Acute heart failure and valvular heart disease: A scientific statement of the Heart Failure Association, the Association for Acute CardioVascular Care and the European Association of Percutaneous Cardiovascular Interventions of the European Society of Cardiology

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Acute heart failure (AHF) represents a broad spectrum of disease states, resulting from the interaction between an acute precipitant and a patient's underlying cardiac substrate and comorbidities. Valvular heart disease (VHD) is frequently associated with AHF. AHF may result from several precipitants that add an acute haemodynamic stress superimposed on a chronic valvular lesion or may occur as a consequence of a new significant valvular lesion. Regardless of the mechanism, clinical presentation may vary from acute decompensated heart failure to cardiogenic shock. Assessing the severity of VHD as well as the correlation between VHD severity and symptoms may be difficult in patients with AHF because of the rapid variation in loading conditions, concomitant destabilization of the associated comorbidities and the presence of combined valvular lesions. Evidence-based interventions targeting VHD in settings of AHF have yet to be identified, as patients with severe VHD are often excluded from randomized trials in AHF, so results from these trials do not generalize to those with VHD. Furthermore, there are not rigorously conducted randomized controlled trials in the setting of VHD and AHF, most of the data coming from observational studies. Thus, distinct to chronic settings, current guidelines are very elusive when patients with severe VHD present with AHF, and a clear-cut strategy could not be yet defined. Given the paucity of evidence in this subset of AHF patients, the aim of this scientific statement is to describe the epidemiology, pathophysiology, and overall treatment approach for patients with VHD who present with AHF.

Graphical Abstract
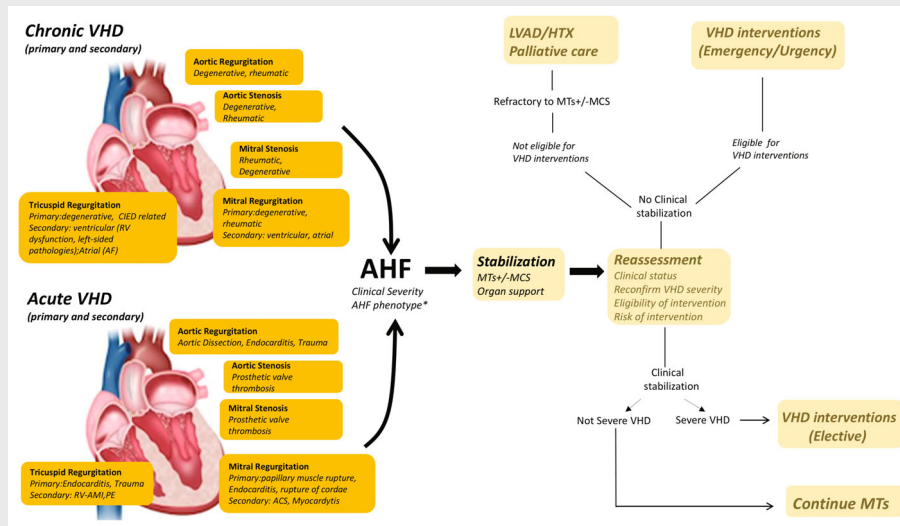
Assessing severity of acute heart failure (AHF) in parallel with evaluation of the aetiology, mechanism and severity of valvular heart disease (VHD). Management follows Heart Team discussion to decide emergency/urgent/elective interventions or palliation. Three possible scenarios should be considered. First, if there is no emergent indication to intervention, patients must receive medical therapy (MT). MT may be appropriate as bridge to early in-hospital or elective intervention or as destination therapy if intervention is contraindicated because of the comorbidities. Second, patients presenting with cardiogenic shock or AHF refractory to medical treatment require interventions on an urgent/emergency basis, when VHD represents the main contributor to the immediate life-threatening haemodynamic deterioration. Third, early use of percutaneous mechanical circulatory support (MCS) may help bridge patients to a decision of delayed VHD repair, left ventricular assist device (LVAD) and/or heart transplantation (HTX). The second and third scenarios are more likely to be considered as patients with AHF and VHD may require emergent surgery, especially in case of valve endocarditis or acute aortic regurgitation caused by aortic dissection or acute mitral regurgitation caused by papillary muscle rupture. ACS, acute coronary syndrome; AF, atrial fibrillation; AMI, acute myocardial infarction; CIED, cardiac implantable electronic device; PE, pulmonary embolism; RV, right ventricular. *AHF phenotypes: cardiogenic shock, acute pulmonary oedema, acute decompensated heart failure; right heart failure.

Introduction

Defined according to guidelines as the new onset or worsening of symptoms and signs of heart failure (HF) in the presence of an underlying structural or functional cardiac dysfunction, one or more precipitating factors can induce acute HF (AHF).[1] Valvular heart disease (VHD) is one of the most common underlying conditions associated with AHF.[2–10] AHF may result from the acute haemodynamic stress superimposed on a chronic valvular lesion or may occur because of a new significant valvular lesion. Patients with VHD presenting with AHF may have significant comorbidities, and it is often difficult to ascribe the contribution of VHD to symptom severity. Assessing aetiology may not be immediately available in critically ill patient and accurate valvular assessment can be challenging with multiple VHD or in those with extreme loading conditions.[11–14]

There are no rigorously conducted randomized controlled trials in the setting of VHD with AHF. Besides, patients with severe VHD are often excluded from AHF randomized controlled trials and this leads to lack of a clear-cut strategy.[15,16] Hence, the current European Society of Cardiology (ESC) and US guidelines emphasize the need of an early referral of patients with HF and valvular disease to a multidisciplinary Heart Team, including HF specialists, for assessment and treatment planning.[1,15,16] The guidelines also recommend the Heart Team must individualize multidisciplinary discussion to offer the best option for each particular case.[1,15,16]

It is therefore the aim of the present scientific statement to focus on the epidemiology, pathophysiology, diagnostic work-up and management of VHD with AHF.

Epidemiology

In hospitalized patients from the EURObservational Research Programme (EORP) VHD II survey,[17] aortic stenosis (AS) was the most common VHD (41.2%), followed by primary mitral regurgitation (MR) (13.8%) and secondary MR (7.8%). Multiple VHD was reported in 26.5% patients. Isolated right-sided VHD was rare (2.5%).

The prevalence of VHD in the setting of AHF has not been clearly embodied. AHF clinical trials generally excluded patients with moderate to severe VHD and in AHF registries (*Table 1*), the VHD prevalence varied according to the methodology of the registries.[2–10]

Among AHF patients, VHD as primary cause of HF was more common in HF with preserved ejection fraction (HFpEF) (20%), as compared to HF with mildly reduced ejection fraction (14%) and HF with reduced ejection fraction (HFrEF) (6.2%).[18]

In the international REPORT-HF registry, VHD was considered as a cause of AHF in 13% of patients (ranging from 7% in Asia and North America to 18% in Western Europe), while in 20% of AHF patients VHD was present as a comorbidity (ranging from 8% in Asia to 30% in Eastern Europe).[19] Also, in-hospital VHD interventions varied substantially by geographic region (7.9% in Western Europe vs. 1.2% in South East Asia).[20]

In the ESC HF Long-Term Registry, VHD was reported as the primary cause of AHF in 11.8% of patients, though moderate/severe MR and tricuspid regurgitation (TR) were found at echo in 45.9% and 35.4% of patients respectively,[21] suggesting dynamic nature of functional regurgitations.

In terms of prognosis, severe AS was an independent predictor of 1-year all-cause mortality.[8] Mild to moderate aortic regurgitation (AR) was linked to all-cause mortality in patients with AHF and preserved ejection fraction.[22]

Moderate/severe MR was associated with a composite of all-cause mortality or HF readmissions in patients with both worsening and *de novo* HF from BIOSTAT-CHF.[23] In the ARIC study, moderate/severe MR was associated with 1-year all-cause mortality only in AHF patients with ejection fraction <50%.[24] Of note, residual functional MR at discharge was associated with prognosis only in the group of AHF patients with high B-type natriuretic peptide at discharge.[25] Interestingly, in patients hospitalized for AHF, dynamic MR (severe on hospital arrival and improved at discharge) was linked to a worse composite outcome including death and HF readmissions.[26]

In hospitalized AHF patients, moderate/severe TR prevented successful decongestion,[9] it was a strong predictor of HF readmissions[27] and it was associated with mortality only in the subset of patients with HFpEF[28] or those with pulmonary hypertension (PH).[29]

Acute heart failure pathophysiology

Primary severe VHD may represent an abnormal substrate or an underlying cause of AHF. Valve lesions often progress gradually over time but manifest clinically or become acutely worsened during the haemodynamic stress from a superimposed precipitant that may vary in severity and can interact additively (*Figure 1*). Furthermore, alteration of the cardiovascular substrate during HF progression may cause functional VHD, especially MR and TR, and coexistence of these two may complicate the clinical picture. In contrast to organic (primary) valve regurgitation, where the valve apparatus is structurally normal, secondary MR and TR develop by structural alterations of the ventricular or atrial geometry. Secondary atrio-ventricular regurgitations may occur in the full spectrum of left ventricular ejection fraction (LVEF) and are dynamic lesions, changing severity with loading conditions.[30,31]

Acute VHD may be responsible for AHF in cases of a new acute valve dysfunction (e.g. papillary muscle rupture, aortic dissection) or acute deterioration of a prior moderate VHD by endocarditis, prosthetic valve thrombosis, and so forth (*Figure 1*). In addition, haemodynamic significance of even moderate VHD might be

Table 1 Prevalence of valvular heart disease in patients hospitalized for acute heart failure in registries with different enrolment strategies

	EHFS II[2] (2004–2005)	RO-AHFS[3] (2008–2009)	AHEAD[4] (2006–2009)	OFICA[6] (2009)	ESC-HFA EORP HF LT[8,9] (2011–2018)	EAHFE[10] (2011–2018)	REPORT-HF[20] (2014–2018)
Patients, n	3580	3224	4153	1468	7865	11 360	18 102
Methodology, time frame of enrolment	133 sites/30 countries, 20 pts/site	13 sites, 1-year all-consecutive	7 sites, consecutive	170 sites, 1-day survey	211 sites/33 countries, periodic consecutive	45 sites, 2 months consecutive	358 sites/44 countries, periodic consecutive
VHD as underlying cause	34.4%	35.8%	11.3%	22.6%	12.0%	26.8%	13%
Echocardiography	44.3% moderate to severe MR 29.9% moderate to severe TR	23.8% severe mitral valve disease 19.8% severe aortic valve disease	–	–	52.5% moderate to severe MR 36.3% moderate to severe TR	–	–

AHEAD, Acute Heart Failure Database; EAHFE, Epidemiology of Acute Heart Failure in Emergency Departments; EHFS II, European Heart Failure Survey II; ESC-HFA EORP HF LT, European Society of Cardiology Heart Failure Association EUROObservational Research Programme Heart Failure Long-Term Registry; MR, mitral regurgitation; OFICA, French Observational Survey on Acute Heart Failure; REPORT-HF, International REgistry to assess medical Practice with lOngitudinal obseRvation for Treatment of Heart Failure; RO-AHFS, Romanian Acute Heart Failure Syndromes; TR, tricuspid regurgitation; VHD, valvular heart disease.

aggravated by the coexistence of diverse precipitants such as acute coronary syndrome, hypertension, arrhythmia, fluid overload, or worsening renal function (*Figure 1*).

Pulmonary hypertension

Pulmonary hypertension is frequently a consequence of left-sided VHD and contributes to, or aggravates, secondary TR.[32–35]

In left-sided VHD, left ventricular pressure and/or volume overload induces left atrial pressure overload and a passive backward rise of pulmonary venous pressure. This sudden increase in pulmonary venous pressure causes alveolar-capillary membrane disruption producing reversible acute alveolar oedema, while chronic adaptation, including left atrial dilatation and alveolar capillary remodelling with collagen deposition, is a partially irreversible process.[33,34] PH induces right ventricular pressure overload causing right ventricular hypertrophy and dilatation and consequently annulus dilatation with secondary TR that further deteriorates right ventricular function.

Pulmonary hypertension due to left heart disease, including VHD, represents group 2 PH defined by an mean pulmonary artery pressure >20 mmHg and a pulmonary capillary wedge pressure >15 mmHg. Within this haemodynamic condition of post-capillary PH, isolated PH is defined by pulmonary vascular resistance (PVR) ≤2 Wood units (WU) and combined PH by PVR >2 WU.[35] Severe PH is defined as >5 WU.[35] In patients with VHD undergoing intervention, increased PVR, particularly if >5 WU, is associated with an increased disease burden and a worse outcome.[35] Furthermore, regression of PH after correction of VHD is frequently incomplete and persistent PH is associated with adverse outcomes.[36]

The prevalence of PH increases with severity of left-sided VHD[37] and severity of symptoms.[33,38] In mitral stenosis (MS), PH is linked to symptom severity and valve area and is associated with long-term prognosis.[39]

The prevalence of PH in primary MR may vary according to clinical severity and reaches 64% for patients with New York Heart Association (NYHA) class III/IV.[33,40,41] Early surgical treatment is advisable in these patients, since pre-existing PH is associated with post-operative left ventricular systolic decline and an almost two-fold increase in post-operative mortality.[15,16,39,42]

In AS, PH prevalence ranges from 6% to 30%.[43] The mechanism of PH in AS is controversial and attributed more to the left ventricular diastolic dysfunction and less to AS severity itself. The reversibility of PH post-operatively correlates with improvement of diastolic function and was linked to better outcomes.[44,45]

In severe AR, the prevalence of PH is between 30% and 37% and represents a predictor of worse prognosis post-intervention.[46]

Investigations and in-hospital monitoring for valvular heart disease

As many of these patients with VHD and atrial fibrillation undergo urgent surgical or percutaneous correction, it is important to
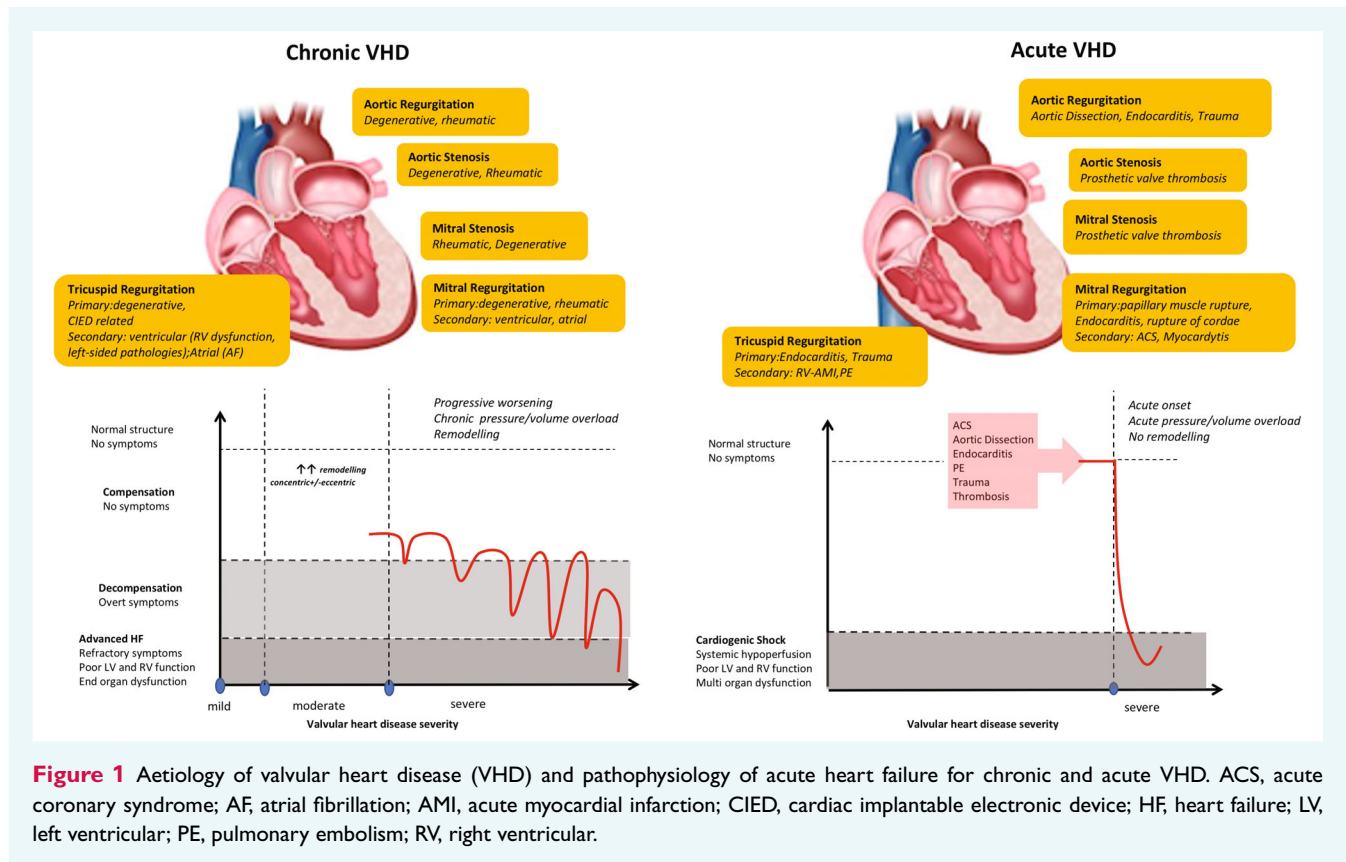
Figure 1 Aetiology of valvular heart disease (VHD) and pathophysiology of acute heart failure for chronic and acute VHD. ACS, acute coronary syndrome; AF, atrial fibrillation; AMI, acute myocardial infarction; CIED, cardiac implantable electronic device; HF, heart failure; LV, left ventricular; PE, pulmonary embolism; RV, right ventricular.

concomitantly evaluate: (i) the clinical status and rapidly identify early signs of hypoperfusion and respiratory distress; (ii) the severity of the valvular disease and its impact on the cardiac chambers and pulmonary circulation and overall haemodynamic status; (iii) markers of end-organ dysfunction; and (iv) the presence/absence of significant coronary artery disease, precipitants, comorbidities.

