surgical and percutaneous mitral valve repair in secondary MR, accurate LV assessment, including LV volumes, LVEF and sphericity index, is mandatory, accompanied by geometric assessment of the MV apparatus (tenting area, coaptation depth, leaflet angles, and inter-papillary muscle distance). Transthoracic and transesophageal echocardiography are the primary modalities; however, detailed information can also be obtained with cardiac CT and CMR. Table 2 summarizes the echocardiographic criteria that suggest increased risk of MR recurrence after mitral valve repair as well as unfavorable anatomical conditions for percutaneous edge-to-edge repair with a MitraClip device (Abbott Vascular, Menlo Park, CA, US).¹⁷ In patients with secondary MR who are undergoing surgery, successful repair is less likely in the presence of severe mitral valve tethering with coaptation depth >1 cm, systolic tenting area >2.5 cm², posterior mitral leaflet angle $>45^\circ$ and distal anterior mitral leaflet angle $>25^\circ$.^{17,19} Furthermore, global and regional LV remodeling, indicated by LV end-diastolic dimension >65 mm, end-systolic dimension >51 mm, systolic sphericity

ty index >0.7 and interpapillary muscle distance >20 mm predict a lower likelihood of successful mitral valve repair.^{17,20} A leaflet coaptation depth >11 mm and coaptation length <2 mm challenge the percutaneous edge-to-edge mitral valve repair since these parameters indicate advanced LV remodeling with excessive tethering of the mitral leaflets.¹⁷ Large regurgitant orifices often require implantation of >1 MitraClip to reduce MR. Short posterior leaflet, cleft, severe annular calcification and calcification in the grasping area are other anatomical conditions that challenge percutaneous edge-to-edge repair.¹⁷ Peri-procedural transesophageal echocardiography is crucial to perform successful percutaneous implantation of a MitraClip device (Figure 3).

Table 2: Unfavorable anatomical conditions for successful surgical and percutaneous edge-to-edge repair in secondary mitral regurgitation.

SURGICAL REPAIR	PERCUTANEOUS REPAIR
Parameters related to mitral valve tethering	
Coaptation depth >1 cm	Coaptation depth >11 mm
Systolic tenting area >2.5 cm ²	Coaptation length <2 mm
Posterior mitral leaflet angle $>45^\circ$	Severe asymmetric tethering
Distal anterior mitral leaflet angle $>25^\circ$	Large ($>50\%$) inter-commissural extension of regurgitant jet
Parameters related to left ventricular remodeling	
LV end-diastolic diameter >65 mm	Severe annular dilatation
LV end-systolic diameter >51 mm	Severe LV remodeling
End-systolic inter-papillary muscle distance >20 mm	
Systolic sphericity index >0.7	
Unfavorable anatomical conditions specific for percutaneous edge-to-edge repair	
	Short posterior leaflet
	Calcification in the grasping area
	Severe annular calcification
	Cleft

