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POSITION PAPER

Management of aortic stenosis and chronic heart failure: A clinical consensus statement of the Heart Failure Association (HFA) and the European Association of Percutaneous Cardiovascular Interventions (EAPCI) of the ESC

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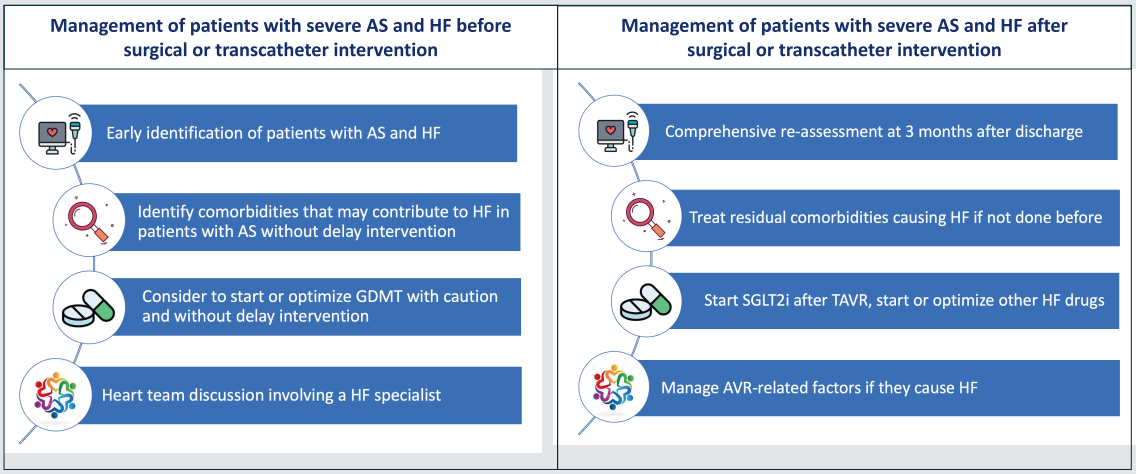
Aortic stenosis (AS) is common and can cause heart failure (HF) or contribute to the progression of pre-existing HF. The management of patients with concomitant AS and HF poses specific clinical challenges. Optimization of guideline-directed medical therapy for HF may be difficult in patients with AS, especially in case of reduced left ventricular ejection fraction. Transcatheter or surgical aortic valve replacement (AVR) is the evidence-based treatment of choice for patients with severe AS and HF. However, advanced cardiac damage, concomitant conditions that can cause HF in addition to AS, as well as some procedure-related factors, may contribute to persistence or worsening of HF after AVR. A multidisciplinary management involving an HF specialist is crucial in this setting and should include a dedicated pre-procedural HF and AS assessment, as well as a careful post-procedural follow-up, including monitoring of HF status. The aim of this clinical consensus statement is to summarize current knowledge on AS and HF, with a focus on pre-procedural and post-procedural management of patients with HF undergoing AVR.

Graphical Abstract



Management of patients with severe aortic stenosis (AS) and heart failure (HF) before and after surgical or transcatheter intervention. AVR, aortic valve replacement; GDMT, guideline-directed medical therapy; SGLT2i, sodium–glucose co-transporter 2 inhibitor; TAVR, transcatheter aortic valve replacement.

Keywords Aortic stenosis • Chronic heart failure

Preamble

Aortic stenosis (AS) is a frequent and treatable cause of heart failure (HF) and may negatively impact the progression of pre-existing HF.[1,2] Transcatheter or surgical aortic valve replacement (AVR) is currently recommended in patients with severe AS and HF. However, the management of these patients can be complex. Guideline-recommended medical therapies for HF, especially those for HF with reduced ejection fraction (HFrEF), may be limited as less tolerated in presence of AS. Moreover, the role of AS as a cause of HF may be difficult to ascertain such that also the clinical course after AVR may be difficult to predict.[3] In addition, HF may persist or worsen after AVR because of pre-existing impairment of cardiac function, long-standing AS leading to advanced cardiac remodelling, comorbidities such as valvular heart disease (VHD), coronary artery disease (CAD), arrhythmias, chronic obstructive pulmonary disease (COPD) as well as AVR-related conditions (i.e. permanent pacemaker implantation). Careful multidisciplinary evaluation of the patient with AS and HF before and after intervention as well as a close interaction between HF specialists interventional cardiologists and surgeons are therefore crucial for patient's management.

Current European Society of Cardiology (ESC) and American College of Cardiology/American Heart Association guidelines emphasize the need for an early referral of patients with severe AS and HF to a multidisciplinary Heart Team for the choice of an individualized treatment strategy.[1,2,4,5] However, specific indications on HF management before and after the intervention are lacking. A recent scientific statement of the Heart Failure Association (HFA), the Association for Acute CardioVascular Care and the European Association of Percutaneous Cardiovascular Interventions of the ESC focused on the management of acute HF and VHD, including AS.[6]

The aim of the present scientific statement is to summarize current knowledge on AS in chronic HF and to provide practical advice on the management. The document will focus on challenging diagnostic aspects, multidisciplinary decision-making and pre-procedural and post-procedural assessment and treatment.