Clinical examination

In general, while all left-sided VHDs contribute to symptoms and signs of pulmonary congestion, right-sided VHDs contribute to symptoms and signs of systemic congestion (*Table 2*).[27,47–56]

To note, clinical examination alone, in particular auscultation, has a limited sensitivity,[57] being insufficient for the diagnosis of VHD, particularly in critically ill patients or in those with acute VHD, when the murmur intensity and duration may be diminished due to systemic hypotension and rapid pressure equilibration between cardiac chambers.[14] However, some symptoms may be especially informative of the underling aetiology (i.e. fever in infective endocarditis, chest pain in aortic dissection).

Biomarkers, arterial blood gas analysis, lactate, electrolytes

The value of natriuretic peptides for diagnosis and prognostic evaluation has been reported in the ESC HF guidelines.[1,58] In very acute settings, such as MS with flash pulmonary oedema,

natriuretic peptide values may not reach the recommended 'likely' cut-offs.[59]

The identification of acidosis and especially elevated lactate remain reliable markers for hypoperfusion and it is advised to be checked routinely.[1,60]

The *electrocardiogram* may help the diagnostic by identification right ventricular hypertrophy (PH), arrhythmias, conduction abnormalities (extension of annular aortic abscesses) and ischaemia.

Cineradiography can aid the diagnosis of mechanical valve obstruction.

Transthoracic echocardiography (TTE) is essential for the diagnosis and precise evaluation of the severity of valvular lesions (online supplementary *Table S1*), the impact on left ventricular size and function, right ventricular function and pulmonary circulation (pulmonary pressure as well as pulmonary resistance).

Careful quantification is required, as the severity of the mitral/aortic lesion may be underestimated when the left ventricular systolic function is depressed as in AHF or cardiogenic shock (CS). Adequate assessment of left ventricular contractile/flow reserve may be difficult when the patient is under inotropic support.[16]

Transoesophageal echocardiography (TEE) is essential before or during mitral and tricuspid valve interventions, in patients with prosthetic valve dysfunction as well as whenever the TTE examination is not informative. TEE remains very sensitive and specific for the diagnosis of valve vegetations (consistently above 95%) and other imaging findings of infective endocarditis.[61,62]

Table 2 Pathophysiology and clinical presentation of valvular heart disease in acute settings

	Pathophysiology	Clinical presentation
Severe AS	• AS represents an increased afterload state for the left ventricle. The reduction of valve area produces a pressure gradient across the aortic valve and consequently an increase in LV systolic wall stress that leads to increased LV diastolic pressure, LV concentric hypertrophy, diastolic stiffness and impaired compliance. LV diastolic filling is impaired and the left ventricle is dependent on increasing filling pressure to maintain cardiac output.[11–16] LV hypertrophy is a key adaptive mechanism to the pressure load but it increases LV mass leading to discrepancy in oxygen demand and supply and relative myocardial ischaemia.[11–16] Afterload mismatch is initially responsible of decreasing in EF and stroke volume, but later on long-term exposure to pressure overload and demand ischaemia produce intrinsic myocardial contractility dysfunction with further decrease of EF, LV dilatation and secondary mitral regurgitation[11–13] • Various precipitants may intervene in different stages of severity and ventricular adaptation and may lead to decompensation, when SV is decreased at rest, and development of AHF[11–16] • Acute obstruction of aortic prosthetic valve may lead to AHF. The acute outflow obstruction, if left untreated, leads to a rapid clinical deterioration with decrease of SV and LV dilatation[11–16]	• May present with any clinical profile[1,13,15,16] • Clinical presentation is more severe in patients with LVEF <50%, peak aortic jet velocity ≥5 m/s, TR pressure gradient ≥40 mmHg, combined valvular disease[17,37] • CS presentation is strongly related to mortality even after interventions[121,123] • RHF may occur in the later stages of AS evolution as consequence of PH or associated right-sided VHD[37]
Severe AR	• Backflow of ejected blood into the LV cavity during diastole and regurgitant volume is dependent on the regurgitant area, diastolic gradient and diastolic time.[11–16] AR may produce relative ischaemia as consequence of the decreasing diastolic coronary flow and as result of elevated end-diastolic pressures and tachycardia that increase myocardial oxygen demand. This supply–demand mismatch is further aggravated when significant coronary lesions are present or if aortic dissection impairs coronary flow.[11–16] Chronic AR: increased LV preload, LV dilatation, LV eccentric hypertrophy; low aortic diastolic pressure and LV eccentric hypertrophy contribute to relative myocardial ischaemia. In compensated stages, SV is maintained via compensatory mechanisms, but several precipitants may lead to decompensation and SV cannot increase in response to demanding conditions (exercise, infection, arrhythmia, etc.) and progressively it decreases at rest.[11–16] Acute AR: acute increase of LVEDP without the chronic adaptive mechanisms of hypertrophy and dilatation. The sudden increase of end-diastolic pressure in a normal sized left ventricle rapidly leads to a decrease in forward cardiac flow.[11–16] Acute AR may occur in settings of endocarditis, either native or prosthetic valve, when detrimental effects of both infection and haemodynamic instability potentiate each other[150,151]	• There is a poor correlation between AR severity and symptoms and in acute settings the auscultation has poor accuracy for diagnosis or estimating severity • May present with any clinical profile but chronic MR presents more frequently as ADHF and acute MR commonly presents as CS or APO[1] • In acute settings, symptoms at presentation may also reflect the underlying pathogenesis of acute AR, such as severe chest pain from aortic dissection or fever from endocarditis • Haemolytic anaemia is the consequence of paravalvular leak[157] • Mixed shock (cardiogenic and septic) may occur in patients with endocarditis and acute MR[154,155] • Septic embolus may occur in 20–50% of patients with endocarditis[80,154] • RHF may occur as a consequence of PH or associated right-sided VHD
Severe MR (primary and secondary)	• Leakage of blood into the left atrium during systole; regurgitant volume depends on the regurgitant orifice area, systolic time, systemic vascular resistance, LA pressure and LVESP[11–16] Chronic MR: increased LV preload, LV dilatation, LV eccentric hypertrophy. In compensated stages, SV is maintained via compensatory mechanisms, but several precipitants may lead to decompensation when SV is decreased at rest[11–16] Acute MR: there is a sudden volume increase into a normal sized and poorly compliant left atrium, an excessive increase in LA pressure and congestion of pulmonary circulation and an acute reduction in the forward cardiac output.[11–16] Acute MR may occur in settings of endocarditis, either native or prosthetic valves, when detrimental effects of both infection and haemodynamic instability potentiate each other.[150,151] In acute secondary MR (in settings of ACS) poor LV compliance aggravate pulmonary congestion[31]	• May present with any clinical profile but chronic MR presents more frequently as ADHF and acute MR commonly presents as CS or APO; unilateral APO may occur in acute MR with eccentric jet.[1,11–14] • Cardiac auscultation has poor accuracy for diagnosis or estimating severity[11–14] • Mixed shock (cardiogenic and septic) may occur in patients with endocarditis and acute MR[154,155] • Haemolytic anaemia is the consequence of paravalvular leak[15,16,157] • RHF may occur as a consequence of PH or associated right-sided VHD

Table 2 (Continued)

	Pathophysiology	Clinical presentation
Severe MS	• Severe MS manifests as obstruction to LV filling, increased LA pressure, LA volume, decreased LV preload and dependence on LA kick[11–16] • In 25% of patients, systolic dysfunction is also present due to chronic decrease of preload but also due to rheumatic cardiomyopathy[11–16] • Acute obstruction of mitral prosthetic valve may lead to AHF. The acute obstruction leads to a rapid clinical deterioration[11–13]	• Resting symptoms usually develop when the valve area is <1.0 cm². However, symptoms often occur in patients with larger valve areas if the time of diastolic filling decreases and/or transmitral flow increases (pregnancy, infection, new-onset or rapid AF, fever, anaemia, hyperthyroidism or haemodynamic shifts in the perioperative period of patients undergoing non-cardiac surgery).[11–16] However, symptom status may change with no change in MS severity because of an increased haemodynamic load • Patients may also present with AF, or an embolic event • RHF may occur as a consequence of PH or associated right-sided VHD
Severe TR	• Very often TR is the consequence of left-sided diseases or left-sided VHD.[59] Chronic volume overload, induced by severe TR, promotes an increase in RV end-diastolic volume, preload and wall tension, resulting in RV ischaemia and, accordingly, RV systolic dysfunction and increased overall mortality.[11–16] The RV remodelling process associated with secondary TR varies tremendously between patients. The different patterns of RV remodelling may be related to the underlying pathophysiology and to the timing in natural history of secondary TR when these patterns are assessed[57] • TR creates a vicious cycle of progressive RV dilatation, annular dilatation and leaflet tethering that results in increased TR severity and RV dilatation, eventually leading to RV dysfunction. Also, significant TR reduces RV SV and, therefore, LV preload and cardiac output[27,52,54,56] • Increase of RV volume and RV pressure produces leftward interventricular septal displacement with LV compression and restricted LV filling, resulting in the subsequent reduction in LV preload with increase in LVEDP and PAP and decrease of cardiac output[55,57,58] • Elevated RA pressure caused by TR determines increase in CVP and systemic venous congestion. Also, high RA pressure can lead to atrial remodelling and to the development of supraventricular tachyarrhythmias, compromising cardiac stability of patients with severe TR[54] • Increase in CVP with systemic venous congestion is the main determinant of worsening renal function, hepatic failure, compromised gastrointestinal function	• Clinical manifestations of TR are characterized by the consequences of increase in CVP with systemic venous congestion and in advanced stages, decrease of cardiac output and signs of end-organ dysfunction.[11–16,55,57–59] However, fatigue, decreased exercise tolerance, peripheral oedema, hepatic congestion, decreased appetite, ascites/anasarca are non-specific and often erroneously considered non-TR-related • Systemic venous congestion is a main determinant of the decline of glomerular filtration rate and of the exhaustion of renal autoregulatory capacity.[51] A pathological rise in renal venous pressure is an independent risk factor for worsening renal function in patients with AHF, even in the absence of impaired cardiac output • Hepatic failure, resulting from both hepatic congestion and reduced hepatic perfusion, is crucially combined to TR severity.[55,57–59] TR is particularly susceptible to result in severe passive congestion,[55] and this leads to atrophy of the hepatocytes and sinusoidal oedema that can directly affect oxygen diffusion to the hepatocyte with subsequent hepatic failure (increased markers of cholestasis and reduced albumin synthesis), leading to a vicious cycle that sustains the increase of hydrostatic pressure and abdominal oedema[57–59] • Compromised gastrointestinal function: visceral oedema and intra-abdominal hypertension can lead to malnutrition, protein-losing enteropathy, bacterial translocation from the intestinal gut and diuretic malabsorption and resistance[53,55,59] • The clinical presentation can also include symptoms mimicking left-sided heart disease because TR-induced RV volume overload impairs LV filling by direct ventricular interaction through the interventricular septum[55,57–59]

ACS, acute coronary syndrome; ADHF, acute decompensated heart failure; AF, atrial fibrillation; AHF, acute heart failure; APO, acute pulmonary oedema; AR, aortic regurgitation; AS, aortic stenosis; CS, cardiogenic shock; CVP, central venous pressure; EF, ejection fraction; LA, left atrial; LV, left ventricular; LVEDP, left ventricular end-diastolic pressure; LVEF, left ventricular ejection fraction; LVESP, left ventricular end-systolic pressure; MR, mitral regurgitation; MS, mitral stenosis; PAP, pulmonary artery pressure; PH, pulmonary hypertension; RA, right atrial; RHF, right heart failure; RV, right ventricular; SV, stroke volume; TR, tricuspid regurgitation; VHD, valvular heart disease.

Multidetector computed tomography (MDCT) is extensively used in perioperative care of percutaneous valve procedures.[61,63] MDCT may diagnose leaflet thrombosis.[61] It has also a role to assess the extent of aortic calcification and 'porcelain aorta' in the elderly[64] and for those requiring redo surgery.[65] MDCT can identify native cusp/prosthetic leaflet vegetations,[62,66,67] though it is more useful as an add-on to TTE and TEE, with sensitivity up to 100% for the detection of perivalvular complications (abscesses/pseudoaneurysms).[62]

18-Fluoro-2-deoxyglucose positron emission tomography-computed tomography improves the diagnostic ability of TEE in prosthetic valve endocarditis (100% sensitivity and 91% specificity),[68] but it is not as sensitive for the native valves.[69]

Magnetic resonance imaging can overcome the shortcomings of echocardiography (i.e. difficult acoustic window) for evaluating the severity of aortic insufficiency, has a very good accuracy for characterization of right ventricular systolic function and precisely characterizes myocardial tissue (including displaced/anomalous/ischaemic papillary muscles).[70]

Right heart catheterization – pulmonary artery catheter

There is no agreement on the optimal method of haemodynamic monitoring in patients with AHF. Pulmonary artery catheter (PAC) measurements guide volume, drug (inotrope, vasopressor) mechanical circulatory support (MCS) and patient's response to these interventions.[71] PAC is guideline-recommended in patients with severe TR prior to surgical or interventional valve repair.[35] In the complex patients with VHD and AHF, PAC may be appropriate for diagnosis and therapeutic management, especially in patients with PH and/or right ventricular failure, in patients deteriorating to CS, in patients with planned MCS, or in cases of additional respiratory distress syndrome or sepsis. In addition, the PAC does provide important diagnostic information in selected patients who fail to respond to initial therapeutic interventions (persistence of hypotension and hypoperfusion), or in case of diagnostic/therapeutic uncertainty (cases of mixed shock or patients with advanced right HF).[72]

As firm evidence is lacking, PAC indication must be checked carefully, its placement and measurements be done with caution, and early removal is advised when patient condition improves.

Specific clinical settings

Prosthesis valve dysfunction

Both mechanical and biological prostheses in any location are vulnerable to acute paravalvular regurgitant disease because of suture failure or valve dehiscence related to endocarditis. Mechanical prostheses are also subject to acute thrombosis (which has the potential to result in stenosis, regurgitation, or both).[11] In biologic prosthesis, infective endocarditis might also lead to acute regurgitation due to leaflet tear/perforation or acute stenosis due to obstructive vegetations.[11]

The sudden occurrence of AHF symptoms in a patient with a valve prosthesis should raise the suspicion of prosthesis malfunctioning, which can be acute, due to thrombosis or endocarditis.

The incidence of thrombosis in mitral valve prosthesis ranges from 0.1 to 5.7 per 100 patient-years,[73] whereas thrombotic obstruction in aortic valve prosthesis has a prevalence of 1% to 3%.[74]

Obstructive valve thrombosis generally leads to a sudden onset of severe HF symptoms and haemodynamic instability. Prognosis is poor in absence of appropriate treatment.

Clinical examination reveals the absence or damping of prosthetic valve sounds. TTE can identify increased transvalvular gradients, reduced valve motion, and valve thrombosis.[73]

Infective endocarditis occurs in 1–6% in patients with prosthetic valve. In early prosthetic valve infective endocarditis (PVIE), which occurs within 1 year of surgery, endocarditis is considered as a perioperative contamination and usually leads to perivalvular abscess, fistulae or pseudo-aneurysms. Early PVIE may also lead to paravalvular leak that may cause haemolysis. Late PVIE occurs more than 1 year after valve replacement and is characterized by infective involvement of the leaflets causing vegetations or perforation. Both conditions may lead to AHF due to bioprosthesis dysfunction (stenosis and/or insufficiency).

Bioprosthesis degeneration can also cause AHF.[75] Time of degeneration depends on patient age and comorbidities, valve position (atrio-ventricular vs. aortic), type and size of bioprosthesis.[75] Different mechanisms of degeneration may occur (calcification, fibrosis, leaflet tear or disruption, pannus or thrombus) leading to valve stenosis or insufficiency.

Native valve endocarditis

Acute HF is among the most frequent complications of native valve endocarditis (NVE) and represents the most common indication for surgery in these patients. AHF occurs secondary as a result of AR or MR (due to leaflet or chordae rupture or leaflet perforation), intracardiac fistulae or valve obstruction caused by vegetations. Tricuspid valve endocarditis is commonly associated with cardiac implantable electronic devices (CIED).

In the ESC-EORP EURO-ENDO (European infective endocarditis registry),[76] congestive HF was observed in 15.9% and CS in 6.2% of patients with NVE. In that registry, both culture positive and negative were associated with valvular destruction, but HF was more common and more severe in patients with culture negative NVE.[77]

In a prospective observational cohort study, Roux *et al.*[78] found that HF was 2.5 times more frequent and mortality two times higher when NVE was complicated with an acute coronary syndrome, due to coronary embolism, coronary compression by an abscess and obstruction of left coronary ostium by a large vegetation.

Secondary mitral and tricuspid regurgitation

Secondary MR is a consequence of left ventricular and/or left atrial remodelling. Many concerns arise regarding the prognostic

benefit of intervening secondary MR in AHF. The only randomized trial showing a benefit of MR correction in patients with chronic HF is the COAPT trial[79] which compared optimal medical therapy and transcatheter edge-to-edge repair (TEER) versus optimal medical therapy alone. A simultaneously published trial, MITRA-FR,[80] showed neutral results though it included a different population with more advanced HF. Therefore, carefully selected patients with a COAPT-like profile should benefit from TEER.[81] However, non-ambulatory NYHA class IV with signs of hypoperfusion or need for inotropes or MCS were exclusion criteria in the COAPT trial. Thus, we do not have strong evidence supporting treatment of secondary MR in AHF setting, with limited data only from observational studies.