LV = left ventricular. Source: De Bonis *et al.*¹⁷

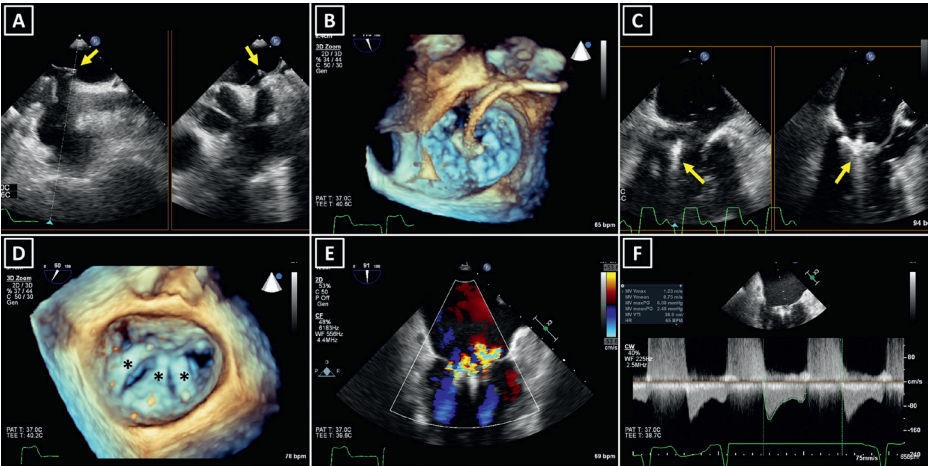


Figure 3: Transesophageal echocardiography during MitraClip implantation: guiding the intervention (A-C) and the assessment of procedural results (D-E). (A) Transseptal puncture. Arrows point at the tenting of the interatrial septum before the puncture in two simultaneous perpendicular image planes. (B) Opening of the Mitraclip device in the left atrium. (C) The MitraClip implantation – orienting the device arms perpendicular to the leaflets (arrows) is essential for successful grasping of the mitral valve. (D) Three MitraClips were implanted (asterisks) in a patient with severe secondary mitral regurgitation. (E) Assessment of residual mitral regurgitation. (F) Transmitral gradient measurement for the evaluation of post-implant mitral valve stenosis.

AORTIC STENOSIS IN HEART FAILURE

The LV pressure overload caused by AS increases LV wall stress and as a consequence the LV responds with myocyte hypertrophy to maintain a normal LVEF. However, this response is counterproductive in the long-term and causes LV diastolic dysfunction, myocardial ischemia in the subendocardium, increased myocardial fibrosis (reactive and replacement) and eventually LV systolic dysfunction.²¹ Clinically, patients with severe AS may present with dyspnea, chest pain and syncope.

The prevalence of HF among patients with severe AS varies largely based on the definition of HF (e.g. reduced LVEF, presence of symptoms) and the characteristics of patients included in the studies. In a large cohort study (n=79,043) involving people with HF symptoms referred for echocardiography, at least mild AS was found in 10.1% and moderate or severe AS in 3.2%.⁴ Furthermore, in the Euro Heart Survey 19.3% of patients with severe AS undergoing surgical aortic valve replacement (SAVR) had LVEF <50%.⁵ In a more contemporary series of 42,776 patients with AS undergoing SAVR included in the German Aortic Valve Registry, LVEF <50% was present

in 26.6% of the patients.²² Data from the American Transcatheter Valve Therapy (TVT) Registry showed a 25.6% prevalence of reduced LVEF (<45%) among 42,988 patients undergoing TAVR.²³

Doppler echocardiography is the preferred technique for the assessment of the severity of AS. The primary hemodynamic parameters defining severe AS with echocardiography are the peak jet velocity ≥ 4 m/s, mean transvalvular pressure gradient ≥ 40 mmHg and aortic valve area (AVA) by continuity equation <1.0 cm² (Table 3).²⁴ In the majority of patients, these criteria coincide. However, up to 30% of patients may show low peak jet velocity and transaortic valve gradient with an AVA <1 cm².²⁵ This is frequently observed among patients with LVEF <50%, the so-called classical low-flow low-gradient severe AS.

Table 3: Echocardiographic criteria for the definition of severe AS.

	Severe AS	Common mistakes in the assessment of LFLG AS	Recommendations to avoid mistakes in the assessment of LFLG AS
Peak velocity (m/s)	≥ 4.0	- Underestimation of peak velocity and mean gradient: - misalignment of the ultrasound beam with the AS jet - high blood pressure	- Multiple acoustic windows to determine the highest velocity - Parallel ultrasound beam alignment with the direction of flow - Measurements when patient has normal blood pressure
Mean gradient (mmHg)	≥ 40		
AVA (cm ²) by continuity equation (LVOT area $\times$ LVOT VTI)	<1.0	- Underestimation of LVOT area: - Elliptical shape of LVOT - Calcifications - Sigmoid septum - Diastolic measurements - Underestimation of LVOT VTI: - PW Doppler sample volume placed too apically	- Systolic LVOT diameter in ≥ 3 beats (sinus rhythm) and in ≥ 5 beats (irregular rhythm) 3D planimetric measurement of the LVOT area (3D TEE, CT) - PW Doppler sample volume should be in the middle of LVOT just below the flow convergence where smooth velocity curve is obtained
AVAi (cm ² /m ²)	<0.6	Underestimation in obese patients	Important measure in children, adolescents, small adults
Velocity ratio (LVOT velocity / peak velocity)	<0.25	Underestimation of LVOT velocity or peak velocity	- Multiple acoustic windows to determine the highest peak velocity - Parallel ultrasound beam alignment with the direction of flow - Measurements when patient has normal blood pressure - PW Doppler sample volume in the middle of LVOT just below the flow convergence where smooth velocity curve is obtained

3D = 3-dimensional; AS = aortic stenosis; AVA = aortic valve area; AVAi = indexed aortic valve area; CT = computed tomography; LFLG = low-flow low-gradient; LVOT = left ventricular outflow tract; PW = pulsed wave; TEE = transesophageal echocardiography; VTI = velocity time integral.