Epidemiology of aortic stenosis and heart failure

Among 5219 patients with native VHD included in the EURObservational Research Programme (EORP) VHD II survey, AS was the most common VHD lesion (41.2%). Among patients with severe AS, 37% had New York Heart Association (NYHA) class III or IV and 16% had a hospitalization for HF in the previous year.[7] Consistent with these observations, in a nationwide registry including the entire Swedish population between 2003 and 2010, AS was the VHD with the highest prevalence in both men and women (37.8 and 24.2 per 100 000 person-years, respectively), accounting for 47.2% of VHD diagnoses. Almost one-third of AS patients had a history of HF.[8]

In the specific setting of HF, moderate or severe AS was reported in 4.3% of 15 216 patients with HF enrolled in the ESC- HFA EORP HF Long-Term Registry, with a prevalence ranging from 3% in patients with HFrEF as well as in those with HF with mildly reduced ejection fraction (HFmrEF) to 8% in patients with HF with preserved ejection fraction (HFpEF).[9] AS had a strong prognostic impact at 1-year follow-up, regardless of ejection fraction category, being associated with a higher adjusted risk of cardiovascular (CV) mortality or HF hospitalization as compared to patients without AS.[9]

Despite a clear indication to intervention for patients with HF and severe AS, the latter condition remains underdiagnosed and undertreated or treated too late.[10–14] Untreated moderate and severe AS is associated with an increased risk of mortality regardless of demographic features, left ventricular ejection fraction (LVEF) and concomitant regurgitation.[15] Advanced versus early stages of cardiac damage due to AS are associated with poorer outcomes despite intervention.[13]

Pathophysiology and clinical presentation of aortic stenosis and heart failure

The pathophysiology of AS may vary depending on the aetiology. In the great majority of cases, AS aetiology is degenerative, which is an active process, with similar underlying pathological processes and risk factors, but different course, as compared to atherosclerosis.[16] Inflammation is followed by leaflet fibrosis and calcification. However, other factors may play a specific role in the development of AS (i.e. mechanical factors and lipoprotein[a] concentrations).[17] Sharing common risk factors, the combination with HF is frequent.[9]

The first and most common response of the left ventricle to AS is a concentric hypertrophy with increase of left ventricular (LV) end-diastolic pressure. Long-standing AS can then lead to overload of pulmonary circulation and, at the later stages, involvement of the right heart. A staging classification of AS based on the extent of cardiac damage has recently been proposed with stage 1 characterized by LV damage (increase in LV mass and/or decrease in LVEF), stage 2 characterized by involvement of the left atrium with atrial fibrillation (AF) and/or mitral regurgitation, stage 3 characterized by pulmonary hypertension and/or tricuspid regurgitation, and stage 4 characterized by right ventricular dysfunction. This classification has important prognostic implications in patients undergoing AVR with an incremental and independent association with mortality.[18] However, in some cases (i.e. pre-existing cardiomyopathy or comorbidities) the cardiac damage can be partially independent of AS and it could be difficult to truly understand the cause–effect relationship between AS and HF.

Patients with AS may remain asymptomatic for a long period of time and, when symptomatic, AS classically presents with angina, syncope and/or HF.[2] When HF symptoms are present, their degree of severity remain subjective and the respective contribution of HF and AS may be difficult to ascertain. A predominant role of HF, myocardial dysfunction and underlying myocardial remodelling (e.g. fibrosis and hypertrophy) may explain the persistence of symptoms and poor clinical outcome of some patients after AVR.[19] The contribution of CV and non-CV comorbidities (i.e. AF, CAD, other VHD, COPD), frequently associated with both AS and HF, may represent an additional challenge for causal relationship between severity of AS and symptoms.

Diagnostic work-up in patients with aortic stenosis and heart failure

Subtypes of aortic stenosis and heart failure

The three subtypes of HF, namely HFrEF, HFmrEF and HFpEF, can all be associated with AS, with HFpEF being the most prevalent, although frequently overlooked.[9,20,21] Notably, it is unexplored whether a supernormal LVEF phenotype is associated with poorer outcome in the setting of AS.[22,23] Several subtypes of symptomatic severe AS based on aortic valve area (AVA), mean transvalvular pressure gradient (MPG), LVEF, and forward flow (i.e. stroke volume [SV]) have been identified. An AVA $\leq$1.0 cm^2 is mandatory for the diagnosis of severe AS. High-gradient AS is characterized by a high MPG ($\geq$40 mmHg) regardless of LVEF and SV. In most patients with HF and high-gradient AS, the HF subtype observed is HFpEF. However, if other causes of HF coexist (i.e. ischaemic heart disease or dilated cardiomyopathy) or in advanced stage of AS, HFmrEF or HFrEF can also be observed. Although most patients with severe AS have high peak velocity and MPG in line with a reduced AVA, there is a subset of patients with reduced LVEF, either due to long-standing severe AS or due to other causes such as ischaemic cardiomyopathy, that present with discordant grading. In these patients with reduced LVEF, the calculated AVA, MPG, and peak velocity are all low (classical low-flow low-gradient [LFLG] AS).[24–26] Patients with LFLG AS may, however, present