The prognostic relevance of secondary TR in the context of AHF depends on the relative contribution of right ventricular dysfunction and the stage of HF. Recent data suggest that it could be a marker of disease severity rather than an independent prognostic factor.[82] For treatment, although retrospective data show promise, further studies are definitely needed to identify the point of no return beyond which TR intervention is futile. To date, indications from current guidelines are valuable also in the AHF setting.[1,15,16]

Combined valvular heart disease

Multiple VHD, defined by the presence of a regurgitant and/or stenotic lesion involving at least two cardiac valves, has a prevalence of 20%, if moderate and/or severe dysfunction is considered[83–85] (*Table 3*). Patients with multiple VHD are more symptomatic with higher mortality than those with single VHD.[85]

Patients with combined VHD represent a particular diagnostic challenge not only for assessing the true severity of the different valvular lesions but also for the optimal timing of the intervention. The haemodynamic interaction between different VHDs generally exacerbate, but also mitigate the expression of a single valvular lesion. 'Flow-dependent' or 'loading condition-dependent' echocardiographic parameters of quantification are sources of error in the context of multiple VHD, particularly in patients with AHF. TEE plays an important role, both to assess the severity of individual valvular lesions and to determine the optimal strategy, based on morphologic features of the valves when is possible.[86] In AHF patients who combine moderate to severe AS with severe MR, transaortic pressure gradient may be reduced, even during dobutamine stress echocardiography, leading to underestimation of AS severity. In this clinical setting, as well as in paradoxical low-flow, low-gradient AS, quantitation of aortic valve calcium score by MDCT may provide more accurate assessment of AS.[16]

Complex clinical judgment is necessary, since the correction of a single valve lesion can exacerbate, or on the contrary, reduce the severity of another valvular lesion through changes in loading conditions and reverse remodelling.[85,87] Current guidelines lack evidence-based recommendations to guide clinical decision-making in multiple VHD, as most studies have focused on single valve disease. It is advised as medical decision to carefully individually evaluate and balance the risk of combined intervention against the evolution of 'left untreated' valve disease with the inherent risk of subsequent intervention.[15,16,86–90]

In patients undergoing surgical intervention for VHD, multivalve disease can be treated during a single procedure, although often with an increase in surgical risk. While surgical intervention to address mixed VHD might be best for some patients, transcatheter interventions offer the option of a stepwise approach when surgery is high risk, treating the most severe lesion first and then reassessment followed by subsequent interventions if needed.[91]

According to current guidelines,[15,16] patients with multiple VHD should be referred to a specialized Heart Valve Centre where a Heart Team, including HF specialists, can offer the best therapeutic option[15,16,86–91] (*Table 3*).

Treatment

It is advised as management principles in AHF patients with VHD[16] to follow a staged approach (*Figure 2*) including the following steps: (i) diagnosis including assessment of VHD severity, identification of the clinical phenotype of AHF and estimation of the patient's prognosis; (ii) stabilization and reassessment; (iii) definitive treatment; and (iv) post-intervention care.

Since AHF is a major risk factor for perioperative mortality, all attempts should be undertaken to stabilize the patient before treatment via Heart Team evaluation. Three possible scenarios should be considered. First, if there is no emergent indication to intervention, patients must receive medical therapy as outlined in current guidelines.[1] Medical therapy may be appropriate as bridge to delayed or elective intervention or as destination therapy if intervention is contraindicated because of the comorbidities and this case is associated with poor prognosis.[12] Second, patients presenting with CS or AHF refractory to medical treatment require interventions on an urgent/emergency basis, when VHD represents the main contributor to the immediate life-threatening haemodynamic deterioration. Third, early use of percutaneous MCS may help bridge patients to a decision of delayed VHD repair, left ventricular assist device (LVAD) and/or transplantation. The second and third scenarios are more likely to be considered as patients with AHF and VHD may require emergent surgery, especially in case of valve endocarditis or acute AR, caused by aortic dissection or acute MR, caused by papillary muscle rupture. Following intervention, if LVEF remains <40%, guideline-directed medical therapies should be initiated during the pre-discharge phase.[1]

Early intravenous medical treatment

The goal of medical therapy is to stabilize the AHF patient prior to definitive correction of the VHD. These therapies aim to optimize left and right ventricular loading conditions and to reduce congestion while maintaining tissue perfusion. In case of persistent haemodynamic instability, urgent intervention (transcatheter or surgical) is guideline-recommended[16] (*Figure 2*).

Aortic regurgitation

In AR, intravenous loop diuretics, generally intravenous furosemide, can be used if there is volume overload. Intravenous

Table 3 Pathophysiology, diagnosis and management of combined valvular heart disease

	Pathophysiology	Diagnosis	Management
AS and MR	• MR may lead to an underestimation of the severity of AS[87,89] • An increased mitral regurgitant volume is to be expected • Secondary MR is common, but even when severe, may regress following AS correction • Secondary MR may improve in up to 50% of cases after aortic valve intervention[88] • Low-flow, low-gradient AS is common[87,89]	• TTE/TEE: increased area of MR jet using colour-flow mapping is unreliable; PISA method is still reliable • Mitral effective regurgitant orifice less affected than MR volume and colour-flow mapping parameters • Underestimation of AS severity will occur with significant MR, as forward LVOT flow is reduced • Aortic valve calcium scoring by CCT for confirming AS severity	• Concomitant surgery of the aortic and mitral valve should be performed for patients with severe AS and severe primary MR whenever possible[15,16] • SAVR and concomitant repair/replacement of the mitral valve in case of severe secondary MR[15,16,87,89] • For moderate secondary MR, TAVI followed by re-evaluation of MR and transcatheter edge-to-edge repair if needed[16,87,89] • TAVI with staged transcatheter edge-to-edge repair is reasonable for patients with severe AS and persistent secondary MR after TAVI[15,16,87,89] • AS correction by TAVI or surgery and secondary MR should be medically treated > percutaneous mitral valve repair indication should be reassessed during follow-up[15,16,87,89]
AS and MS	• Usually due to reumathismal disease which causes extreme fusion of commissures, and calcification beyond valve tissues; patients are especially exposed to low cardiac output • It is very difficult to assess the severity of AS in patients with severe MS[87,89] • Very common, patients with severe AS and MS have an unfavourable anatomy with heavily calcified annulus and leaflets[87,89,92]	• TTE/TEE • Underestimation of lesions may occur as forward flow is severely depressed • TEE may be essential for evaluation of calcification criteria that may make the valves amenable to percutaneous therapies • 3D mitral valve anatomic area can be used to confirm MS severity • DSE and/or aortic valve calcium scoring by CCT can be used to confirm AS severity	• The treatment strategy is largely dependent on mitral valve morphology and the presence of concomitant MR[15,16,87–89] • Concomitant surgical replacement of the aortic and mitral valve is indicated. If patient can be stabilized and there is no high/prohibitive surgical risk • In cases of high or prohibitive surgical risk and unfavourable valve morphology such as severe mitral annular calcification, TAVI followed by transcatheter mitral valve replacement is an option in experienced heart valve centres[15,16,87–90] • Surgery is mainstay as rheumatic AS may not be amenable by percutaneous therapy; TAVI and percutaneous mitral valvuloplasty could be accomplished when echo criteria are present[15,16,87–90] • Agents that promote tachycardia should be avoided, as filling may be dependent on cycle length duration
AR and MS	• MS may blunt the increase of pulse pressure commonly associated with AR	• TTE/TEE • LV dilatation associated with AR may not be as significant • Pulmonic flow could be used as reference for the continuity equation • Severity of MS may be underrecognized by the increase in LV pressure • 3D mitral valve anatomic area can be useful for confirming MS severity	• Surgery is mainstay therapy • Bradicardic agents should be best avoided in acute settings

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Table 3 (Continued)

	Pathophysiology	Diagnosis	Management
AR and MR	• Secondary MR may be commonly present due to long lasting LV dilatation and dysfunction • Low output may be more frequent than in other multiple valve diseases • In acute setting with only mild LV dilation, an acute etiology such as infective endocarditis should be searched for • When AR is severe, MR will worsen LV remodelling and dysfunction	• TTE and TEE for AR mechanism evaluation • Doppler volumetric method using left-sided assessment of net forward flow may be invalid; mitral-to-aortic velocity time integral ratio is unreliable, but the PISA method remains accurate for the assessment of MR	• Bradicardic agents should be best avoided in AHF setting • Surgery is ussualy needed for both valves • There are no evidence-based recommendations regarding the management of moderate AR during mitral surgery [15,16]
AS and AR	• Decreased LV compliance with disproportionate increase in LV diastolic pressure • The left ventricle will not dilate as expected with isolated AR	• TTE/TEE • For AR severity, PHT method may be unreliable, especially in acute settings • Peak aortic jet velocity and Doppler mean gradient will be increased disproportionally from AS severity as may reflect severity of both AR and AS	• Percutaneous procedures could be preferred for at least intermediate and high-risk patients • Early intervention may be warranted as disease may be poorly tolerated [15,16]
MS and MR	• Aetiology is mainly rheumatic [16] • LA pressure and pulmonary pressures may be markedly increased [16,87,89]	• TTE and TEE • Continuity equation unreliable for MS evaluation • PHT method may not be reliable • Doppler mitral gradient reflects severity of both MS and MR • Assessement of mitral ring calcification is required	• Surgery is mainstay of treatment • Percutaneous procedures are under development and mitral TAVI could be inserted if the rheumatic mitral ring provide enough support [87,89]
TR and left-sided VHD	• Secondary TR associated with left-sided VHD is common and severity is highly variable	• TTE and TEE • Evaluation of right atrium, right ventricle and pulmonary pressure and resistance are equally significant • TR should be best evaluated with euvolaemia	• A low threshold for identification of the criteria requiring surgery of TR • Previous evidence of right heart failure may be an indication as well • The response of TR to aortic or mitral valve interventions is unpredictable and in view of the high peri-operative mortality of reoperation for severe TR after left-sided valve surgery, current guidelines support the addition of tricuspid valve surgery when performing left-sided valvular surgery among patients with severe TR or among patients with moderate TR in the presence of a dilated annulus (≥40 mm) [15,16] • If patients are deemed at high surgical risk or inoperable, staged transcatheter tricuspid valve intervention for persistent or worsening TR after TAVI or mitral TEER can be considered [15,16,87,89]

3D, three-dimensional; AHF, acute heart failure; AR, aortic regurgitation; AS, aortic stenosis; CCT, cardiac computed tomography; DSE, dobutamine stress echocardiography; LA, left atrial; LV, left ventricular; LVOT, left ventricular outflow tract; MR, mitral regurgitation; MS, mitral stenosis; PHT, pressure half-time; PISA, proximal isovelocity surface area; SAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation; TEE, transoesophageal echocardiography; TR, tricuspid regurgitation; TTE, transthoracic echocardiography; VHD, valvular heart disease.
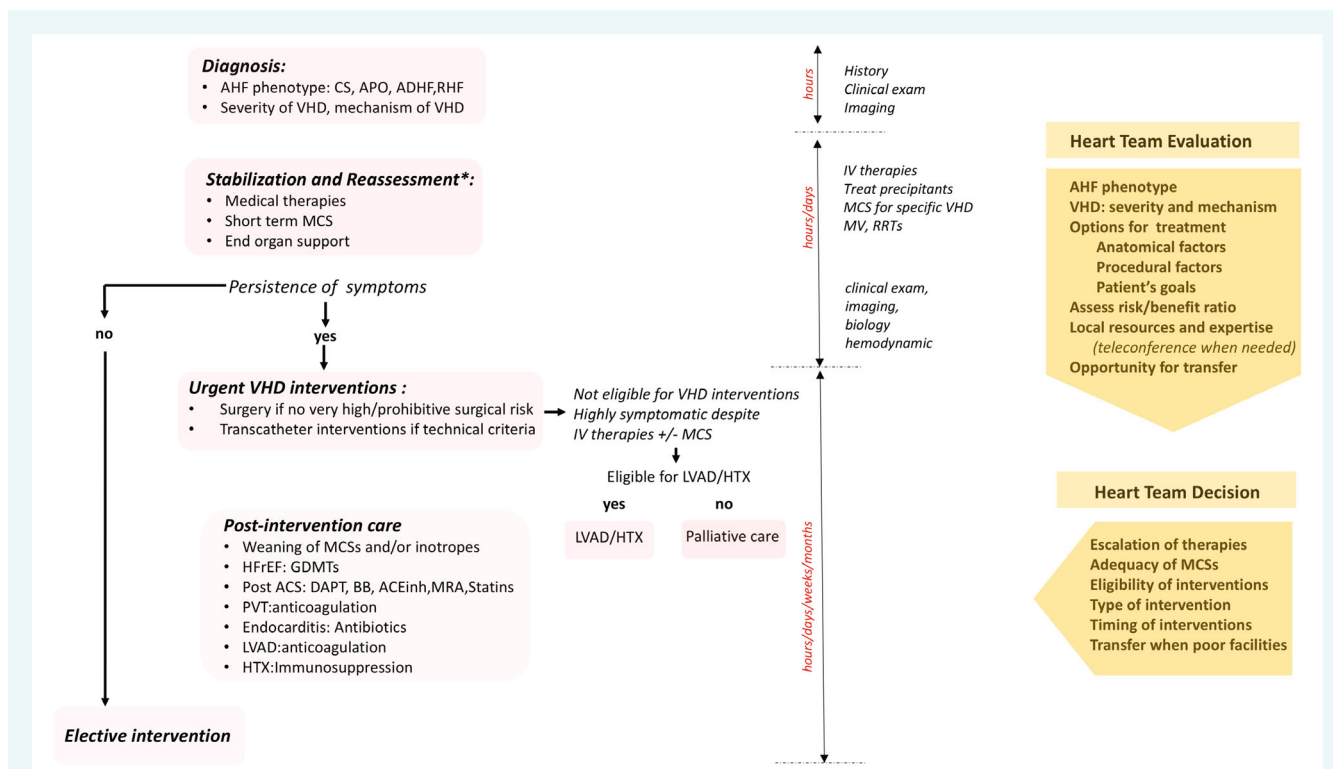
Figure 2 The management of patients with valvular heart disease (VHD) and acute heart failure (AHF) and the role of the Heart Team. The staged management approach in AHF patients with VHD includes the following steps: (i) diagnosis, including assessment of VHD severity, identification of the clinical phenotype of AHF and estimation of the patient's prognosis; (ii) stabilization with continuous reassessment; (iii) definitive VHD treatment; (iv) post-intervention care. Medical therapy can be used as bridge to elective intervention or as destination therapy if intervention is contraindicated because of very high procedural risk, severe comorbidities or futility. Highly symptomatic patients, despite intravenous (IV) therapies +/− mechanical circulatory support (MCS), but not eligible for VHD interventions should be evaluated for heart transplant (HTX) and left ventricular assist device (LVAD) implantation. The Heart Team must individualize multidisciplinary discussion to offer the best option for each particular case. ACS, acute coronary syndrome; ACEinh, angiotensin-converting enzyme inhibitor; ADHF, acute decompensated heart failure; APO, acute pulmonary oedema; BB, beta-blocker; CS, cardiogenic shock; DAPT, dual antiplatelet therapy; GDMT, guideline-directed medical therapy; HFrEF, heart failure with reduced ejection fraction; MRA, mineralocorticoid receptor antagonist; PVT, prosthetic valve thrombosis; RHF, right heart failure; RRT, renal replacement therapy. *Continuous reassessment after initial therapies is mandatory in order to evaluate congestion and perfusion status, to confirm VHD severity, to decide the need for further escalation and to establish indication of VHD intervention on an emergency or elective basis.

vasodilators can be used in normotensive or hypertensive patients to improve forward flow.[12] In particular, nitroprusside, reducing both left ventricular afterload and preload, can reduce aortic regurgitant volume.[92] Inotropic agents, such as milrinone or dobutamine, can be used in patients with AHF and hypotension to increase stroke volume.[12] However, when CS ensues, norepinephrine represents the first choice.[14] In general, beta-blockers are not appropriate in acute AR, as they can prolong diastolic regurgitation time and decrease stroke volume.[12] In case of CS and severe bradycardia, temporary cardiac pacing is advised.[14]

Aortic stenosis

Intravenous therapy for severe AS is limited by the presence of a fixed obstruction and left ventricular hypertrophy that make the ventricle preload sensitive.[14] In normotensive or hypertensive

patients with AS and congestion, the cautious use of vasodilators and diuretics can safely mitigate congestion,[12] but excessive doses may result in decreased cardiac output with hypotension. Mixed vasodilators, such as nitroglycerine, should be avoided. Nitroprusside was found to be effective in reducing left ventricular filling pressure and improving cardiac output in a small set of patients with severe AS and severe left ventricular dysfunction and was safe as a bridge to aortic valve replacement.[93] Inotropes (dobutamine)[14] and levosimendan[94] may be used in extremely selected patients with severely impaired cardiac output, but their use is limited as they may increase transvalvular gradient without increasing forward stroke volume and may worsen myocardial ischaemia in patients with concomitant coronary artery disease. However, the increase in the valve gradient and stroke volume due to inotropes can help to confirm severity of AS in patients with HFrEF. In patients with severe AS and hypotension, intravenous norepinephrine increases blood pressure and can restore coronary

perfusion pressure. Phenylephrine is useful for counteracting the vasodilatory effects of anaesthesia.[14]

Mitral regurgitation

The left ventricular function in severe MR is highly afterload sensitive and vasodilators are first-line therapy in patients with AHF and MR unless hypotensive.[95,96] They are effective in reducing left ventricular afterload, increasing forward stroke volume and reducing MR. For the remaining patients, carefully titrated intravenous diuretics are effective to achieve adequate decongestion. Inotropic (dobutamine) and inodilator (milrinone) drugs may be appropriate to improve stroke volume in patients with hypotension and/or signs of hypoperfusion.[14] In AHF patients with secondary MR, levosimendan acutely improves systolic and diastolic function and reduces MR degree and might be particularly useful in patients already on beta-blockers and in those with PH and/or right ventricular dysfunction.[97] Intravenous vasopressors may worsen MR, and even in hypotensive patients it is advised as the lowest possible dose to be used.[14]

Mitral stenosis

In MS, intravenous diuretics reduce pulmonary congestion and improve symptoms.[12] Intravenous vasodilators and inotropes are ineffective at reducing congestion or increasing cardiac output in MS with impaired left ventricular filling, but with relatively preserved left ventricular function.[98] In hypotensive patients, cautiously titrated intravenous norepinephrine or vasopressors without tachycardic effects, such as vasopressin, increase forward flow.[14,60,72] The most common reason for HF decompensation in patients with MS is atrial fibrillation with rapid ventricular rate. Parenteral beta-blockers (i.e. esmolol, landiolol) decrease heart rate, prolong diastolic filling time, reduce left atrial pressure and transmitral gradient. Intravenous digoxin and amiodarone may be appropriate for rate control in hypotensive patients with atrial fibrillation. A rhythm control strategy using electrical cardioversion is guideline-recommended,[1,16] if there is haemodynamic instability, though anticoagulation and TEE are needed frequently.[99]

Tricuspid regurgitation

In secondary TR, the underlying aetiology should be addressed. Diuretics, intravenous furosemide alone or in combination with thiazides, decrease volume overload and may improve symptoms in severe TR with signs of right HF.[16] Adding an aldosterone antagonist represents a possible treatment option, in particular for patients with hepatic congestion and secondary hyperaldosteronism.[1] However, the benefit of aldosterone antagonists or angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers on right ventricular remodelling or functional improvement in patients with severe secondary TR has not been validated in clinical studies.