Source: Baumgartner *et al.*²⁴

Low-dose dobutamine stress echocardiography is the primary diagnostic method to differentiate between true severe AS and pseudo-severe AS in patients with reduced LVEF.²⁴ In patients with true severe AS, intravenous infusion of low-dose dobutamine will increase the LV contractility and stroke volume leading to an increase in mean transvalvular gradient while the AVA will remain narrow (Figure 4). In contrast, pseudo-severe AS is diagnosed when the

increase in LV contractility and stroke volume is accompanied by an increase in AVA $>1.0 \text{ cm}^2$ (Figure 5). While patients with true severe low-flow low-gradient AS should undergo prompt aortic valve intervention, the course of action for patients with pseudo-severe AS is less clear. Fougères *et al.*²⁶ demonstrated comparable survival of patients with pseudo-severe AS to that of propensity-matched patients with systolic HF and no evidence of VHD. However, this has recently been challenged by another study that demonstrated a very high risk for clinical events (defined as the composite of all-cause death, aortic valve replacement and HF hospitalization) among patients with HF and moderate AS.²⁷ Furthermore, in a retrospective analysis of 1,090 patients with moderate AS and LVEF $\leq 50\%$ aortic valve surgery was associated with a higher 5-year survival compared to medical therapy.²⁸ While current guidelines do not recommend aortic valve intervention in HF patients with moderate AS, this view might change after the results of the ongoing international, multicenter, randomized, clinical trial TAVR UNLOAD (NCT02661451), which has been designed to compare the efficacy and safety of transfemoral TAVR in addition to optimal HF therapy vs HF therapy alone in HF patients with moderate AS.²⁹

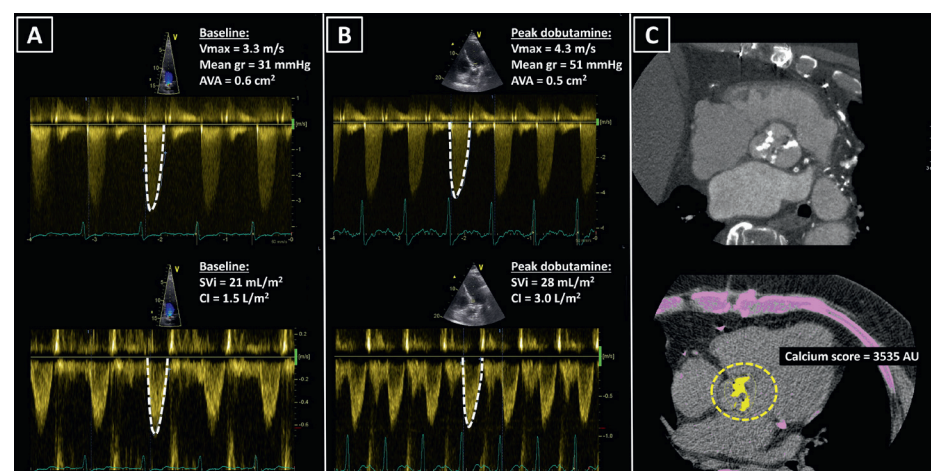


Figure 4: Classical low-flow low-gradient severe aortic stenosis. (A) A 75-year old male with ischemic cardiomyopathy, reduced left ventricular ejection fraction (32%) and low cardiac output. At rest, echocardiography showed calcified aortic valve with severely narrowed valve area $<1.0 \text{ cm}^2$, while peak velocity and mean gradient were in the range of moderate aortic stenosis. (B) During low-dose dobutamine stress echocardiography peak jet velocity and mean gradient increased $\geq 4.0 \text{ m/s}$ and $\geq 40 \text{ mmHg}$ respectively, and the aortic valve area remained $<1.0 \text{ cm}^2$, revealing true severe aortic stenosis. Furthermore, an increase in cardiac output demonstrated left ventricular contractile reserve. (C) Computed tomography showed a tricuspid aortic valve with high calcium score, suggesting high likelihood of severe aortic stenosis. AU = arbitrary units; AVA = aortic valve area; CI = cardiac index; Mean gr = mean gradient; SVI = stroke volume index; Vmax = peak velocity.