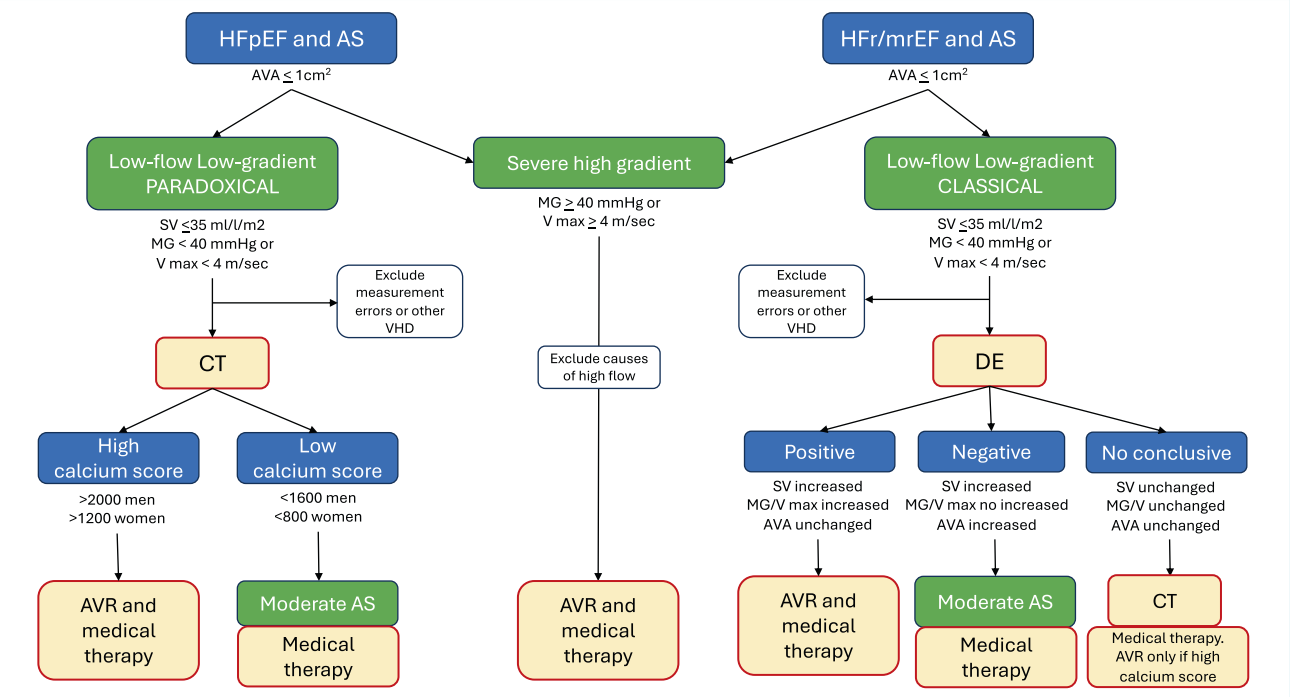


Figure 1 Diagnostic work-up and management of aortic stenosis (AS) in patients with heart failure. The figure shows the diagnostic and therapeutic flow chart according to heart failure and AS subtypes. AVA, aortic valve area; AVR, aortic valve replacement; CT, computed tomography; DE, dobutamine echocardiography; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; MG, mean gradient; SV, stroke volume; VHD, valvular heart disease.

also with preserved LVEF (paradoxical LFLG-AS), so that the low flow is not expected based on LVEF. These patients are often elderly with a history of hypertension, small LV cavity, concentric LV hypertrophy and HFpEF, or may have significant mitral or tricuspid valve diseases.[27] Differential diagnosis between AS subtypes in HF is of utmost importance to avoid overtreatment and/or calibrate treatment expectations. A detailed algorithm for diagnosis of different phenotypes of HF and AS is reported in *Figure 1*.

Challenges in the diagnosis of low-flow low-gradient aortic stenosis

Many challenges can be found in the diagnosis of LFLG AS. We advise to carefully rule out measurement errors (underestimation of the LV outflow tract [LVOT] diameter,[28] misalignment of the continuous-wave Doppler with the aortic jet, or lack of correction to 'the pressure recovery phenomenon' in patients with small ascending aorta [i.e. <30 mm][29–32]) as a first step of the diagnostic work-up. Calculating the effective orifice area index, and the net pressure gradient (adjusted for pressure recovery) can provide more accurate assessment.[33] The use of the dimensionless index or Doppler velocity index (ratio between aortic and LVOT velocity-time integral) as well as the projected effective orifice area may aid in distinguishing true versus pseudo-severe LFLG AS.[34] Then, according to current guidelines,[2] the diagnosis is based on dobutamine echocardiography and/or computed tomography (CT) (*Figure 1*).