Inotropic and vasopressor agents may support right ventricular contractility. Dobutamine up to 5 µg/kg/min, milrinone and levosimendan improve cardiac output without increasing PVR in patients with PH. In patients with PH, pulmonary vasodilators may lead to a reduction in TR severity.[35,100]

Specific conditions

When AHF is caused by prosthetic valve endocarditis, appropriate antibiotic therapies should be initiated and continued 4–6 weeks after intervention.[15,16,101] However, for patients with CS and prosthetic valve endocarditis, urgent cardiac surgery remains the only option unless contraindicated in Heart Team.[15,16] In presence of obstructive thrombosis of a mechanical prosthesis, intravenous unfractionated heparin is indicated in case of inadequate recent anticoagulation and with absence of haemodynamic instability. According to guideline recommendations, fibrinolysis should be considered if the patient presents with severe haemodynamic instability and surgery is not immediately available or is deemed high risk.[16]

Mechanical ventilation

The assessment of respiratory status and anticipating a need for airway management with either intubation or non-invasive positive pressure ventilation (NIPPV) is critically important in patients with VHD presenting with AHF.[1,12,16] There are no particular indications for any modality or technique of mechanical ventilation in patients with VHD and AHF.[102–104] However, the most common condition requiring invasive mechanical ventilation in patients with significant VHD and AHF remains cardiac surgery.[104] General anaesthesia with mechanical ventilation via intubation is also recommended during percutaneous procedures, such as complex mitral and tricuspid transcatheter interventions, when TEE is essential to guide procedures and to detect early potential complications.

According to guideline recommendations, NIPPV should be considered in patients with AHF when oxygen therapy is not sufficient to control hypoxaemia and hypercapnia.[1] It should be started as soon as possible to decrease respiratory distress and reduce the need for endotracheal intubation.[58] NIPPV can potentially improve MR severity by reducing left ventricular preload and afterload.[103] Patients with severe AS and MS and AHF may not tolerate intubation with mechanical ventilation as positive intra-thoracic pressure may result in reduced preload with hypotension. Therefore, non-invasive ventilation is preferred. Moreover, positive intra-thoracic pressure may precipitate right ventricular failure in patients with severe PH, and aggravates functional TR and right ventricular dysfunction secondary to VHD, and low pressures should be used in this setting.[102,104]

To note, significant VHD, mainly MR and AS, may preclude weaning from mechanical ventilation, requiring prolonged intubation coupled with weaning strategies.[61,104]

Short-term mechanical circulatory support

Short-term MCS may be appropriate in patients VHD and refractory HF or CS[1,58] to support cardiac output and peripheral perfusion pressure, decrease myocardial oxygen demand and, possibly,

increase coronary perfusion.[105] Early escalation of MCS is preferred to reduce the need for vasopressors and inotropes, which may have unfavourable effects on cardiac loading conditions,[72] but this strategy is not yet supported by the results of clinical trials in patients with CS and diverse aetiologies. Given the complex decision-making required for management of VHD emergencies, referral to a comprehensive Heart Valve Centre is advised. Data from randomized controlled trials do not allow drawing definitive conclusions in favour of one device versus the others in the setting of VHD.[105]

All short-term MCS are contraindicated in presence of significant AR since they can worsen severity of regurgitation and decrease cardiac output. Intra-aortic balloon pump (IABP), TandemHeart and peripheral extra-corporeal membrane oxygenation (ECMO) will all result in an increase of left ventricular end-diastolic pressure due to the incompetent aortic valve, and there will be recirculation with the Impella.[14,72]

In AHF patients with severe AS, IABP and ECMO can be used as bridge to intervention or as support during and after high-risk procedures.[12] Impella can also be used in patients with severe AS, although placement across the stenotic aortic valve might be challenging.[106,107]

In MS, peripheral ECMO can be used, while IABP and Impella are typically ineffective. TandemHeart is theoretically ideal due to direct left atrial unloading.[14,72]

In AHF patients with MR, short-term MCS can be used as bridge to intervention (i.e. papillary muscle rupture), as bridge to recovery (i.e. acute myocarditis with severe MR) or as bridge to long-term MCS or heart transplantation (i.e. advanced HF). Notably, ECMO can worsen functional MR due to left ventricular distension if no venting is provided.

Small studies reported the role of IABP in improving technical success in patients with secondary MR and poor leaflet coaptation undergoing TEER.[108,109] Impella and ECMO have also been described in a few case reports showing their effectiveness in high-risk percutaneous mitral valve procedures.[110] However, cases reporting damage to the subvalvular apparatus after Impella device positioning are also described.[111]

Valvular surgery and percutaneous interventions

Distinct to valvular surgery in chronic settings,[16] there are many challenging aspects in the context of AHF including varying cause−effect relationship between AHF and VHD, timing of intervention (before or after stabilization), type of intervention (repair or replacement, surgical or percutaneous).

Although the current scores for the assessment of the operative risk in patients undergoing cardiac surgery include variables associated with increased risk of mortality,[112] these variables were not specifically validated in the setting of AHF. Since AHF patients with VHD, especially those with multiple organ dysfunctions or severe comorbidities, may have high or prohibitive surgical risk,[16] percutaneous strategies must be integrated into the therapeutic spectrum.

However, there are some acute conditions, such as prosthetic valve thrombosis, acute endocarditis, in which surgery, even at high risk, remains the only therapeutic option when medical treatment is not sufficient.

Aortic regurgitation

In AHF patients with isolated severe AR without dissection, surgery after initial stabilization remains the gold standard (*Figure 3*). Emergency surgery is the only solution in acute severe AR due to aortic dissection, unless contraindicated.[16]
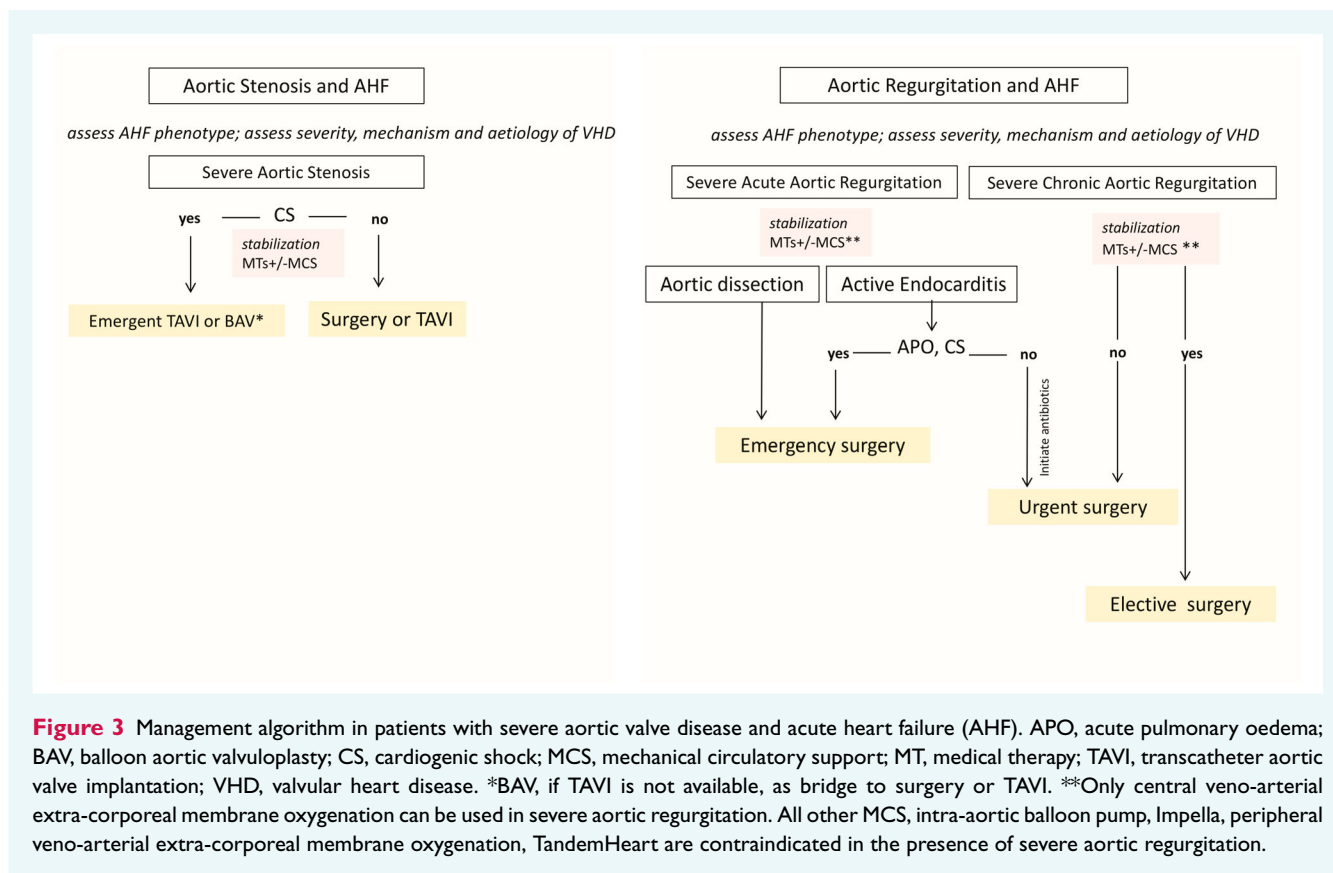
Transcatheter aortic valve implantation (TAVI) represents an appropriate option in AHF patients with AR if (i) surgical risk is prohibitive, and (ii) there are no clinical or anatomical contraindications to TAVI (i.e. active endocarditis, aortic dissection or excessive dilated aortic annulus). Currently, there are no dedicated and approved devices to treat isolated AR (*Figure 3*). Devices used for treating AS are adapted to isolated AR, but these procedures should be considered off-label. The main technical challenge is valve anchoring due to the absence of calcifications. Data from two large multicentre registries reported feasibility and efficacy of TAVI in AR, but most of the patients were electively treated.[113,114] Although the second-generation JenaValve has recently received a CE mark for the transcatheter treatment of severe symptomatic AR, the results of the ALIGN-AR EFS trial,[115] evaluating the safety and effectiveness of the transfemoral JenaValve in the treatment of patients with symptomatic severe AR, will better inform the clinical practice.

Few case reports described treating acute AR with TAVI in the emergency setting.[116,117]

Aortic stenosis

In AHF patients with severe AS, according to guidelines, the choice between TAVI and surgical aortic valve replacement (SAVR) should be based on Heart Team decisions (*Figures 1* and *3*).[16,20] Although there are no specific randomized controlled trials to evaluate the role of TAVI in the setting of AHF, most of the patients undergoing TAVI in randomized trials and observational studies were in NYHA class III or IV. NYHA class IV was found to be associated with poor outcome within 3 months after TAVI, but TAVI recipients with baseline NYHA class IV who survived at 3 months had a long-term outcome comparable to that of patients with baseline NYHA class I−III.[118] Similarly, emergent or urgent TAVI in patients with severe AS and CS has worse prognosis compared to elective TAVI.[119–121] Nevertheless, this difference seems limited to the first months after the procedure and is probably linked to the very high-risk profile.[120]

In patients with severe AS and significant proximal coronary artery disease who are candidates for cardiac surgery, the guideline recommendation for concomitant SAVR and complete revascularization has not recently changed.[16] For TAVI candidates, current guidelines mentioned that percutaneous coronary intervention (PCI) should be considered in patients with a primary indication for TAVI and coronary artery diameter stenosis >70% in proximal segments,[16] but did not make any recommendations for the timing of PCI, pre-, concomitant or post-TAVI. Routine revascularization of all significant coronary artery disease before TAVI in patients with no or minimal angina is not supported by the latest evidence.[122] In addition, other factors such as symptom severity, haemodynamic

Figure 3 Management algorithm in patients with severe aortic valve disease and acute heart failure (AHF). APO, acute pulmonary oedema; BAV, balloon aortic valvuloplasty; CS, cardiogenic shock; MCS, mechanical circulatory support; MT, medical therapy; TAVI, transcatheter aortic valve implantation; VHD, valvular heart disease. *BAV, if TAVI is not available, as bridge to surgery or TAVI. **Only central veno-arterial extra-corporeal membrane oxygenation can be used in severe aortic regurgitation. All other MCS, intra-aortic balloon pump, Impella, peripheral veno-arterial extra-corporeal membrane oxygenation, TandemHeart are contraindicated in the presence of severe aortic regurgitation.

instability (either ischaemia-induced or associated with AS), bleeding risk associated with antiplatelet therapy, amount of contrast use, duration of procedure and coronary access (very challenging post-TAVI when a prosthesis with a supra-annular leaflet position is chosen), are decisional for the appropriate timing.[123] However, there is currently insufficient evidence regarding the role and timing of PCI in AHF patients undergoing TAVI to inform clinical practice and the role of the Heart Team remains essential in this complex patient group.

In patients with CS, balloon aortic valvuloplasty (BAV) remains a reasonable option as a bridge to a definitive intervention in centres without availability for TAVI or SAVR.[15,16] Although acute procedural success, measured as a reduction ≥50% of transaortic pressure gradient, was consistently reported, early restenosis is frequent.[124,125] However, BAV carries risk of significant complications and short- and mid-term outcomes remained poor, with more than half of patients dying at 1 year, with a steady trend over time. In particular, excess risk of mortality was observed when BAV was not followed by definitive therapy (SAVR or TAVI), if the delay to SAVR or TAVI was long or the patient required repeat procedure.[126,127] Thus, it is crucial to only perform BAV at experienced centres, ideally where access to TAVI is available. If TAVI is not available, then transferring the patient to a centre with SAVR or TAVI capabilities is an important consideration when performing BAV. In addition, urgent BAV showed a higher rate of 30- and 90-day HF readmission compared to TAVI performed in urgency settings.[125,128,129] If pre-procedural computed tomography scan is

not available for urgent TAVI, Doppler echocardiography of the ileo-femoral arterial axis and three-dimensional echocardiography can be used for access choice and valve sizing. BAV can be performed as palliative measure when general conditions prohibit any further intervention, and it may be also appropriate in patients with multifactorial causes of acute decompensation and for whom the expected benefit of valve replacement is limited.

Mitral regurgitation

In acute ischaemic MR, papillary muscle rupture needs immediate repair (*Figure 4*). Papillary muscle rupture occurs in 0.25% of patients following acute myocardial infarction (AMI) and represents up to 7% of patients in CS following AMI.[130] Unpredictability and rapid deterioration with death makes surgery for papillary muscle rupture necessary. Short-term MCS can be used to support the intervention. In this context, mitral valve replacement represents the first choice and surgical repair may be appropriate only in carefully selected cases. In case of severe MR due to papillary muscle rupture, percutaneous TEER may be appropriate in expert centres, if the Heart Team deems the surgical option prohibitive.[131–135]

In primary severe MR with AHF, according to guidelines, surgery remains the gold standard and only patients deemed at high or prohibitive risk should be considered for alternative therapies.[16]

A series of such patients with acute severe MR undergoing emergency surgery showed that patients with acute endocarditis, coronary artery disease, pre-operative atrial fibrillation and chronic
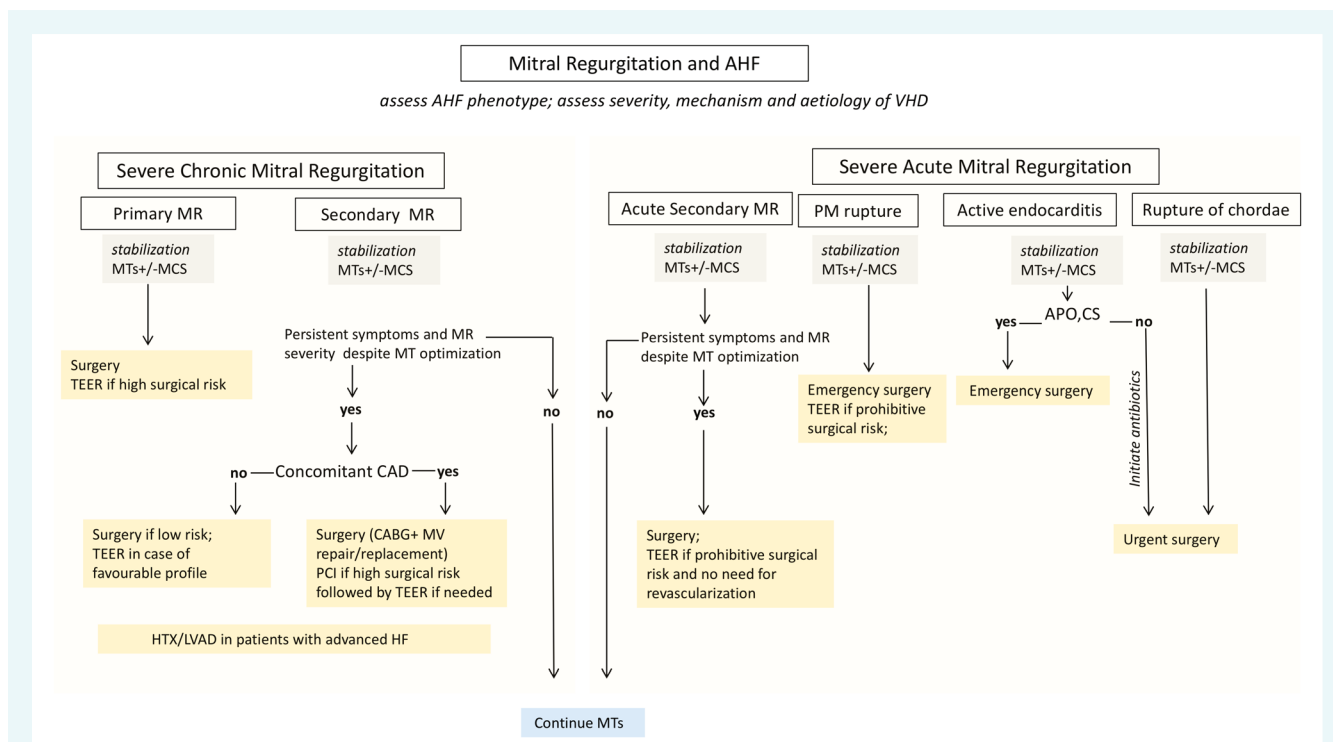
Figure 4 Management algorithm in patients with severe mitral regurgitation (MR) and acute heart failure (AHF). APO, acute pulmonary oedema; CABG, coronary artery bypass graft; CAD, coronary artery disease; CS, cardiogenic shock; HF, heart failure; HTX, heart transplant; LVAD, left ventricular assist device; MCS, mechanical circulatory support; MT, medical therapy; MV, mitral valve; PCI, percutaneous coronary intervention; PM, papillary muscle; SMR, secondary mitral regurgitation; TEER, transcatheter edge-to-edge repair; VHD, valvular heart disease.

renal failure make up the most vulnerable group, with highest risk for early and late adverse cardiac events.[135–138] Thus, according to guidelines, AHF patients with acute primary MR, at high or prohibitive surgical risk may be considered by the Heart Team for percutaneous treatment.[16] TEER is the most used technique, though other devices may be appropriate according to the expertise of the centre.[16,135–137]

Acute secondary MR (i.e. after AMI) requires mitral valve intervention, possibly after initial stabilization. The prognostic impact of surgery in this setting is unproven, and 1-year mortality remains high (19−31%).[134–140] Timing of intervention depends on response to medical therapy and clinical and haemodynamic characteristics of the patient. Short reports showed feasibility and efficacy of TEER in patients with AMI treated by primary PCI, complicated by acute MR,[133,136,141,142] but careful evaluation by a multidisciplinary Heart Team is advised.