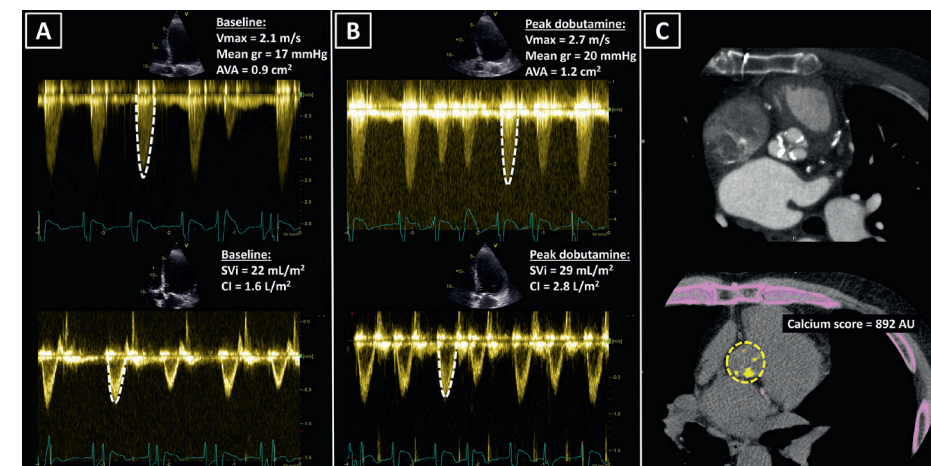


Figure 5: Pseudo-severe low-flow low-gradient aortic stenosis. (A) An 80-year old male with dilated cardiomyopathy, reduced left ventricular ejection fraction (21%) and low cardiac output. At rest, echocardiography showed calcified aortic valve with an area $<1.0 \text{ cm}^2$ (suggesting severe aortic stenosis), while peak velocity and mean gradient were representative of mild aortic stenosis. (B) During low-dose dobutamine stress echocardiography, the peak jet velocity and mean gradient marginally increased and the aortic valve area increased $>1.0 \text{ cm}^2$, revealing pseudo-severe aortic stenosis. (C) Computed tomography showed tricuspid aortic valve with low calcium score, suggesting non-severe aortic stenosis. AU = arbitrary units; AVA = aortic valve area; CI = cardiac index; Mean gr = mean gradient; SVI = stroke volume index; Vmax = peak velocity.

In patients without contractile reserve, defined as failure to increase stroke volume $>20\%$ during dobutamine stress echocardiography, the assessment of aortic valve calcification burden with cardiac CT may help to estimate the severity of AS (Figure 4 and 5).²⁴ Aortic valve calcium score is quantified using the Agatston method and expressed in arbitrary units (AU).³⁰ Cueff *et al.*³¹ demonstrated a good overall correlation between the degree of aortic valve calcification and hemodynamic parameters of AS severity assessed by the AVA ($r=-0.63$, $P<0.001$), indexed AVA ($r=-0.67$, $P<0.001$), mean gradient ($r=0.78$, $P<0.001$) and peak velocity ($r=0.79$, $P<0.001$). The proposed cut-off value of 1,651 AU yielded a 93% sensitivity and 75% specificity in grading AS severity in patients with classical low-flow low-gradient AS. Clavel *et al.*³² proposed different cut-off values to define severe AS for men and women, 2,065 AU and 1,274 AU, respectively. The joint European and American recommendations for the assessment of AS consider the aortic valve calcium score as a continuum – a very high calcium score suggests severe AS and low calcium score suggests severe AS is unlikely (Table 4).²⁴

Table 4: Calcium score by computed tomography in grading of aortic stenosis.