Additional diagnostic tools

In the diagnostic work-up of patients with concomitant AS and HF, regardless of the LVEF category, in addition to echocardiography and multi-slice CT, in selected situations (i.e. young patients with severe LV hypertrophy or suspicion of a specific cardiomyopathy), cardiac magnetic resonance (CMR) may be useful. It can be used for LV tissue characterization, differential diagnosis of HF, and the identification of fibrosis (diffuse or focal).[35] In patients with severe AS undergoing AVR, the myocardial scar (whether ischaemic or non-ischaemic) is independently associated with all-cause and CV mortality beyond 10 years of follow-up; the presence of myocardial scar reduces median survival by a third or 3.5 years, underscoring the importance of its evaluation for post-intervention risk assessment in this patient population.[36] Finally, CMR or nuclear imaging may be helpful to exclude specific diseases such as cardiac transthyretin (TTR) amyloidosis.

Management of patients with severe aortic stenosis and heart failure

Beyond the indication for AVR, the co-existence of severe AS and HF poses some challenges in terms of pre-procedural and post-procedural management. In general, an early identification of patients with severe AS and HF is advised to avoid treating

long-standing disease associated with advanced myocardial damage (evidence-based guidance).[13,18]

Management before intervention

Assessment of comorbidities

Comorbidities or concomitant conditions that may contribute to or cause HF in patients with AS need to be carefully identified and treated, if possible, taking into consideration the HF category (expert opinion).

In patients with severe AS and HFrEF, it would be important to understand, according to the patient history, whether LV dysfunction is the consequence of AS or pre-existing, although this may be challenging in some cases. CAD needs to be ruled out if it is supposed to have an active role in the pathophysiology of HF.

In patients with severe AS and LVEF ≥50%, the integration of the HFpEF scores may be predictive of prognosis in patients undergoing transcatheter AVR (TAVR).[37,38] In these patients, HFpEF can be: (i) entirely secondary to AS because of concentric LV hypertrophy and remodelling; (ii) secondary to both AS and other conditions (i.e. cardiac amyloidosis) with different possible contributions to HF signs and symptoms; (iii) entirely or partially primary and unrelated or poorly related to AS.[39–41] However, the only strategy to distinguish between these three scenarios is the re-assessment of HF status after AVR.

Medical therapy

In patients with HF and severe AS, AVR is recommended according to current guidelines.[2]

Our expert opinion is to consider guideline-directed medical therapy (GDMT) while performing diagnostic tests and planning the intervention. However, it should be administered with caution, without delaying the intervention. Factors limiting GDMT optimization before AVR are reported in *Figure 2*. Drugs with effects on blood pressure (i.e. renin–angiotensin–aldosterone system inhibitors) may not be well tolerated in patients with severe AS.[42,43] Our expert opinion is to (1) avoid hypotension maintaining systolic blood pressure above 110–120 mmHg, (2) avoid excessive preload decrease, that is, possible caused by relatively high diuretic doses,[1,44–47] and (3) avoid or up-titrate with caution beta-blockers because of their negative inotropic effect in presence of a fix afterload. Since sodium–glucose co transporter 2 inhibitors (SGLT2i) might be better tolerated than other HF drugs, it would be speculated that SGLT2i could be used as a first-line therapy in these patients.[48,49] However, studies specifically evaluating SGLT2i in patients with HF and severe AS before AVR are not available.

Multidisciplinary evaluation

Our expert opinion is that, in presence of HF, the Heart Team discussion should include a dedicated HF specialist who provides a major contribution in the evaluation of pre-AVR HF status and in the risk assessment of persistence or worsening of HF after AVR. Depending on the HF mechanisms, aetiology, and severity, as well as comorbidity burden, frailty and life expectancy, the Heart Team may decide either to prompt AVR for preventing evolution of HF or to deny AVR, as in case of too advanced stages of HF for avoiding futility.[1,2,4,5,50] Also, the risk of AVR-related complications, even if rare in the modern era, must be taken into account (i.e. patient–prosthesis mismatch after surgical AVR (SAVR) in small annuli, permanent pacemaker after TAVR)[51] as possibly associated with persistence or worsening of HF signs and symptoms after AVR. The experts decided not to discuss here in detail the factors to consider in the choice between TAVR versus SAVR since these aspects are extensively covered in the 2021 ESC/European Association for Cardio-Thoracic Surgery (EACTS) guidelines.[2]

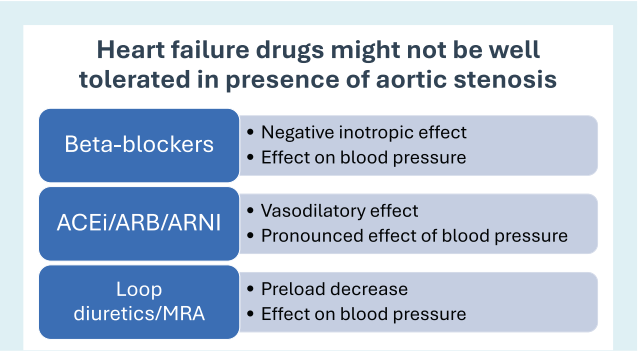


Figure 2 Limitations of medical therapy optimization in patients with heart failure and aortic stenosis. The figure shows the factors limiting the use of heart failure drugs in patients with heart failure and aortic stenosis. ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor–neprilysin inhibitor; MRA, mineralocorticoid receptor antagonist.