Patients with chronic secondary MR who develop AHF during HF progression represent a more challenging group. Efficacy of percutaneous techniques was not demonstrated by randomized trials in this setting but recent multicentre registries suggested a possible beneficial effect of TEER on prognosis of unstable patients presenting with CS.[139,140,143]
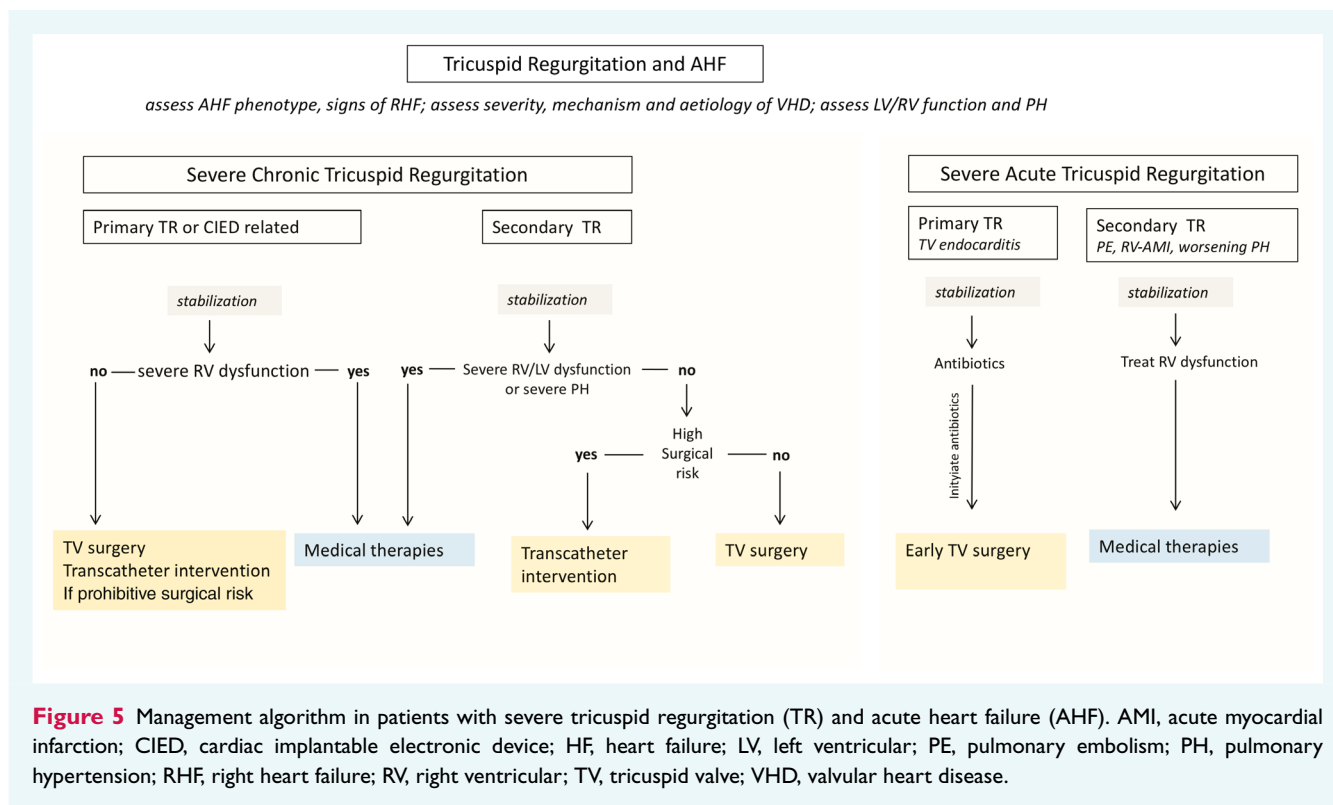
Mitral stenosis

In general, percutaneous mitral commissurotomy (PMC) is indicated in patients with clinically significant and symptomatic MS

having favourable clinical and anatomic characteristic for PMC[16,88] (*Figure 4*). Although evidence is limited, PMC seems feasible also in the AHF setting. PMC is very effective during pregnancy since many of these patients have AHF and surgery is contraindicated.[144] Emergent PMC has high mortality (about 30%), though survivors seem to have a significant haemodynamic and clinical benefit from the procedure.[144,145] According to guidelines, in patients in whom PMC is contraindicated or have unfavourable clinical and anatomical characteristics, surgery should be considered.[15,16]

Tricuspid regurgitation

Most patients remain asymptomatic for a protracted span of time with moderate-to-severe TR. Moreover, when symptoms occur they can initially be insidious and difficult to ascribe to the TR. Fatigue, decreased exercise tolerance, peripheral oedema, hepatic congestion, decreased appetite, ascites/anasarca are non-specific and late findings. Surgery is the treatment of choice in patients with isolated TR presenting with right AHF (*Figure 5*). It has the potential to reduce central venous pressure, halt right ventricular remodelling, increase stroke volume, improve peripheral perfusion and, theoretically, permit the recovery of renal and hepatic function.[52,56,89] However, in-hospital mortality remains high (9%) due to the advanced disease.[146] To note, correcting TR in patients with PH (non-valvular) left heart disease with significantly elevated PVR and/or right ventricular dysfunction is hazardous, and associated with severe post-procedural outcomes.[147,148]

Figure 5 Management algorithm in patients with severe tricuspid regurgitation (TR) and acute heart failure (AHF). AMI, acute myocardial infarction; CIED, cardiac implantable electronic device; HF, heart failure; LV, left ventricular; PE, pulmonary embolism; PH, pulmonary hypertension; RHF, right heart failure; RV, right ventricular; TV, tricuspid valve; VHD, valvular heart disease.

For percutaneous tricuspid valve interventions, a propensity-matched analysis from the largest international multicentre registry showed a better outcome in patients receiving transcatheter tricuspid valve interventions compared to those managed medically. More than 90% of these patients were in NYHA class III or IV and about one-third had right ventricular failure and/or PH.[89] Although not including patients with AHF, in the recent open-label TRILUMINATE trial, tricuspid TEER compared to medical therapy was associated with an improvement in quality of life, but not significant benefit in terms of mortality, HF readmissions and 6-min walk distance.[149] This suggests that in patients with severe HF, TR can be caused by a number of different underlying conditions and its reduction with TEER may not address the root causes of the valvular disease.

Although percutaneous devices for treating TR are spreading, appropriate patient selection, type of device and timing are still unclear. Once a tricuspid valve intervention is considered, it should be performed in a VHD centre with experienced operators and with the potential to offer all treatment modalities with proof of excellent outcomes.[149] In these VHD centres, the multidisciplinary VHD Heart Teams will evaluate the need, timing, and type of intervention.[16,150] Although, transcatheter TV replacement or repair represent novel and less invasive alternatives to surgery and have shown early promising results, larger randomized studies are needed to define the clinical and procedural endpoints and outcomes, in order to draw more solid conclusions, particularly for the subset of patients presenting with AHF.[151,152]

Infective endocarditis

Emergent/urgent surgery is indicated in infective aortic, mitral or tricuspid valve endocarditis with severe regurgitation, obstruction or fistula causing AHF.[15,16,101,153,154] Surgery must be performed on an emergency basis, irrespective of the status of infection, when patients are in persistent pulmonary oedema or CS despite medical therapy.[15,16] Surgery for CS and infective endocarditis has been associated with higher 30-day mortality than patients without shock (19.5% vs. 14.6%), but this mortality is significantly lower than mitral valve infective endocarditis complicated by septic shock who underwent surgery (65.8%).[153] Identifying the primary aetiology of shock in these haemodynamically unstable patients has important treatment and prognostic implications.[154]

When tricuspid valve endocarditis is caused by an infected CIED, extraction of the CIED is guideline-recommended[16] and surgery is typically not needed for removal of the infected device.[101,153]

Prosthetic valve dysfunction

Emergency reintervention (<24 h) is guideline-recommended in critically ill patients with obstructive thrombosis of a mechanical prosthesis in absence of contraindications.[15,16,155]

Fibrinolysis may be considered if the patient presents with severe haemodynamic instability and surgery is not immediately available or if there is very high risk for the treatment of thrombosis of right-sided prostheses.[15,16] A recent observational study suggested a benefit of slow/ultraslow administration of low-dose fibrinolysis.[15,155]

For patients with AHF in settings of prosthetic valve endocarditis, urgent surgery (within days) is guideline-recommended, while emergency surgery is indicated only in cases with refractory pulmonary oedema or CS, as in NVE.[156] Reoperation is also guideline-recommended as first-line therapy in patients with prosthesis dysfunction and severe paravalvular leak causing AHF.[15,16] In acute settings, there is very limited experience with transcatheter closure of paravalvular leaks and this therapy may be appropriate for anatomically suitable paravalvular leaks in candidates selected by the Heart Team.[156]

Transcatheter valve-in-valve procedures are feasible in aortic, mitral and tricuspid position for bioprosthesis failure.[157] These interventions may be appropriate only in selected cases where reoperation is contraindicated or deemed at high risk by the Heart Team or in the acute settings of HF such as bioprosthesis degeneration leading to acute decompensation or CS.[157–159] Valve thrombosis or active endocarditis represent contraindications to percutaneous procedures.

Left ventricular assist devices and heart transplantation

Left ventricular assist devices and heart transplantation are indicated in patients with acute advanced HF when medical therapy and short-term MCS are insufficient to avoid HF progression and multi-organ impairment.[1,160] Type and severity of VHD should be carefully assessed before LVAD implant. In the setting of LVAD, AR creates a circulatory shunt or a 'closed circulatory loop' between the pump, valve, the left ventricle, and back to the pump again.[161] This phenomenon ultimately reduces pump efficiency and decreases left ventricular unloading, cardiac output, and organ perfusion. The presence of AR is likely detrimental to right ventricular function, especially in patients with moderate to severe pre-operative right ventricular failure. The incomplete left ventricular unloading increases right ventricular afterload and worsens right ventricular failure. Concomitant aortic valve procedures at the time of LVAD implantation, in patients with moderate or severe AR is justified and very often performed particularly when the anticipated duration of support is more than 1 year.[162]

Patients with AS associated with moderate/severe AR are treated similarly as patients with AR. Aortic valve replacement in patients with severe isolated AS may potentially optimize chances of left ventricular recovery but does not provide clinical or physiological benefits.[163]

Management of pre-existent severe MR in patients undergoing LVAD remains controversial. In the INTERMACS database, concomitant mitral valve procedures for severe MR were not associated with increased survival compared to no intervention cohorts.[164] In a recent study, there was no significant difference in mortality following MCS in those with or without pre-existing severe MR. In the absence of mitral intervention, 93% of patients showed resolution of MR at 30 days.[165] In addition, a sub-analysis of MOMENTUM 3 including patients who had preoperative severe MR demonstrated residual MR in only 6.2% of patients with Heart-Mate 3.[166] In conclusion, overall data support no intervention for pre-existing severe MR.

Persistent moderate/severe TR seems to be detrimental to LVAD patients, though the benefit of a concomitant tricuspid valve procedure remains unclear and the decision should be based on a multidisciplinary Heart Team discussion.

The International Society for Heart and Lung Transplantation guidelines suggest that moderate/severe TR should be considered for surgical repair at the time of MCS implantation but more recent studies demonstrated no survival benefit and an increase in post-operative morbidity when addressing significant TR.[163,167,168] In a recent clinical trial, tricuspid valve surgery was successful in reducing post-implant TR compared with no tricuspid valve surgery, but was not associated with a lower incidence of right HF.[169]

Cardiac pacing

According to the guidelines, cardiac resynchronization therapy (CRT) is recommended for symptomatic patients with HF and LVEF ≤35% in sinus rhythm with a QRS duration >150 ms and left bundle branch block morphology despite optimal medical therapy and in those with HFrEF and indication for ventricular pacing for high-degree atrio-ventricular block. In presence of AHF with severe AR and/or AS, primary MR, CRT may be appropriate only if these criteria persist after valve treatment.[1,58] On the other hand, in presence of secondary MR, CRT is advised to be performed first if indicated.

Implantation or extraction of pacemaker or defibrillator leads, including CRT, can cause or worsen TR in up to 18% of recipients[170] and possibly lead to AHF. When medical therapy is not sufficient to control symptoms and surgical risk is high, repositioning (via coronary sinus) or extraction of CIED leads can be envisaged in selected patients with disturbed tricuspid leaflet motion.[171] However, the efficacy of lead extraction in reducing TR is uncertain and additional damage to the tricuspid valve can occur.[151,171] If severe and symptomatic TR persists after lead extraction, transcatheter interventions are feasible with different technologies in well-selected patients in experienced centres.[151,171] Tricuspid TEER is advised when there is only commissural jet, while in patients with tricuspid annular dilatation and large leaflet gap (>8.5 mm), transcatheter annuloplasty plus TEER or transcatheter tricuspid valve replacement is advised.[151]

Palliative care

A palliative care approach within the VHD setting is currently clinically relevant. Increasing age, frailty and associated comorbidities, such as cancer, end-stage renal disease, frailty, put an increasing number of patients with VHD at very high or prohibitive surgical risk.[16,172] Also, for VHD patients with complex comorbidities, cardiac disease might not be the primary driver of symptoms and reduced quality of life and in these cases, valve interventions have only marginal effects on a patient's overall clinical course, despite procedural success.[172,173]

The decision not to offer surgery/intervention, when treatment is deemed futile, should not mean abandoning care as these patients require transition to palliative care and continuity of health

services. Ideally, palliative care should continue throughout the disease course and should be instituted alongside disease-modifying interventions.[173,174]

A collaborative approach is advised whereby multidisciplinary team members from cardiology (Structural Heart Team) and palliative care, work together to plan management.[172] A number of service models, utilizing this shared care approach, have been tested within HF and found to yield positive outcomes in terms of improved symptom burden, depression and spiritual well-being.[173,174] The care priorities include treating pain, other symptoms, and psychological distress, using advanced communication skills to establish goals of care and to match treatment options to individualized goals.

Conclusions

Acute HF in the setting of VHD generates several diagnostic challenges, including difficulties in assessing VHD severity because of the rapid change in loading conditions, and the interference with acute precipitants and associated comorbidities that makes problematic to ascertain whether the VHD is the only contributor to the patient's clinical deterioration. Furthermore, therapeutic interventions in patients with VHD and AHF are not rigorously evidence-based because there are no randomized controlled trials in this setting and even more, patients with severe VHD are often excluded from AHF randomized trials. Thus, a clear-cut strategy regarding timing of intervention (before or after stabilization) or type of intervention (repair or replacement, surgical or percutaneous) cannot yet be defined. However, since AHF patients with VHD, especially those with multiple organ dysfunction or severe comorbidities, may have very high or prohibitive surgical risk, percutaneous strategies must be integrated into the therapeutic spectrum, following the Heart Team decision aiming to offer the best option for each particular case.

Supplementary Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Conflict of interest: none declared.