	Men	Women
Severe aortic stenosis very likely	≥3,000	≥1,600
Severe aortic stenosis likely	≥2,000	≥1,200
Sever aortic stenosis unlikely	<1,600	<800

Source: Baumgartner *et al.*²⁴

TREATMENT OPTIONS FOR AORTIC STENOSIS

Current therapeutic options for patients with severe AS and HF are conservative medical therapy, SAVR and TAVR. For patients with symptomatic high-gradient severe AS there is no lower LVEF limit for aortic valve intervention (Class I recommendation), since LV function will likely improve after relief of stenosis.^{6,7} Asymptomatic severe AS patients with an LVEF <50% should undergo aortic valve replacement (Class I recommendation).^{6,7} In patients with classical low-flow low-gradient severe AS (with reduced LVEF) aortic valve intervention is indicated when dobutamine stress echocardiography shows evidence of LV contractile reserve (Class I recommendation in European guidelines and Class IIa in American guidelines).^{6,7} An intervention should also be considered in patients without LV contractile reserve, particularly when CT calcium score is high (Class IIa recommendation in European guidelines, while the American guidelines stress the importance of individualized decisions in these high-risk patients).^{6,7} Tribouilloy *et al.*³³ demonstrated that patients with low-flow low-gradient severe AS without contractile reserve experience high operative mortality, but SAVR was associated with better outcomes compared with patients who were treated conservatively. Only symptomatic patients with severe comorbidities, in whom aortic valve intervention is unlikely to improve survival or quality of life, should be treated with medical therapy.⁶

The choice of the intervention in patients with symptomatic severe AS and HF should be made by the specialist heart team and should take into account patient’s cardiac and extra-cardiac characteristics, the individual risk of surgery, the feasibility of TAVR, as well as the local experience and outcome data.^{6,8} Table 5 lists the imaging-derived characteristics that guide the decision to choose TAVR or SAVR. Multi-slice CT has become the imaging modality of choice for pre-procedural evaluation of TAVR candidates in most centers due to its low invasiveness and comprehensive evaluation.⁶ It allows assessment of the size and the shape of the aortic annulus, its distance to the coronary ostia, the distribution of calcifications and the dimensions of the aortic root, which is of paramount importance to determine feasibility of TAVR and to choose appropriate prosthesis size (Figure 6). However, if CT is contraindicat-

ed (e.g., if the patient has severely impaired renal function), 3D transesophageal echocardiography can be used to determine the aortic annulus size. It is important to remember that the obtained annulus dimensions with 3D transesophageal echocardiography are smaller than those measured with cardiac CT and the echocardiographic accuracy can be reduced in heavily calcified aortic valves.^{34,35} Cardiac CT also allows assessment of the peripheral arteries to determine feasibility of transfemoral access, which is the least invasive TAVR approach, used in the majority of patients.^{23,36} Cardiac CT allows detailed visualization of iliofemoral arteries and aorta with the assessment of size, tortuosity, degree of calcification and plaque burden (Figure 6). For currently available TAVR delivery catheters, a 6.0-6.5 mm minimal luminal vessel diameter of femoral arteries is considered acceptable.³⁷ In case of contraindications to CT, invasive angiography or, less commonly, CMR angiography might be employed.

Table 5: Imaging-derived characteristics that guide the decision between TAVR and SAVR in patient at increased surgical risk.

	Favours TAVR	Favours SAVR
Peripheral arteries anatomy favorable for transfemoral TAVR	+	
Unfavorable access (any) for TAVR		+
Porcelain aorta	+	
Expected patient-prosthesis mismatch	+	
Short distance between coronary ostia and aortic valve annulus		+
Size of aortic valve annulus out of range for TAVR		+
Aortic root morphology unfavorable for TAVR		+
Valve morphology (bicuspid, degree of calcification, calcification pattern) unfavorable for TAVR		+
Presence of thrombi in aorta or left ventricle		+

SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement.