Notably, in symptomatic HFrEF patients with severe AS and left bundle branch block (LBBB), AVR can be considered prior to cardiac resynchronization therapy (CRT) (expert opinion).[5]

Management after intervention

Treatment of AS by means of TAVR or SAVR is associated with a well-established mortality benefit.[52] Furthermore, LV reverse remodelling and improvement in health status have been previously reported.[53,54] In most cases, patients with severe AS experience an improvement after AVR. However, it is known that signs and symptoms of HF may persist or worsen after AVR. Readmission for congestive HF has been observed in up to 24% of patients after TAVR.[55,56] Thus, in some cases the response to AVR can be partial or absent. Rarely an early or late worsening of HF status can be observed (*Figure 3*). Changes in HF status after AVR can differ according to several factors. Lack of improvement or worsening can be due to advanced stages of myocardial damage, other factors contributing to HF beyond AS, lack of GDMT optimization, and/or AVR-related factors (*Figure 3*).

Our expert opinion is to (1) treat comorbidities if not done before AVR, (2) start or optimize GDMT, and (3) treat AVR-related factors (*Figure 4*). Therefore, a comprehensive patient evaluation after AVR (*Table 1*) is advised before discharge and within 3 months

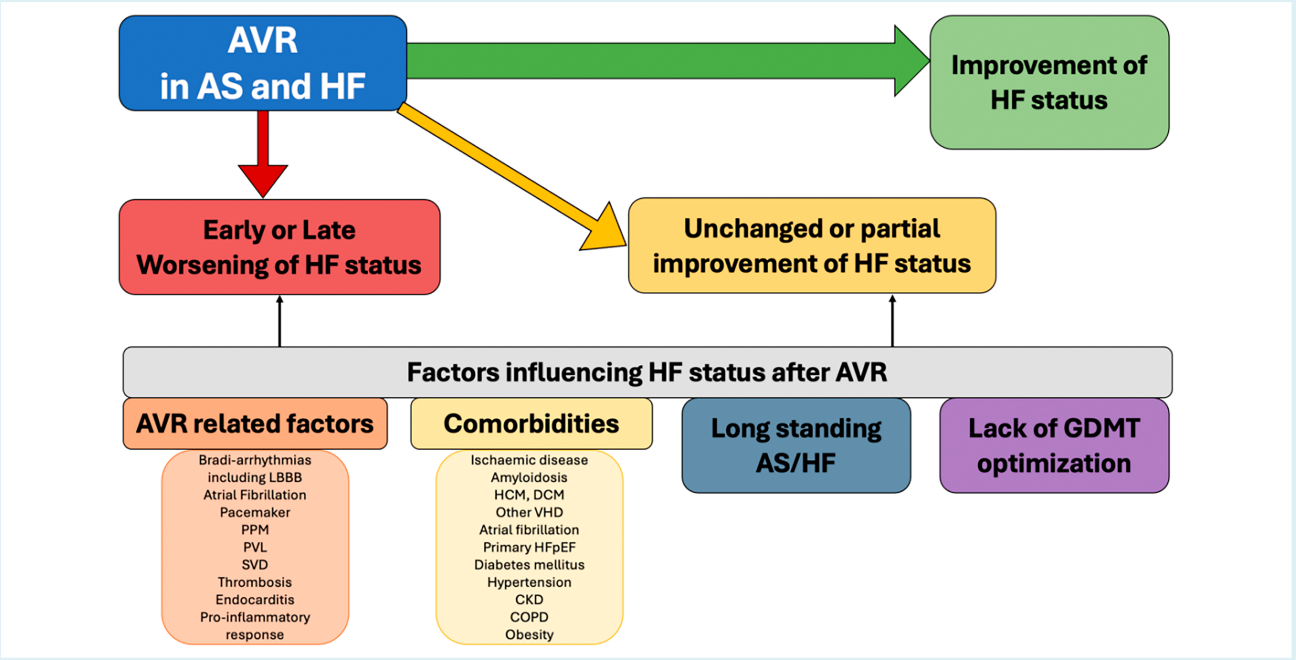


Figure 3 Changes and factors influencing heart failure (HF) status after aortic valve replacement (AVR). The figure shows changes in HF status after surgical or transcatheter AVR, as well as factors that can contribute to the lack of improvement, partial improvement or worsening of HF after aortic valve intervention. AS, aortic stenosis; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DCM, dilated cardiomyopathy; GDMT, guideline-directed medical therapy; HCM, hypertrophic cardiomyopathy; HFpEF, heart failure with preserved ejection fraction; LBBB, left bundle brunch block; PPM, patient–prosthesis mismatch; PVL, paravalvular leak; SVD, structural valve deterioration; VHD, valvular heart disease.