References

1. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Bohm M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). With the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur J Heart Fail*. 2022;**24**:4–131. https://doi.org/10.1002/ejhf.2333
2. Nieminen MS, Brutsaert D, Dickstein K, Drexler H, Follath F, Harjola VP, et al.; EuroHeart Survey Investigators; Heart Failure Association, European Society of Cardiology. EuroHeart Failure Survey II (EHFS II): A survey on hospitalized acute heart failure patients: Description of population. *Eur Heart J*. 2006;**27**:2725–2736. https://doi.org/10.1093/eurheartj/ehl193
3. Chioncel O, Vinereanu D, Datcu M, Ionescu DD, Capalneanu R, Brukner I, et al. The Romanian Acute Heart Failure Syndromes (RO-AHFS) registry. *Am Heart J*. 2011;**162**:142–53.e1. https://doi.org/10.1016/j.ahj.2011.03.033
4. Spinar J, Parenica J, Vitovec J, Widimsky P, Linhart A, Fedorco M, et al. Baseline characteristics and hospital mortality in the Acute Heart Failure Database (AHEAD) Main registry. *Crit Care*. 2011;**15**:R291. https://doi.org/10.1186/cc10584
5. Oliva F, Mortara A, Cacciatore G, Chinaglia A, Di Lenarda A, Gorini M, et al.; IN-HF Outcome Investigators. Acute heart failure patient profiles, management and in-hospital outcome: Results of the Italian Registry on Heart Failure Outcome. *Eur J Heart Fail*. 2012;**14**:1208–1217. https://doi.org/10.1093/eurjhf/hfs117
6. Logeart D, Isnard R, Resche-Rigon M, Seronde MF, de Groote P, Jondeau G, et al. Current aspects of the spectrum of acute heart failure syndromes in a real-life setting: The OFICA study. *Eur J Heart Fail*. 2013;**15**:465–476. https://doi.org/10.1093/eurjhf/hfs189
7. Ambrosy AP, Fonarow GC, Butler J, Chioncel O, Greene SJ, Vaduganathan M, et al. The global health and economic burden of hospitalizations for heart failure: Lessons learned from hospitalized heart failure registries. *J Am Coll Cardiol*. 2014;**63**:1123–1133. https://doi.org/10.1016/j.jacc.2013.11.053
8. Crespo-Leiro MG, Anker SD, Maggioni AP, Coats AJ, Filippatos G, Ruschitzka F, et al. European Society of Cardiology Heart Failure Long-Term Registry (ESC-HF-LT): 1-year follow-up outcomes and differences across regions. *Eur J Heart Fail*. 2016;**18**:613–625. https://doi.org/10.1002/ejhf.566
9. Chioncel O, Mebazaa A, Maggioni AP, Harjola VP, Rosano G, Laroche C, et al.; ESC-EORP-HFA Heart Failure Long-Term Registry Investigators. Acute heart failure congestion and perfusion status – impact of the clinical classification on in-hospital and long-term outcomes; insights from the ESC-EORP-HFA Heart Failure Long-Term Registry. *Eur J Heart Fail*. 2019;**21**:1338–1352. https://doi.org/10.1002/ejhf.1492
10. Javaloyes P, Miro O, Gil V, Martin-Sanchez FJ, Jacob J, Herrero P, et al.; ICA-SEMES Research Group. Clinical phenotypes of acute heart failure based on signs and symptoms of perfusion and congestion at emergency department presentation and their relationship with patient management and outcomes. *Eur J Heart Fail*. 2019;**21**:1353–1365. https://doi.org/10.1002/ejhf.1502
11. McClung JA. Native and prosthetic valve emergencies. *Cardiol Rev*. 2016;**24**:14–18. https://doi.org/10.1097/CRD.0000000000000079
12. Maheshwari V, Barr B, Srivastava M. Acute valvular heart disease. *Cardiol Clin*. 2018;**36**:115–127. https://doi.org/10.1016/j.ccl.2017.08.006
13. Akodad M, Schurtz G, Adda J, Leclercq F, Roubille F. Management of valvulopathies with acute severe heart failure and cardiogenic shock. *Arch Cardiovasc Dis*. 2019;**112**:773–780. https://doi.org/10.1016/j.acvd.2019.06.009
14. Jentzer JC, Ternus B, Eleid M, Rihal C. Structural heart disease emergencies. *J Intensive Care Med*. 2021;**36**:975–988. https://doi.org/10.1177/0885066620918776
15. Otto CM, Nishimura RA, Bonow RO, Carabello BA, Erwin JP 3rd, Gentile F, et al. 2020 ACC/AHA Guideline for the management of patients with valvular heart disease: A report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2021;**143**:e72–e227. https://doi.org/10.1161/CIR.0000000000000923
16. Vahanian A, Beyersdorf F, Praz F, Milojevic M, Baldus S, Bauersachs J, et al. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J*. 2022;**43**:561–632. https://doi.org/10.1093/eurheartj/ehab395
17. Iung B, Delgado V, Rosenhek R, Price S, Prendergast B, Wendler O, et al.; EORP VHD II Investigators. Contemporary presentation and management of valvular heart disease: The EURObservational Research Programme Valvular Heart Disease II survey. *Circulation*. 2019;**140**:1156–1169. https://doi.org/10.1161/CIRCULATIONAHA.119.041080
18. Kaplon-Cieslicka A, Benson L, Chioncel O, Crespo-Leiro MG, Coats AJS, Anker SD, et al.; Heart Failure Association (HFA) of the European Society of Cardiology (ESC) and the ESC Heart Failure Long-Term Registry Investigators. A comprehensive characterization of acute heart failure with preserved versus mildly reduced versus reduced ejection fraction – insights from the ESC-HFA EORP Heart Failure Long-Term Registry. *Eur J Heart Fail*. 2022;**24**:335–350. https://doi.org/10.1002/ejhf.2408
19. Tromp J, Bamadhaj S, Cleland JGF, Angermann CE, Dahlstrom U, Ouwerkerk W, et al. Post-discharge prognosis of patients admitted to hospital for heart failure by world region, and national level of income and income disparity (REPORT-HF): A cohort study. *Lancet Glob Health*. 2020;**8**:e411–e422. https://doi.org/10.1016/S2214-109X(20)30004-8
20. Filippatos G, Angermann CE, Cleland JGF, Lam CSP, Dahlstrom U, Dickstein K, et al. Global differences in characteristics, precipitants, and initial management of patients presenting with acute heart failure. *JAMA Cardiol*. 2020;**5**:401–410. https://doi.org/10.1001/jamacardio.2019.5108
21. Chioncel O, Mebazaa A, Harjola VP, Coats AJ, Piepoli MF, Crespo-Leiro MG, et al.; ESC Heart Failure Long-Term Registry Investigators. Clinical phenotypes and outcome of patients hospitalized for acute heart failure: The ESC Heart Failure Long-Term Registry. *Eur J Heart Fail*. 2017;**19**:1242–1254. https://doi.org/10.1002/ejhf.890

22. Abdurashidova T, Monney P, Tzimas G, Soborun N, Regamey J, Daux A, et al. Non-severe aortic regurgitation increases short-term mortality in acute heart failure with preserved ejection fraction. *ESC Heart Fail*. 2020;**7**:3901–3909. https://doi.org/10.1002/ehf2.12983

23. Pagnesi M, Adamo M, Sama IE, Anker SD, Cleland JG, Dickstein K, et al. Impact of mitral regurgitation in patients with worsening heart failure: Insights from BIOSTAT-CHF. *Eur J Heart Fail*. 2021;**23**:1750–1758. https://doi.org/10.1002/ejhf.2276

24. Arora S, Sivaraj K, Hendrickson M, Chang PP, Weickert T, Qamar A, et al. Prevalence and prognostic significance of mitral regurgitation in acute decompensated heart failure: The ARIC study. *JACC Heart Fail*. 2021;**9**:179–189. https://doi.org/10.1016/j.jchf.2020.09.015

25. Wada Y, Ohara T, Funada A, Hasegawa T, Sugano Y, Kanzaki H, et al. Prognostic impact of functional mitral regurgitation in patients admitted with acute decompensated heart failure. *Circ J*. 2016;**80**:139–147. https://doi.org/10.1253/circj.CJ-15-0663

26. Kubo S, Kawase Y, Hata R, Maruo T, Tada T, Kadota K. Dynamic severe mitral regurgitation on hospital arrival as prognostic predictor in patients hospitalized for acute decompensated heart failure. *Int J Cardiol*. 2018;**273**:177–182. https://doi.org/10.1016/j.ijcard.2018.09.093

27. De la Espriella R, Santas E, Chorro FJ, Minana G, Soler M, Bodi V, et al. Functional tricuspid regurgitation and recurrent admissions in patients with acute heart failure. *Int J Cardiol*. 2019;**291**:83–88. https://doi.org/10.1016/j.ijcard.2019.03.051

28. Santas E, Chorro FJ, Minana G, Mendez J, Munoz J, Escribano D, et al. Tricuspid regurgitation and mortality risk across left ventricular systolic function in acute heart failure. *Circ J*. 2015;**79**:1526–1533. https://doi.org/10.1253/circj.CJ-15-0129

29. Mutlak D, Lessick J, Khalil S, Yalonetsky S, Agmon Y, Aronson D. Tricuspid regurgitation in acute heart failure: Is there any incremental risk? *Eur Heart J Cardiovasc Imaging*. 2018;**19**:993–1001. https://doi.org/10.1093/ehjci/jex343

30. Lancellotti P, Gerard PL, Pierard LA. Long-term outcome of patients with heart failure and dynamic functional mitral regurgitation. *Eur Heart J*. 2005;**26**:1528–1532. https://doi.org/10.1093/eurheartj/ehi189

31. Bartko PE, Hulsmann M, Hung J, Pavo N, Levine RA, Pibarot P, et al. Secondary valve regurgitation in patients with heart failure with preserved ejection fraction, heart failure with mid-range ejection fraction, and heart failure with reduced ejection fraction. *Eur Heart J*. 2020;**41**:2799–2810. https://doi.org/10.1093/eurheartj/ehaa129

32. Galie N, Humbert M, Vachiery JL, Gibbs S, Lang I, Torbicki A, et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). *Eur Heart J*. 2016;**37**:67–119. https://doi.org/10.1093/eurheartj/ehv317

33. Magne J, Pibarot P, Sengupta PP, Donal E, Rosenhek R, Lancellotti P. Pulmonary hypertension in valvular disease: A comprehensive review on pathophysiology to therapy from the HAVEC Group. *JACC Cardiovasc Imaging*. 2015;**8**:83–99. https://doi.org/10.1016/j.jcmg.2014.12.003

34. Yamamoto K, Ikeda U, Mito H, Fujikawa H, Sekiguchi H, Shimada K. Endothelin production in pulmonary circulation of patients with mitral stenosis. *Circulation*. 1994;**89**:2093–2098. https://doi.org/10.1161/01.cir.89.5.2093

35. Humbert M, Kovacs G, Hoeper MM, Badagliacca R, Berger RMF, Brida M, et al. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Heart J*. 2022;**43**:3618–3731. https://doi.org/10.1093/eurheartj/ehac237

36. Bermejo J, Yotti R, Garcia-Orta R, Sanchez-Fernandez PL, Castano M, Segovia-Cubero J, et al.; Sildenafil for Improving Outcomes after VAlvular Correction (SIOVAC) investigators. Sildenafil for improving outcomes in patients with corrected valvular heart disease and persistent pulmonary hypertension: A multicenter, double-blind, randomized clinical trial. *Eur Heart J*. 2018;**39**:1255–1264. https://doi.org/10.1093/eurheartj/ehx700

37. Tichelbacker T, Dumitrescu D, Gerhardt F, Stern D, Wissmuller M, Adam M, et al. Pulmonary hypertension and valvular heart disease. *Herz*. 2019;**44**:491–501. https://doi.org/10.1007/s00059-019-4823-6

38. Al-Omary MS, Sugito S, Boyle AJ, Sverdlov AL, Collins NJ. Pulmonary hypertension due to left heart disease: Diagnosis, pathophysiology, and therapy. *Hypertension*. 2020;**75**:1397–1408. https://doi.org/10.1161/HYPERTENSIONAHA.119.14330

39. Fawzy ME, Hassan W, Stefadouros M, Moursi M, El Shaer F, Chaudhary MA. Prevalence and fate of severe pulmonary hypertension in 559 consecutive patients with severe rheumatic mitral stenosis undergoing mitral balloon valvotomy. *J Heart Valve Dis*. 2004;**13**(6):942–947. PMID: 15597587

40. Le Tourneau T, Richardson M, Juthier F, Modine T, Fayad G, Polge AS, et al. Echocardiography predictors and prognostic value of pulmonary artery systolic pressure in chronic organic mitral regurgitation. *Heart*. 2010;**96**:1311–1317. https://doi.org/10.1136/hrt.2009.186486

41. Barbieri A, Bursi F, Grigioni F, Tribouilloy C, Avierinos JF, Michelena HI, et al.; Mitral Regurgitation International DAtabase (MIDA) Investigators. Prognostic and therapeutic implications of pulmonary hypertension complicating degenerative mitral regurgitation due to flail leaflet: A multicenter long-term international study. *Eur Heart J*. 2011;**32**:751–759. https://doi.org/10.1093/eurheartj/ehq294

42. Kusunose K, Popovic ZB, Motoki H, Marwick TH. Prognostic significance of exercise-induced right ventricular dysfunction in asymptomatic degenerative mitral regurgitation. *Circ Cardiovasc Imaging*. 2013;**6**:167–176. https://doi.org/10.1161/CIRCIMAGING.112.000162

43. Faggiano P, Antonini-Canterin F, Ribichini F, D'Aloia A, Ferrero V, Cervesato E, et al. Pulmonary artery hypertension in adult patients with symptomatic valvular aortic stenosis. *Am J Cardiol*. 2000;**85**:204–208. https://doi.org/10.1016/s0002-9149(99)00643-8

44. Cam A, Goel SS, Agarwal S, Menon V, Svensson LG, Tuzcu EM, et al. Prognostic implications of pulmonary hypertension in patients with severe aortic stenosis. *J Thorac Cardiovasc Surg*. 2011;**142**:800–808. https://doi.org/10.1016/j.jtcvs.2010.12.024

45. Lancellotti P, Magne J, Donal E, O'Connor K, Dulgheru R, Rosca M, et al. Determinants and prognostic significance of exercise pulmonary hypertension in asymptomatic severe aortic stenosis. *Circulation*. 2012;**126**:851–859. https://doi.org/10.1161/CIRCULATIONAHA.111.088427

46. Khandhar S, Varadarajan P, Turk R, Sampat U, Patel R, Kamath A, et al. Survival benefit of aortic valve replacement in patients with severe aortic regurgitation and pulmonary hypertension. *Ann Thorac Surg*. 2009;**88**:752–756. https://doi.org/10.1016/j.athoracsur.2009.05.025

47. Lau GT, Tan HC, Kritharides L. Type of liver dysfunction in heart failure and its relation to the severity of tricuspid regurgitation. *Am J Cardiol*. 2002;**90**:1405–1409. https://doi.org/10.1016/s0002-9149(02)02886-2

48. Mullens W, Abrahams Z, Francis GS, Sokos G, Taylor DO, Starling RC, et al. Importance of venous congestion for worsening of renal function in advanced decompensated heart failure. *J Am Coll Cardiol*. 2009;**53**:589–596. https://doi.org/10.1016/j.jacc.2008.05.068

49. Topilsky Y, Khanna A, Le Tourneau T, Park S, Michelena H, Suri R, et al. Clinical context and mechanism of functional tricuspid regurgitation in patients with and without pulmonary hypertension. *Circ Cardiovasc Imaging*. 2012;**5**:314–323. https://doi.org/10.1161/CIRCIMAGING.111.967919

50. Verbrugge FH, Dupont M, Steels P, Grieten L, Malbrain M, Tang WH, et al. Abdominal contributions to cardiorenal dysfunction in congestive heart failure. *J Am Coll Cardiol*. 2013;**62**:485–495. https://doi.org/10.1016/j.jacc.2013.04.070

51. Shiran A, Najjar R, Adawi S, Aronson D. Risk factors for progression of functional tricuspid regurgitation. *Am J Cardiol*. 2014;**113**:995–1000. https://doi.org/10.1016/j.amjcard.2013.11.055

52. Mangieri A, Montalto C, Pagnesi M, Jabbour RJ, Rodes-Cabau J, Moat N, et al. Mechanism and implications of the tricuspid regurgitation: From the pathophysiology to the current and future therapeutic options. *Circ Cardiovasc Interv*. 2017;**10**:e005043. https://doi.org/10.1161/CIRCINTERVENTIONS.117.005043

53. Bartko PE, Arfsten H, Frey MK, Heitzinger G, Pavo N, Cho A, et al. Natural history of functional tricuspid regurgitation: Implications of quantitative Doppler assessment. *JACC Cardiovasc Imaging*. 2019;**12**:389–397. https://doi.org/10.1016/j.jcmg.2018.11.021

54. Dietz MF, Prihadi EA, van der Bijl P, Goedemans L, Mertens BJA, Gursoy E, et al. Prognostic implications of right ventricular remodeling and function in patients with significant secondary tricuspid regurgitation. *Circulation*. 2019;**140**:836–845. https://doi.org/10.1161/CIRCULATIONAHA.119.039630

55. Sanz J, Sanchez-Quintana D, Bossone E, Bogaard HJ, Naeije R. Anatomy, function, and dysfunction of the right ventricle: JACC state-of-the-art review. *J Am Coll Cardiol*. 2019;**73**:1463–1482. https://doi.org/10.1016/j.jacc.2018.12.076

56. Margonato D, Ancona F, Ingallina G, Melillo F, Stella S, Biondi F, et al. Tricuspid regurgitation in left ventricular systolic dysfunction: Marker or target? *Front Cardiovasc Med*. 2021;**8**:702589. https://doi.org/10.3389/fcvm.2021.702589

57. Arden C, Chambers JB, Sandoe J, Ray S, Prendergast B, Taggart D, et al. Can we improve the detection of heart valve disease? *Heart*. 2014;**100**:271–273. https://doi.org/10.1136/heartjnl-2013-304223

58. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J*. 2016;**37**:2129–2200. https://doi.org/10.1093/eurheartj/ehw128

59. Mueller C, McDonald K, de Boer RA, Maisel A, Cleland JGF, Kozhuharov N, et al. Heart Failure Association of the European Society of Cardiology practical guidance on the use of natriuretic peptide concentrations. *Eur J Heart Fail.* 2019;**21**:715–731. https://doi.org/10.1002/ejhf.1494

60. Fuernau G, Desch S, de Waha-Thiele S, Eitel I, Neumann FJ, Hennersdorf M, et al. Arterial lactate in cardiogenic shock: Prognostic value of clearance versus single values. *JACC Cardiovasc Interv.* 2020;**13**:2208–2216. https://doi.org/10.1016/j.jcin.2020.06.037

61. Jilaihawi H, Asch FM, Manasse E, Ruiz CE, Jelnin V, Kashif M, et al. Systematic CT methodology for the evaluation of subclinical leaflet thrombosis. *JACC Cardiovasc Imaging.* 2017;**10**:461–470. https://doi.org/10.1016/j.jcmg.2017.02.005

62. Hryniewiecki T, Zatorska K, Abramczuk E, Zakrzewski D, Szymanski P, Kusmierczyk M, et al. The usefulness of cardiac CT in the diagnosis of perivalvular complications in patients with infective endocarditis. *Eur Radiol.* 2019;**29**:4368–4376. https://doi.org/10.1007/s00330-018-5965-2