Source: Baumgartner *et al.*⁶

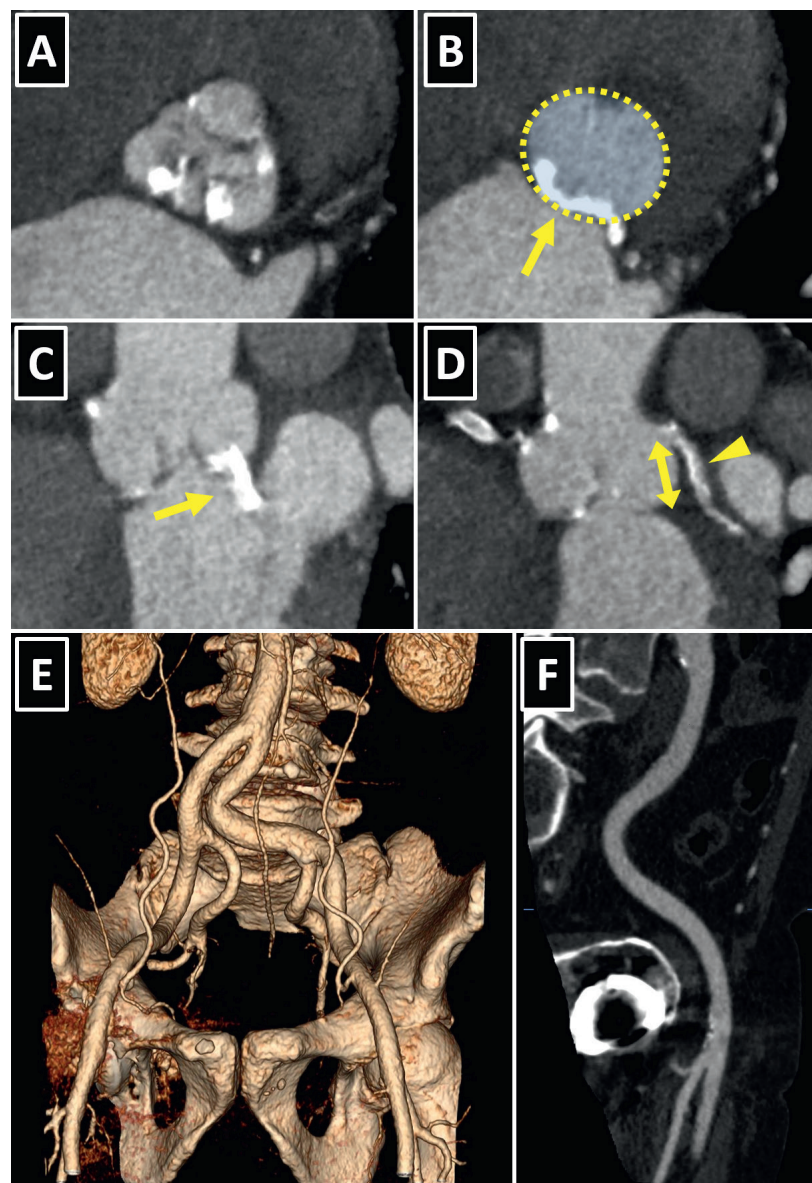


Figure 6: Computed tomography (CT) in pre-procedural assessment for transcatheter aortic valve replacement (TAVR). (A) Double oblique transverse view of a calcified tricuspid aortic valve. (B) Planimetry of the aortic annulus. The posterior part of the annulus was severely calcified (arrow), increasing the likelihood of aortic rupture in case of an oversized TAVR prosthesis implantation or post-dilatation with an oversized balloon. (C) The calcification extended from the aortic annulus into the left ventricular outflow tract towards the anterior mitral valve leaflet (arrow). (D) Measurement of the distance between left main coronary artery and the aortic annulus (arrow). A calcified plaque in the left coronary artery is visible (arrowhead). (E) Tortuous bilateral iliofemoral arteries. (F) Multi-planar reconstruction revealed only mildly calcified right iliofemoral artery with adequate lumen diameter to allow for transfemoral TAVR.

CONCLUSION

Accurate grading of valvular lesion and reliable assessment of LV dysfunction is of paramount importance when deciding the most appropriate therapy for patients with VHD and HF. Trans-thoracic echocardiography is the first-line imaging modality to quantify LV systolic function and grade of valvular stenosis and regurgitation, as well as characterizing the mechanism of valvular dysfunction. However, in HF patients, quantification of valvular dysfunction remains challenging and the use of other imaging techniques such as 3D transesophageal echocardiography, CMR and CT is needed to determine whether the valve stenosis and regurgitation are severe. The integration of multimodality cardiovascular imaging is even more important when assessing suitability for transcatheter valve repair and replacement therapies. CT has become the key imaging modality for pre-procedural evaluation of patients undergoing TAVR, and 3D transesophageal echocardiography is crucial to guide percutaneous edge-to-edge mitral valve repair.

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