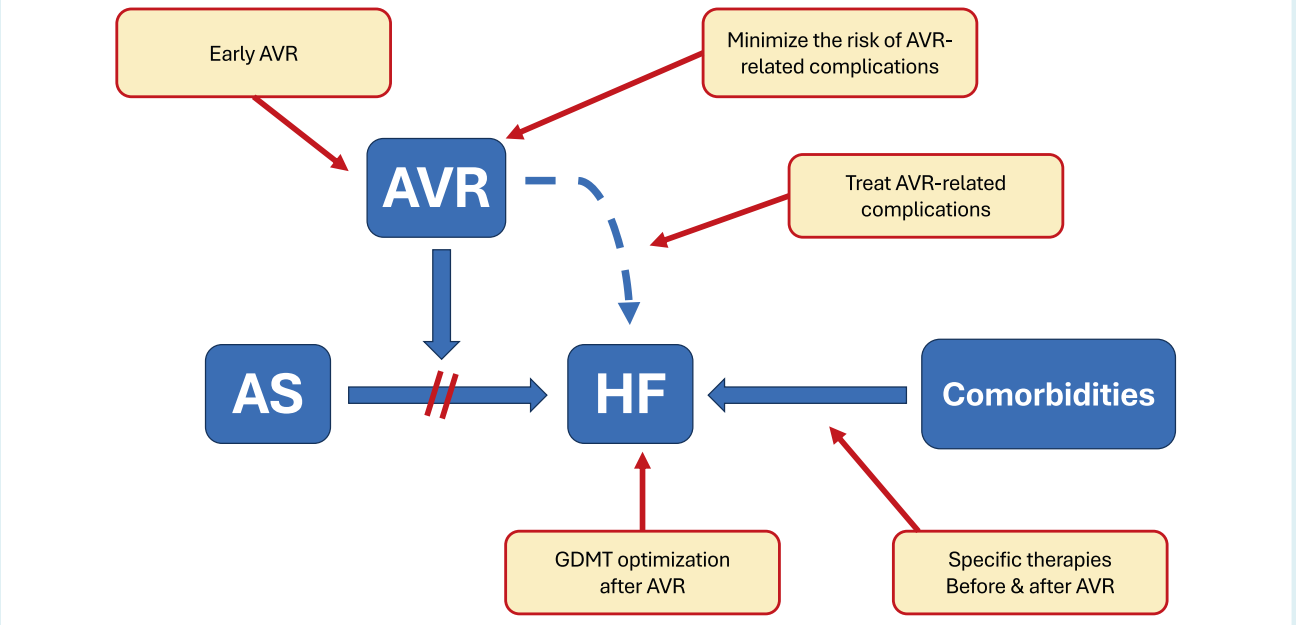


Figure 4 Actions to prevent or treat heart failure (HF) in patients with aortic stenosis (AS) undergoing aortic valve replacement (AVR). The figure shows the possible cause of HF in patients with AS (blue) and possible actions to prevent the risk of HF before intervention or treat HF after intervention (red). GDMT, guideline-directed medical therapy.

Table 1 Check-list for patient follow-up assessments after aortic valve replacement

Clinical assessment
NYHA class
Vital signs (BP, HR)
Signs of congestion (including body weight)
Quality of life
Electrocardiogram
AF vs. SR
Bradi-arrhythmias, including LBBB
Ventricular pacing (check the ventricular pacing rate in patients with permanent PM)
Echocardiogram
Aortic valve prosthesis performance • Mean gradient, EOA, DVI • Intra-valvular and/or peri-valvular aortic regurgitation • Prosthesis valve dysfunction (structural valve deterioration, non-structural dysfunction, thrombosis, endocarditis)
LV dimensions, remodelling and LVEF
Estimated pulmonary artery pressure, right ventricular dimensions/function
Assessment of other valvular heart diseases
Laboratory assessments
Natriuretic peptides (serial measurement)
Renal function, hepatic function
Electrolytes (potassium)

AF, atrial fibrillation; BP, blood pressure; DVI, Doppler velocity index; EOA, effective orifice area; HR, heart rate; LBBB, left bundle branch block; LV, left ventricular; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PM, pacemaker; SR, sinus rhythm.

after discharge. The timing of the following evaluations depends on the persistence of HF, HF phenotype and severity.