63. Blanke P, Weir-McCall JR, Achenbach S, Delgado V, Hausleiter J, Jilaihawi H, et al. Computed tomography imaging in the context of transcatheter aortic valve implantation (TAVI)/transcatheter aortic valve replacement (TAVR): An expert consensus document of the Society of Cardiovascular Computed Tomography. *JACC Cardiovasc Imaging.* 2019;**12**:1–24. https://doi.org/10.1016/j.jcmg.2018.12.003

64. Osaka S, Tanaka M. Strategy for porcelain ascending aorta in cardiac surgery. *Ann Thorac Cardiovasc Surg.* 2018;**24**:57–64. https://doi.org/10.5761/atcs.ra.17-00181

65. Aviram G, Sharony R, Kramer A, Nesher N, Loberman D, Ben-Gal Y, et al. Modification of surgical planning based on cardiac multidetector computed tomography in reoperative heart surgery. *Ann Thorac Surg.* 2005;**79**:589–595. https://doi.org/10.1016/j.athoracsur.2004.07.012

66. Koo HJ, Yang DH, Kang JW, Lee JY, Kim DH, Song JM, et al. Demonstration of infective endocarditis by cardiac CT and transoesophageal echocardiography: Comparison with intra-operative findings. *Eur Heart J Cardiovasc Imaging.* 2018;**19**:199–207. https://doi.org/10.1093/ehjci/jex010

67. Ouchi K, Sakuma T, Ojiri H. Cardiac computed tomography as a viable alternative to echocardiography to detect vegetations and perivalvular complications in patients with infective endocarditis. *Jpn J Radiol.* 2018;**36**:421–428. https://doi.org/10.1007/s11604-018-0740-5

68. Swart LE, Gomes A, Scholtens AM, Sinha B, Tanis W, Lam M, et al. Improving the diagnostic performance of ^{18}F-fluorodeoxyglucose positron-emission tomography/computed tomography in prosthetic heart valve endocarditis. *Circulation.* 2018;**138**:1412–1427. https://doi.org/10.1161/CIRCULATIONAHA.118.035032

69. Ricciardi A, Sordillo P, Ceccarelli L, Maffongelli G, Calisti G, Di Pietro B, et al. 18-Fluoro-2-deoxyglucose positron emission tomography-computed tomography: An additional tool in the diagnosis of prosthetic valve endocarditis. *Int J Infect Dis.* 2014;**28**:219–224. https://doi.org/10.1016/j.ijid.2014.04.028

70. Rajiah P, Fulton NL, Bolen M. Magnetic resonance imaging of the papillary muscles of the left ventricle: Normal anatomy, variants, and abnormalities. *Insights Imaging.* 2019;**10**:83. https://doi.org/10.1186/s13244-019-0761-3

71. Gidwani UK, Mohanty B, Chatterjee K. The pulmonary artery catheter: A critical reappraisal. *Cardiol Clin.* 2013;**31**:545–565. https://doi.org/10.1016/j.ccl.2013.07.008

72. Chioncel O, Parissis J, Mebazaa A, Thiele H, Desch S, Bauersachs J, et al. Epidemiology, pathophysiology and contemporary management of cardiogenic shock – a position statement from the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail.* 2020;**22**:1315–1341. https://doi.org/10.1002/ejhf.1922

73. Lin SS, Tiong IY, Asher CR, Murphy MT, Thomas JD, Griffin BP. Prediction of thrombus-related mechanical prosthetic valve dysfunction using transesophageal echocardiography. *Am J Cardiol.* 2000;**86**:1097–1101. https://doi.org/10.1016/s0002-9149(00)01166-8

74. Roudaut R, Serri K, Lafitte S. Thrombosis of prosthetic heart valves: Diagnosis and therapeutic considerations. *Heart.* 2007;**93**:137–142. https://doi.org/10.1136/hrt.2005.071183

75. Kostyunin AE, Yuzhalin AE, Rezvova MA, Ovcharenko EA, Glushkova TV, Kutikhin AG. Degeneration of bioprosthetic heart valves: Update 2020. *J Am Heart Assoc.* 2020;**9**:e018506. https://doi.org/10.1161/JAHA.120.018506

76. Habib G, Erba PA, Iung B, Donal E, Cosyns B, Laroche C, et al.; EURO-ENDO Investigators. Clinical presentation, aetiology and outcome of infective endocarditis. Results of the ESC-EORP EURO-ENDO (European infective endocarditis) registry: A prospective cohort study. *Eur Heart J.* 2019;**40**:3222–3232. https://doi.org/10.1093/eurheartj/ehz620

77. Kong WKF, Salsano A, Giacobbe DR, Popescu BA, Laroche C, Duval X, et al. Outcomes of culture-negative vs. culture-positive infective endocarditis: The ESC-EORP EURO-ENDO registry. *Eur Heart J.* 2022;**43**:2770–2780. https://doi.org/10.1093/eurheartj/ehac307

78. Roux V, Salaun E, Tribouilloy C, Hubert S, Bohbot Y, Casalta JP, et al. Coronary events complicating infective endocarditis. *Heart.* 2017;**103**:1906–1910. https://doi.org/10.1136/heartjnl-2017-311624

79. Stone GW, Lindenfeld J, Abraham WT, Kar S, Lim DS, Mishell JM, et al.; COAPT Investigators. Transcatheter mitral-valve repair in patients with heart failure. *N Engl J Med.* 2018;**379**:2307–2318. https://doi.org/10.1056/NEJMoa1806640

80. Obadia JF, Messika-Zeitoun D, Leurent G, Iung B, Bonnet G, Piriou N, et al.; MITRA-FR Investigators. Percutaneous repair or medical treatment for secondary mitral regurgitation. *N Engl J Med.* 2018;**379**:2297–2306. https://doi.org/10.1056/NEJMoa1805374

81. Adamo M, Fiorelli F, Melica B, D'Ortona R, Lupi L, Giannini C, et al. COAPT-like profile predicts long-term outcomes in patients with secondary mitral regurgitation undergoing MitraClip implantation. *JACC Cardiovasc Interv.* 2021;**14**:15–25. https://doi.org/10.1016/j.jcin.2020.09.050

82. Neuhold S, Huelsmann M, Pernicka E, Graf A, Bonderman D, Adlbrecht C, et al. Impact of tricuspid regurgitation on survival in patients with chronic heart failure: Unexpected findings of a long-term observational study. *Eur Heart J.* 2013;**34**:844–852. https://doi.org/10.1093/eurheartj/ehs465

83. Iung B, Baron G, Butchart EG, Delahaye F, Gohlke-Barwolf C, Levang OW, et al. A prospective survey of patients with valvular heart disease in Europe: The Euro Heart Survey on Valvular Heart Disease. *Eur Heart J.* 2003;**24**:1231–1243. https://doi.org/10.1016/s0195-668x(03)00201-x

84. Andell P, Li X, Martinsson A, Andersson C, Stagmo M, Zoller B, et al. Epidemiology of valvular heart disease in a Swedish nationwide hospital-based register study. *Heart.* 2017;**103**:1696–1703. https://doi.org/10.1136/heartjnl-2016-310894

85. Tribouilloy C, Bohbot Y, Kubala M, Ruschitzka F, Popescu B, Wendler O, et al. Characteristics, management, and outcomes of patients with multiple native valvular heart disease: A substudy of the EURObservational Research Programme Valvular Heart Disease II Survey. *Eur Heart J.* 2022;**43**:2756–2766. https://doi.org/10.1093/eurheartj/ehac209

86. Windecker S, Okuno T, Unbehaun A, Mack M, Kapadia S, Falk V. Which patients with aortic stenosis should be referred to surgery rather than transcatheter aortic valve implantation? *Eur Heart J.* 2022;**43**:2729–2750. https://doi.org/10.1093/eurheartj/ehac105

87. Vahanian A, Himbert D, Brochet E. Multiple valve disease – assessment, strategy and intervention. *EuroIntervention.* 2015;**11**:W14–W16. https://doi.org/10.4244/EIJV11SWA3

88. Sinning JM, Mellert F, Schiller W, Welz A, Nickenig G, Hammerstingl C. Transcatheter mitral valve replacement using a balloon-expandable prosthesis in a patient with calcified native mitral valve stenosis. *Eur Heart J.* 2013;**34**:2609. https://doi.org/10.1093/eurheartj/eht254

89. Taramasso M, Benfari G, van der Bijl P, Alessandrini H, Attinger-Toller A, Biasco L, et al. Transcatheter versus medical treatment of patients with symptomatic severe tricuspid regurgitation. *J Am Coll Cardiol.* 2019;**74**:2998–3008. https://doi.org/10.1016/j.jacc.2019.09.028

90. Okuno T, Asami M, Khan F, Praz F, Heg D, Lanz J, et al. Does isolated mitral annular calcification in the absence of mitral valve disease affect clinical outcomes after transcatheter aortic valve replacement? *Eur Heart J Cardiovasc Imaging.* 2020;**21**:522–532. https://doi.org/10.1093/ehjci/jez208

91. Hahn RT, Pibarot P, Otto CM. Transcatheter interventions spark a paradigm change for management of patients with mixed valve disease. *Eur Heart J.* 2022;**43**:2767–2769. https://doi.org/10.1093/eurheartj/ehac229

92. Miller RR, Vismara LA, DeMaria AN, Salel AF, Mason DT. Afterload reduction therapy with nitroprusside in severe aortic regurgitation: Improved cardiac performance and reduced regurgitant volume. *Am J Cardiol.* 1976;**38**:564–567. https://doi.org/10.1016/s0002-9149(76)80003-3

93. Khot UN, Novaro GM, Popovic ZB, Mills RM, Thomas JD, Tuzcu EM, et al. Nitroprusside in critically ill patients with left ventricular dysfunction and aortic stenosis. *N Engl J Med.* 2003;**348**:1756–1763. https://doi.org/10.1056/NEJMoa022021

94. Garcia-Gonzalez MJ, Jorge-Perez P, Jimenez-Sosa A, Acea AB, Lacalzada Almeida JB, Ferrer Hita JJ. Levosimendan improves hemodynamic status in critically ill patients with severe aortic stenosis and left ventricular dysfunction: An interventional study. *Cardiovasc Ther.* 2015;**33**:193–199. https://doi.org/10.1111/1755-5922.12132

95. Stevenson LW, Bellil D, Grover-McKay M, Brunken RC, Schwaiger M, Tillisch JH, et al. Effects of afterload reduction (diuretics and vasodilators) on left ventricular volume and mitral regurgitation in severe congestive heart failure secondary to ischemic or idiopathic dilated cardiomyopathy. *Am J Cardiol.* 1987;**60**:654–658. https://doi.org/10.1016/0002-9149(87)90376-6

96. Hamilton MA, Stevenson LW, Child JS, Moriguchi JD, Walden J, Woo M. Sustained reduction in valvular regurgitation and atrial volumes with tailored vasodilator therapy in advanced congestive heart failure secondary to dilated

(ischemic or idiopathic) cardiomyopathy. *Am J Cardiol.* 1991;**67**:259–263. https://doi.org/10.1016/0002-9149(91)90556-z

97. Branzi G, Malfatto G, Villani A, Ciambellotti F, Revera M, Giglio A, et al. Acute effects of levosimendan on mitral regurgitation and diastolic function in patients with advanced chronic heart failure. *J Cardiovasc Med (Hagerstown).* 2010;**11**:662–668. https://doi.org/10.2459/JCM.0b013e32833832f6

98. Wunderlich NC, Dalvi B, Ho SY, Kux H, Siegel RJ. Rheumatic mitral valve stenosis: Diagnosis and treatment options. *Curr Cardiol Rep.* 2019;**21**:14. https://doi.org/10.1007/s11886-019-1099-7

99. Iung B, Leenhardt A, Extramiana F. Management of atrial fibrillation in patients with rheumatic mitral stenosis. *Heart.* 2018;**104**:1062–1068. https://doi.org/10.1136/heartjnl-2017-311425

100. Kholdani CA, Fares WH. Management of right heart failure in the intensive care unit. *Clin Chest Med.* 2015;**36**:511–520. https://doi.org/10.1016/j.ccm.2015.05.015

101. Habib G, Lancellotti P, Antunes MJ, Bongiorni MG, Casalta JP, Del Zotti F, et al. 2015 ESC Guidelines for the management of infective endocarditis: The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). *Eur Heart J.* 2015;**36**:3075–3128. https://doi.org/10.1093/eurheartj/ehv319

102. Harjola VP, Mebazaa A, Celutkiene J, Bettex D, Bueno H, Chioncel O, et al. Contemporary management of acute right ventricular failure: A statement from the Heart Failure Association and the Working Group on Pulmonary Circulation and Right Ventricular Function of the European Society of Cardiology. *Eur J Heart Fail.* 2016;**18**:226–241. https://doi.org/10.1002/ejhf.478

103. Alviar CL, Miller PE, McAreavey D, Katz JN, Lee B, Moriyama B, et al. Positive pressure ventilation in the cardiac intensive care unit. *J Am Coll Cardiol.* 2018;**72**:1532–1553. https://doi.org/10.1016/j.jacc.2018.06.074

104. Masip J, Peacock WF, Price S, Cullen L, Martin-Sanchez FJ, Seferovic P, et al. Indications and practical approach to non-invasive ventilation in acute heart failure. *Eur Heart J.* 2018;**39**:17–25. https://doi.org/10.1093/eurheartj/ehx580

105. Balthazar T, Vandenbriele C, Verbrugge FH, Den Uil C, Engström A, Janssens S, et al. Managing patients with short-term mechanical circulatory support: JACC review topic of the week. *J Am Coll Cardiol.* 2021;**77**:1243–1256. https://doi.org/10.1016/j.jacc.2020.12.054

106. Singh V, Mendirichaga R, Inglessis-Azuaje I, Palacios IF, O'Neill WW. The role of Impella for hemodynamic support in patients with aortic stenosis. *Curr Treat Options Cardiovasc Med.* 2018;**20**:44. https://doi.org/10.1007/s11936-018-0644-9

107. Alkhalil A, Hajjar R, Ibrahim H, Ruiz CE. Mechanical circulatory support in transcatheter aortic valve implantation in the United States (from the National Inpatient Sample). *Am J Cardiol.* 2019;**124**:1615–1620. https://doi.org/10.1016/j.amjcard.2019.08.013

108. Adamo M, Chiari E, Curello S, Maiandi C, Chizzola G, Fiorina C, et al. Mitraclip therapy in patients with functional mitral regurgitation and missing leaflet coaptation: Is it still an exclusion criterion? *Eur J Heart Fail.* 2016;**18**:1278–1286. https://doi.org/10.1002/ejhf.520

109. Eliaz R, Turyan A, Beeri R, Shuvy M. Utilization of intra-aortic balloon pump to allow MitraClip procedure in patients with non-coapting mitral valve leaflets: A case series. *Eur Heart J Case Rep.* 2019;**3**:ytz045. https://doi.org/10.1093/ehjcr/ytz045

110. Vandenbriele C, Balthazar T, Wilson J, Adriaenssens T, Davies S, Droogne W, et al. Left Impella®-device as bridge from cardiogenic shock with acute, severe mitral regurgitation to MitraClip®-procedure: A new option for critically ill patients. *Eur Heart J Acute Cardiovasc Care.* 2021;**10**:415–421. https://doi.org/10.1093/ehjacc/zuaa031

111. Elhussein TA, Hutchison SJ. Acute mitral regurgitation: Unforeseen new complication of the Impella LP 5.0 ventricular assist device and review of literature. *Heart Lung Circ.* 2014;**23**:e100–e104. https://doi.org/10.1016/j.hlc.2013.10.098

112. Nashef SA, Roques F, Sharples LD, Nilsson J, Smith C, Goldstone AR, et al. EuroSCORE II. *Eur J Cardiothorac Surg.* 2012;**41**:734–745. https://doi.org/10.1093/ejcts/ezs043

113. Yoon SH, Schmidt T, Bleiziffer S, Schofer N, Fiorina C, Munoz-Garcia AJ, et al. Transcatheter aortic valve replacement in pure native aortic valve regurgitation. *J Am Coll Cardiol.* 2017;**70**:2752–2763. https://doi.org/10.1016/j.jacc.2017.10.006

114. De Backer O, Pilgrim T, Simonato M, Mackensen GB, Fiorina C, Veulemanns V, et al. Usefulness of transcatheter aortic valve implantation for treatment of pure native aortic valve regurgitation. *Am J Cardiol.* 2018;**122**:1028–1035. https://doi.org/10.1016/j.amjcard.2018.05.044

115. ClinicalTrials.gov. THE ALIGN-AR EFS TRIAL: JenaValve Pericardial TAVR Aortic Regurgitation Study, [NCT02732704].

116. Achkouty G, Amabile N, Zannis K, Veugeois A, Caussin C. Transcatheter aortic valve replacement for severe aortic regurgitation with acute refractory cardiogenic shock. *Can J Cardiol.* 2018;**34**:342.e5–342.e7. https://doi.org/10.1016/j.cjca.2017.11.024

117. Branca L, Adamo M, Fiorina C, Ettori F, Chizzola G, Scodro M, et al. Life-saving transcatheter aortic valve implantation for acute severe aortic regurgitation due to rheumatoid arthritis and complicated by cardiogenic shock. *J Cardiovasc Med (Hagerstown).* 2020;**21**:268–271. https://doi.org/10.2459/JCM.0000000000000873

118. Adamo M, Fiorina C, Petronio AS, Giannini C, Tamburino C, Barbanti M, et al. Comparison of early and long-term outcomes after transcatheter aortic valve implantation in patients with New York Heart Association functional class IV to those in class III and less. *Am J Cardiol.* 2018;**122**:1718–1726. https://doi.org/10.1016/j.amjcard.2018.08.006

119. Frerker C, Schewel J, Schluter M, Schewel D, Ramadan H, Schmidt T, et al. Emergency transcatheter aortic valve replacement in patients with cardiogenic shock due to acutely decompensated aortic stenosis. *EuroIntervention.* 2016;**11**:1530–1536. https://doi.org/10.4244/EIJY15M03_03

120. Kolte D, Khera S, Vemulapalli S, Dai D, Heo S, Goldsweig AM, et al. Outcomes following urgent/emergent transcatheter aortic valve replacement: Insights from the STS/ACC TVT Registry. *JACC Cardiovasc Interv.* 2018;**11**(12):1175–1185. https://doi.org/10.1016/j.jcin.2018.03.002.