Management of comorbidities

Treatment of factors contributing to HF has to be continued after AVR. Patients with cardiac amyloidosis should receive specific pharmacological therapies according to current indications. Other comorbidities, which are known to be risk factors for HFpEF, have to be addressed (i.e. obesity, hypertension, diabetes). Treatment of iron deficiency seems not to provide additional benefit in patients with or without HF undergoing TAVR.[57] However, according to current HF guidelines, ferritin and transferrin saturation have to be periodically evaluated and intravenous supplementation is indicated in all HFrEF and HFmrEF patients to prevent HF hospitalizations.[1] Thus, our expert opinion is that, in case of persistence of HF after AVR it is reasonable to assess iron status and provide specific therapies, if indicated. CAD, other VHDs, as well as AF, are treated simultaneously to SAVR in case of surgery. If a transcatheter approach is adopted (i.e. TAVR), CAD, VHD and AF may contribute to the persistence of HF after the intervention. Notably, secondary mitral and tricuspid regurgitation as well as AF can improve after TAVR.[58–60] This should be taken into account in the decision-making. A staged personalized transcatheter approach can be adopted to treat residual CV comorbidities. Specific management of these conditions goes beyond the aim of this document.

Optimization of guideline-directed medical therapy

Our expert opinion is that (1) in patients with HFpEF and small LV cavity, hypovolaemia must be avoided during and after AVR, and initiation or up-titration of beta-blockers may be useful to prevent dynamic obstruction under careful consideration of the brady-arrhythmic risk, and (2) afterload reduction secondary to AVR may enable optimization of GDMT in patients with HF, especially those with HFrEF.

In the Dapagliflozin in Patients Undergoing Transcatheter Aortic-Valve Implantation (DapaTAVI) trial, 1222 patients with history of HF and at least one risk factor between diabetes, CKD and LV dysfunction, were randomly assigned to receive either dapagliflozin or standard of care. At 1-year follow-up, the risk of the primary endpoint (death from any cause or worsening HF events) was reduced by 28% in the treatment arm as compared to the control arm, mainly driven by worsening HF events.[61] Therefore, it is advised, as evidence-based guidance, that patients with HF who receive TAVR for severe AS will receive dapagliflozin before discharge to prevent HF events. Renin-Angiotensin System Blockade Benefits in Clinical Evolution and Ventricular Remodeling After Transcatheter Aortic Valve Implantation (RASTAVI) was a small randomized trial comparing ramipril administration versus usual care in patients with LVEF >40% after successful TAVR. It did not meet the primary endpoint of cardiac death, HF readmission and stroke at 1 year as compared to placebo, but was associated with a significant reduction in HF readmissions at 1 year and LV reverse remodelling without improvement in fibrosis.[62] RASTAVI does not lead to specific advices.

Management of aortic valve replacement-related factors

Aortic valve replacement complications, in particular arrhythmic complications, can be associated with a lack of improvement or

worsening of the HF status. New-onset LBBB is the most common complication after TAVR[63] and has been reported as a predictor of mortality.[64] It can develop, even if more rarely, after SAVR as well[65] and may lead to dyssynchrony, LV dysfunction and secondary mitral regurgitation. The possible benefit of CRT in this setting is not supported by evidence since documented only in a few case reports.[66–68] However, if the cause–effect relationship between LBBB and worsening of HF after AVR is clear and not responsive to medical therapy, CRT can be considered as a reasonable option (expert opinion). In particular, CRT can be considered in patients with HFrEF and persistent LBBB after AVR. In this context, CRT implantation might be immediate in patients with associated significant bradyarrhythmia, and delayed after GDMT optimization in patients without significant bradyarrhythmia. In patients with HFpEF, LBBB and significant bradyarrhythmia, the choice between pacemaker and CRT should be discussed case by case by the Heart Team including an electrophysiologist and an HF specialist.

New-onset AF can occur after both TAVR and SAVR, but is more common in the latter.[69] It is associated with impaired outcome and one of the major predictors of AF persistence at 1-year follow-up is LV dysfunction, whereas beta-blocker therapy seems to have a protective role.[59,70] AF has to be recognized and treated according to current guidelines.[71] However, in this specific setting and in line with HF guidelines, a rhythm control strategy should be preferred if a clear association between new-onset AF and lack of HF status improvement is documented.[1]

Finally, complete atrioventricular block requiring new permanent pacemaker implantation is a possible post-AVR complication, more commonly in patients undergoing TAVR. It has been associated with impaired outcome, especially in patients with reduced LVEF, with implantation depth and right bundle brunch block as major independent predictors.[72–74] It may contribute to LV dysfunction and impaired outcomes in case of a high rate of right ventricular pacing.[75] Thus, our expert opinion is that an upgrading to biventricular pacing or the systematic implantation of CRT device can be considered in case of high ventricular pacing. On the other hand, given the low rates of long-term dependency on pacing, current guidelines suggesting algorithms promoting spontaneous atrioventricular conduction should be adopted.[76] Of note, in this setting a His–Purkinje conduction system pacing may have a major role.[77]

Bioprosthetic valve dysfunction is rare.[78,79] Valve deterioration, either structural (i.e. bioprosthesis degeneration or valve thrombosis) or non-structural (i.e. patient–prosthesis mismatch, paravalvular leak), may rarely require a reintervention if graded as significant and clinically relevant according to the most recent definitions (i.e. HF signs and symptoms).[78–82]

Cardiac amyloidosis and aortic stenosis

Recent studies have shown that cardiac amyloidosis (typically TTR amyloidosis) is common in patients with AS, since it coexists with AS in approximately 15% of the patients older than 65 years.[41,83,84] The coexistence of cardiac amyloidosis and AS is associated with worse clinical presentation and outcome as compared to lone AS.[41,85] Multimodality imaging, including nuclear imaging and CMR, may be helpful to identify TTR amyloidosis in patients with AS and 'red flags' raising the suspicion of its coexistence.[41,86] A clinical score (RAISE) including parameters related to systemic involvement, electrical abnormalities and ventricular remodelling has been developed to predict the presence of concomitant AS and cardiac amyloidosis.[85] Patients with TTR cardiac amyloidosis should receive specific pharmacological therapies according to current indications, as soon as the diagnosis is confirmed, even in presence of concomitant AS. TAVR may be preferred to SAVR in patients with severe AS and cardiac amyloidosis. Recent studies have shown that TAVR improved survival versus medical management in patients with severe AS and cardiac amyloidosis, and post-TAVR survival did not differ between patients with lone AS and those with both AS and amyloidosis.[85,87,88] Therefore, TAVR should not be withheld in these patients.

Moderate aortic stenosis

Moderate AS is common in patients with HF[9,89] and, albeit frequently underdiagnosed, HF seems frequent in patients with moderate AS, considering the high prevalence of HF-related symptoms (i.e. NYHA class II–IV) and cardiac functional/structural abnormalities (i.e. LV systolic dysfunction, left atrial dilatation, or LV diastolic dysfunction).[90–92] The presence and extent of extra-valvular cardiac abnormalities have been associated with worse prognosis in patients with moderate AS.[91] Furthermore, several recent studies have demonstrated the prognostic impact of moderate AS in patients with LV systolic dysfunction, defined as LVEF <50%, either asymptomatic or with evidence of HFrEF/HFmrEF.[92–94] The current management of patients with moderate AS is based on close clinical follow-up even in the presence of HF. Careful exclusion of undiagnosed severe AS in case of discordant parameters (by means of dobutamine echocardiography and/or cardiac CT) is mandatory in these patients.[95] In patients with HF symptoms despite a true moderate AS, the identification and treatment of comorbidities and underlying HF is of paramount importance.[95] Preliminary observational evidence suggests a potential benefit of early TAVR or SAVR in patients with moderate AS and LVEF <50%.[93,96,97] However, the randomized Transcatheter Aortic Valve Replacement to UNload the Left ventricle in patients with ADvanced heart failure (TAVR UNLOAD) trial has recently shown that TAVR was not superior to AS surveillance in patients with moderate AS and HFrEF/HFmrEF, that is, NYHA class ≥II and LVEF between 20% and 50%, with respect to a primary hierarchical composite endpoint including all-cause death, disabling stroke, disease-related hospitalizations and HF hospitalization equivalents, and change in the Kansas City Cardiomyopathy Questionnaire overall summary score.[98] Although the trial was negative with respect to the primary endpoint, pre-emptive TAVR was safe and improved quality of life, since it resulted in a greater improvement in the Kansas City Cardiomyopathy Questionnaire overall summary score as compared to AS surveillance.[98] The ongoing Evolut™ EXPAND TAVR II Pivotal Trial (NCT05149755) and A Prospective, Randomized, Controlled Trial to Assess the Management of Moderate Aortic Stenosis by Clinical Surveillance or Transcatheter

Aortic Valve Replacement (PROGRESS; NCT04889872) trials are enrolling patients with moderate AS, symptoms and/or evidence of cardiac functional/structural abnormalities, and LVEF >20%, to evaluate whether early TAVR is superior to a conservative strategy. Treating moderate AS in patients with HF and reduced LVEF, beyond the unloading effect, may also increase the room for medical therapy up-titration, especially in case of drug intolerance due to hypoperfusion (hypotension, renal dysfunction, malabsorption). However, early intervention cannot be currently advised as an evidence-based strategy in patients with moderate AS due to the lack of positive dedicated trials.

Conclusions

Management of patients with AS and HF is complex. The use of medical therapies for HF might be particularly challenging in patients with AS, and AVR may enable GDMT optimization, especially in the context of HFrEF. However, HF can persist or worsen after AVR. Intervention at early stages of cardiac damage is crucial. Furthermore, specific actions are needed to identify and treat concomitant factors contributing to HF and to prevent or treat AVR-related complications. In all these contexts the interaction between HF specialists, imagers and interventionists is crucial to optimize patient management.

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