121. Masha L, Vemulapalli S, Manandhar P, Balan P, Shah P, Kosinski AS, et al. Demographics, procedural characteristics, and clinical outcomes when cardiogenic shock precedes TAVR in the United States. *JACC Cardiovasc Interv.* 2020;**13**:1314–1325. https://doi.org/10.1016/j.jcin.2020.02.033

122. Patterson T, Clayton T, Dodd M, Khawaja Z, Morice MC, Wilson K, et al. ACTIVATION (PercutAneous coronary inTervention prIor to transcatheter aortic VAlve implantaTION): A randomized clinical trial. *JACC Cardiovasc Interv.* 2021;**14**:1965–1974. https://doi.org/10.1016/j.jcin.2021.06.041

123. Tarantini G, Tang G, Nai Fovino L, Blackman D, Van Mieghem NM, Kim WK, et al. Management of coronary artery disease in patients undergoing transcatheter aortic valve implantation. A clinical consensus statement from the European Association of Percutaneous Cardiovascular Interventions in collaboration with the ESC Working Group on Cardiovascular Surgery. *EuroIntervention.* 2023;**19**:37–52. https://doi.org/10.4244/EIJ-D-22-00958

124. Williams T, Hildick-Smith DJR. Balloon aortic valvuloplasty: Indications, patient eligibility, technique and contemporary outcomes. *Heart.* 2020;**106**:1102–1110. https://doi.org/10.1136/heartjnl-2019-315904

125. Debry N, Kone P, Vincent F, Lemesle G, Delhaye C, Schurtz G, et al. Urgent balloon aortic valvuloplasty in patients with cardiogenic shock related to severe aortic stenosis: Time matters. *EuroIntervention.* 2018;**14**:e519–e525. https://doi.org/10.4244/EIJ-D-18-00029

126. Eugene M, Urena M, Abtan J, Carrasco JL, Ghodbane W, Nataf P, et al. Effectiveness of rescue percutaneous balloon aortic valvuloplasty in patients with severe aortic stenosis and acute heart failure. *Am J Cardiol.* 2018;**121**:746–750. https://doi.org/10.1016/j.amjcard.2017.11.048

127. Bularga A, Bing R, Shah AS, Adamson PD, Behan M, Newby DE, et al. Clinical outcomes following balloon aortic valvuloplasty. *Open Heart.* 2020;**7**:e001330. https://doi.org/10.1136/openhrt-2020-001330

128. Bongiovanni D, Kuhl C, Bleiziffer S, Stecher L, Poch F, Greif M, et al. Emergency treatment of decompensated aortic stenosis. *Heart.* 2018;**104**:23–29. https://doi.org/10.1136/heartjnl-2016-311037

129. Chakraborty S, Patel N, Bandyopadhyay D, Hajra A, Amgai B, Zaid S, et al. Readmission following urgent transcatheter aortic valve implantation versus urgent balloon aortic valvuloplasty in patients with decompensated heart failure or cardiogenic shock. *Catheter Cardiovasc Interv.* 2021;**98**:607–612. https://doi.org/10.1002/ccd.29690

130. Thompson CR, Buller CE, Sleeper LA, Antonelli TA, Webb JG, Jaber WA, et al. Cardiogenic shock due to acute severe mitral regurgitation complicating acute myocardial infarction: A report from the SHOCK Trial Registry. SHould we use emergently revascularize Occluded Coronaries in cardiogenic shocK? *J Am Coll Cardiol.* 2000;**36**:1104–1109. https://doi.org/10.1016/s0735-1097(00)00846-9

131. Wolff R, Cohen G, Peterson C, Wong S, Hockman E, Lo J, et al. MitraClip for papillary muscle rupture in patient with cardiogenic shock. *Can J Cardiol.* 2014;**30**:1461.e13–1461.e14. https://doi.org/10.1016/j.cjca.2014.07.015

132. Bahlmann E, Frerker C, Kreidel F, Thielsen T, Ghanem A, van der Schalk H, et al. MitraClip implantation after acute ischemic papillary muscle rupture in a patient with prolonged cardiogenic shock. *Ann Thorac Surg.* 2015;**99**:e41–e42. https://doi.org/10.1016/j.athoracsur.2014.09.075

133. Komatsu I, Cohen EA, Cohen GN, Czarnecki A. Transcatheter mitral valve edge-to-edge repair with the new MitraClip XTR system for acute mitral regurgitation caused by papillary muscle rupture. *Can J Cardiol.* 2019;**35**:1604.e5–1604.e7. https://doi.org/10.1016/j.cjca.2019.06.024

134. McGee EC Jr. Should moderate or greater mitral regurgitation be repaired in all patients with LVEF <30%? Surgery, mitral regurgitation, and heart failure: The

valves are all repairable but the patients are not. *Circ Heart Fail*. 2008;**1**:285–289. https://doi.org/10.1161/CIRCHEARTFAILURE.108.800185

135. Lavall D, Hagendorff A, Schirmer SH, Bohm M, Borger MA, Laufs U. Mitral valve interventions in heart failure. *ESC Heart Fail*. 2018;**5**:552–561. https://doi.org/10.1002/ehf2.12287

136. Haberman D, Taramasso M, Czarnecki A, Kerner A, Chrissoheris M, Spargias K, et al. Salvage MitraClip in severe secondary mitral regurgitation complicating acute myocardial infarction: Data from a multicentre international study. *Eur J Heart Fail*. 2019;**21**:1161–1164. https://doi.org/10.1002/ejhf.1565

137. Haberman D, Estevez-Loureiro R, Benito-Gonzalez T, Denti P, Arzamendi D, Adamo M, et al. Conservative, surgical, and percutaneous treatment for mitral regurgitation shortly after acute myocardial infarction. *Eur Heart J*. 2022;**43**:641–650. https://doi.org/10.1093/eurheartj/ehab496

138. Estevez-Loureiro R, Shuvy M, Taramasso M, Benito-Gonzalez T, Denti P, Arzamendi D, et al. Use of MitraClip for mitral valve repair in patients with acute mitral regurgitation following acute myocardial infarction: Effect of cardiogenic shock on outcomes (IREMMI Registry). *Catheter Cardiovasc Interv*. 2021;**97**:1259–1267. https://doi.org/10.1002/ccd.29552

139. Falasconi G, Melillo F, Pannone L, Adamo M, Ronco F, Latib A, et al. Use of edge-to-edge percutaneous mitral valve repair for severe mitral regurgitation in cardiogenic shock: A multicenter observational experience (MITRA-SHOCK study). *Catheter Cardiovasc Interv*. 2021;**98**:E163–E170. https://doi.org/10.1002/ccd.29683

140. Jung RG, Simard T, Kovach C, Flint K, Don C, Di Santo P, et al. Transcatheter mitral valve repair in cardiogenic shock and mitral regurgitation: A patient-level multicentre analysis. *JACC Cardiovasc Interv*. 2021;**14**:1–11. https://doi.org/10.1016/j.jcin.2020.08.037

141. Adamo M, Curello S, Chiari E, Fiorina C, Chizzola G, Magatelli M, et al. Percutaneous edge-to-edge mitral valve repair for the treatment of acute mitral regurgitation complicating myocardial infarction: A single centre experience. *Int J Cardiol*. 2017;**234**:53–57. https://doi.org/10.1016/j.ijcard.2017.02.072

142. Estevez-Loureiro R, Adamo M, Arzamendi D, Denti P, Freixa X, Nombela-Franco L, et al. Transcatheter mitral valve repair in patients with acute myocardial infarction: Insights from the European Registry of MitraClip in Acute Mitral Regurgitation following an acute myocardial infarction (EREMMI). *EuroIntervention*. 2020;**15**:1248–1250. https://doi.org/10.4244/EIJ-D-19-00653

143. Tang GHL, Estevez-Loureiro R, Yu Y, Prillinger JB, Zaid S, Psotka MA. Survival following edge-to-edge transcatheter mitral valve repair in patients with cardiogenic shock: A nationwide analysis. *J Am Heart Assoc*. 2021;**10**:e019882. https://doi.org/10.1161/JAHA.120.019882

144. Ananthakrishna Pillai A, Ramasamy C, Kottyath H. Outcomes following balloon mitral valvuloplasty in pregnant females with mitral stenosis and significant sub valve disease with severe decompensated heart failure. *J Interv Cardiol*. 2018;**31**:525–531. https://doi.org/10.1111/joic.12507

145. Galusko V, Ionescu A, Edwards A, Sekar B, Wong K, Patel K, et al. Management of mitral stenosis: A systematic review of clinical practice guidelines and recommendations. *Eur Heart J Qual Care Clin Outcomes*. 2022;**8**:602–618. https://doi.org/10.1093/ehjqcco/qcab083

146. Dreyfus J, Audureau E, Bohbot Y, Coisne A, Lavie-Badie Y, Bouchery M, et al. TRI-SCORE: A new risk score for in-hospital mortality prediction after isolated tricuspid valve surgery. *Eur Heart J*. 2022;**43**:654–662. https://doi.org/10.1093/eurheartj/ehab679

147. Lurz P, Orban M, Besler C, Braun D, Schlotter F, Noack T, et al. Clinical characteristics, diagnosis, and risk stratification of pulmonary hypertension in severe tricuspid regurgitation and implications for transcatheter tricuspid valve repair. *Eur Heart J*. 2020;**41**:2785–2795. https://doi.org/10.1093/eurheartj/ehaa138

148. Brener MI, Lurz P, Hausleiter J, Rodes-Cabau J, Fam N, Kodali SK, et al. Right ventricular-pulmonary arterial coupling and afterload reserve in patients undergoing transcatheter tricuspid valve repair. *J Am Coll Cardiol*. 2022;**79**:448–461. https://doi.org/10.1016/j.jacc.2021.11.031

149. Sorajja P, Whisenant B, Hamid N, Naik H, Makkar R, Tadros P, et al.; TRI-LUMINATE Pivotal Investigators. Transcatheter repair for patients with tricuspid regurgitation. *N Engl J Med*. 2023;**388**:1833–1842. https://doi.org/10.1056/NEJMoa2300525

150. Messika-Zeitoun D, Baumgartner H, Burwash IG, Vahanian A, Bax J, Pibarot P, et al. Unmet needs in valvular heart disease. *Eur Heart J*. 2023;**44**:1862–1873. https://doi.org/10.1093/eurheartj/ehad121

151. Praz F, Muraru D, Kreidel F, Lurz P, Hahn RT, Delgado V, et al. Transcatheter treatment for tricuspid valve disease. *EuroIntervention*. 2021;**17**:791–808. https://doi.org/10.4244/EIJ-D-21-00695

152. Russo G, Taramasso M, Pedicino D, Gennari M, Gavazzoni M, Pozzoli A, et al. Challenges and future perspectives of transcatheter tricuspid valve interventions: Adopt old strategies or adapt to new opportunities? *Eur J Heart Fail*. 2022;**24**:442–454. https://doi.org/10.1002/ejhf.2398

153. Gelsomino S, Maessen JG, van der Veen F, Livi U, Renzulli A, Luca F, et al. Emergency surgery for native mitral valve endocarditis: The impact of septic and cardiogenic shock. *Ann Thorac Surg*. 2012;**93**:1469–1476. https://doi.org/10.1016/j.athoracsur.2011.11.025

154. Thuny F, Grisoli D, Collart F, Habib G, Raoult D. Management of infective endocarditis: Challenges and perspectives. *Lancet*. 2012;**379**:965–975. https://doi.org/10.1016/S0140-6736(11)60755-1

155. Özkan M, Gündüz S, Güner A, Kalçık M, Gürsoy MO, Uygur B, et al. Thrombolysis or surgery in patients with obstructive mechanical valve thrombosis: The multicenter HATTUSHA study. *J Am Coll Cardiol*. 2022;**79**:977–989. https://doi.org/10.1016/j.jacc.2021.12.027

156. Ruiz CE, Hahn RT, Berrebi A, Borer JS, Cutlip DE, Fontana G, et al.; Paravalvular Leak Academic Research Consortium. Clinical trial principles and endpoint definitions for paravalvular leaks in surgical prosthesis: An expert statement. *J Am Coll Cardiol*. 2017;**69**:2067–2087. https://doi.org/10.1016/j.jacc.2017.02.038

157. Raval J, Nagaraja V, Eslick GD, Denniss AR. Transcatheter valve-in-valve implantation: A systematic review of literature. *Heart Lung Circ*. 2014;**23**:1020–1028. https://doi.org/10.1016/j.hlc.2014.06.001

158. Hanson ID, Dalal PK, Renard BM, Hanzel GS, Vivacqua A. Emergency valve-in-valve transcatheter aortic valve implantation for the treatment of acute stentless bioprosthetic aortic insufficiency and cardiogenic shock. *Case Rep Cardiol*. 2018;**2018**:6872748. https://doi.org/10.1155/2018/6872748

159. Rufian-Andujar S, Iftikhar O, Salinger M, Saucedo J, Feldman T, Guerrero M. Transseptal transcatheter mitral valve-in-valve for treatment of severe mitral regurgitation in failed bioprosthesis complicated with cardiogenic shock: Case report and review of the literature. *Cardiovasc Revasc Med*. 2018;**19**:874–878. https://doi.org/10.1016/j.carrev.2018.02.011

160. Noly PE, Pagani FD, Noiseux N, Stulak JM, Khalpey Z, Carrier M, et al. Continuous-flow left ventricular assist devices and valvular heart disease: A comprehensive review. *Can J Cardiol*. 2020;**36**:244–260. https://doi.org/10.1016/j.cjca.2019.11.022

161. Bouabdallaoui N, El-Hamamsy I, Pham M, Giraldeau G, Parent MC, Carrier M, et al. Aortic regurgitation in patients with a left ventricular assist device: A contemporary review. *J Heart Lung Transplant*. 2018;**37**:1289–1297. https://doi.org/10.1016/j.healun.2018.07.002

162. Cowger J, Rao V, Massey T, Sun B, May-Newman K, Jorde U, et al. Comprehensive review and suggested strategies for the detection and management of aortic insufficiency in patients with a continuous-flow left ventricular assist device. *J Heart Lung Transplant*. 2015;**34**:149–157. https://doi.org/10.1016/j.healun.2014.09.045

163. Feldman D, Pamboukian SV, Teuteberg JJ, Birks E, Lietz K, Moore SA, et al. The 2013 International Society for Heart and Lung Transplantation Guidelines for mechanical circulatory support: Executive summary. *J Heart Lung Transplant*. 2013;**32**:157–187. https://doi.org/10.1016/j.healun.2012.09.013

164. Robertson JO, Naftel DC, Myers SL, Tedford RJ, Joseph SM, Kirklin JK, et al. Concomitant mitral valve procedures in patients undergoing implantation of continuous-flow left ventricular assist devices: An INTERMACS database analysis. *J Heart Lung Transplant*. 2018;**37**:79–88. https://doi.org/10.1016/j.healun.2017.09.016

165. Coyan GN, Pierce BR, Rhinehart ZJ, Ruppert KM, Katz W, Kilic A, et al. Impact of pre-existing mitral regurgitation following left ventricular assist device implant. *Semin Thorac Cardiovasc Surg*. 2021;**33**:988–995. https://doi.org/10.1053/j.semtcvs.2020.12.007

166. Kanwar MK, Rajagopal K, Itoh A, Silvestry SC, Uriel N, Cleveland JC Jr, et al. Impact of left ventricular assist device implantation on mitral regurgitation: An analysis from the MOMENTUM 3 trial. *J Heart Lung Transplant*. 2020;**39**:529–537. https://doi.org/10.1016/j.healun.2020.03.003

167. Maltais S, Topilsky Y, Tchantchaleishvili V, McKellar SH, Durham LA, Joyce LD, et al. Surgical treatment of tricuspid valve insufficiency promotes early reverse remodeling in patients with axial-flow left ventricular assist devices. *J Thorac Cardiovasc Surg*. 2012;**143**:1370–1376. https://doi.org/10.1016/j.jtcvs.2011.07.014

168. Dunlay SM, Deo SV, Park SJ. Impact of tricuspid valve surgery at the time of left ventricular assist device insertion on postoperative outcomes. *ASAIO J*. 2015;**61**:15–20. https://doi.org/10.1097/MAT.0000000000000145

169. Mendiola Pla M, Chiang Y, Nicoara A, Poehlein E, Green CL, Gross R, et al. Surgical treatment of tricuspid valve regurgitation in patients undergoing left ventricular assist device implantation: Interim analysis of the TVVAD trial. *J Thorac Cardiovasc Surg*. https://doi.org/10.1016/j.jtcvs.2022.10.054 Published online ahead of print 16/11/22.

170. Trankle CR, Gertz ZM, Koneru JN, Kasirajan V, Nicolato P, Bhardwaj HL, et al. Severe tricuspid regurgitation due to interactions with right

ventricular permanent pacemaker or defibrillator leads. *Pacing Clin Electrophysiol.* 2018;**41**:845–853. https://doi.org/10.1111/pace.13369

171. Taramasso M, Gavazzoni M, Pozzoli A, Alessandrini H, Latib A, Attinger-Toller A, et al. Outcomes of TTVI in patients with pacemaker or defibrillator leads: Data from the TriValve registry. *JACC Cardiovasc Interv.* 2020;**13**:554–564. https://doi.org/10.1016/j.jcin.2019.10.058

172. Hill L, Prager Geller T, Baruah R, Beattie JM, Boyne J, de Stoutz N, et al. Integration of a palliative approach into heart failure care: A European Society of Cardiology Heart Failure Association position paper. *Eur J Heart Fail.* 2020;**22**:2327–2339. https://doi.org/10.1002/ejhf.1994

173. Brannstrom M, Boman K. Effects of person-centred and integrated chronic heart failure and palliative home care. PREFER: A randomized controlled study. *Eur J Heart Fail.* 2014;**16**:1142–1151. https://doi.org/10.1002/ejhf.151

174. Sidebottom AC, Jorgenson A, Richards H, Kirven J, Sillah A. Inpatient palliative care for patients with acute heart failure: Outcomes from a randomized trial. *J Palliat Med.* 2015;**18**:134–142. https://doi.org/10.1089/jpm.2014.0192