Review Article

Sex-related disparities in aortic stenosis from disease awareness to treatment: a state-of-the-art review

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Abstract: This state-of-the-art review aimed to synthesize evidence from various sex-stratified studies on aortic stenosis (AS), focusing on the difference in clinical presentation, anatomical characteristics, pathophysiology, and management of AS. In comparison to men, women with AS are present at later stages, are older, more symptomatic, frailer, and exhibit higher operative risk [Society of Thoracic Surgeons (STS) score]. Women tend to have smaller aortic valve (AV) areas and left ventricular (LV) outflow tract, leading to lower stroke volumes (SVs) than men and have a higher prevalence of paradoxical, low-flow, low-gradient AS. In women, chronic pressure overload due to AS results in concentric LV remodelling and hypertrophy, characterized by reduced LV cavities, higher filling pressures, lower wall stress, and more diastolic dysfunction. Conversely, men exhibit more dilated eccentric LV remodelling and hypertrophy. AVs in women are less calcified but more fibrotic. Moreover, women are often underdiagnosed, have severity underestimated, and experience delays or receive fewer referrals for AV replacement (AVR). However, women tend to benefit from transcatheter AVR (TAVR) with a long-term survival advantage over men, although the incidence of vascular complications and bleeding events in 30 days after TAVR is higher in women. Surgical AVR (SAVR) in women has high operative risk, is technically demanding and has poorer outcomes with increased mortality at 30 days compared to men. According to the STS score and EuroSCORE, the female sex itself is considered a risk factor for SAVR. Therefore, addressing sex-related disparities in AS and increasing awareness among physicians promises improved diagnosis and treatment, facilitating equitable care and the development of sex-specific personalized medicine.

Keywords: Aortic stenosis (AS); women; surgical aortic valve replacement (SAVR); transcatheter aortic valve replacement (TAVR); sex differences

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Introduction

Recently, sex-related disparities in aortic stenosis (AS) have gained increasing prominence when considering disease presentation, diagnosis, management, and outcome after aortic valve (AV) interventions. Although epidemiological studies have not detected any difference in the prevalence of AS among men and women, including the new onset of diseases (1-3), crucial sex-related differences tend to exist. They are not being fully appreciated due to the widespread underdiagnosis of AS in women (4). This state-of-the-art review aims to summarize current evidence concerning sex-related disparities in AS to guide future treatment decisions.

Epidemiology of AS

AS is a highly prevalent valvular heart disease worldwide (5). It is a progressive, degenerative heart disease that significantly impacts physical function, quality-of-life and overall lifespan in both men and women (6,7). The epidemiology of AS varies greatly between low- and high-income countries (8). Rheumatic valvular heart disease is the most common cause of AS worldwide (9), so in developing countries (8), and degenerative AV calcification (AVC) is the leading cause in developed countries and is expected to increase due to the rapidly ageing population (8,9).

A recently published study on the United States adult population diagnosed with severe AS over 20 years [1997–2016] showed a population incidence of severe AS as 52.5 per 100,000 patients, with a slightly higher incidence in men than women. However, the incident trend remained stable in men (incidence rate ratio 0.99, P=0.7) and declined in women (incidence rate ratio 0.93, P=0.02) (10). Another cohort study (AGES-Reykjavik study) on a randomly selected population of elderly individuals (67–95 years of age) representing the general population of Iceland, AV area (AVA) index by echocardiography on individuals of age ≥70 years revealed severe AS (AVA index <0.6 cm^2/m^2) was more prevalent in women than in men (4.5% *vs.* 4.1%) and 4.3% in combined sexes. However, assessment of AV calcium score (AVCS) on computed tomography (CT) showed a higher prevalence of severe AS (AVCS ≥500 signifying severe AS of AVA index <0.6 cm^2/m^2) in men compared to women (8.5% *vs.* 4.0%) and 5.9% in both sexes (11). Research indicates AS is one of the common valvular abnormalities in developed countries, affecting >40% of patients (both males and females) with native valvular disease (12,13). The progressive and degenerative nature of the disease necessitates interventions, either surgical AV replacement (SAVR) or transcatheter AV replacement (TAVR), to replace the affected valve to prevent irreversible haemodynamic changes and damage to the heart (14).

Underdiagnosis and undertreatment of AS in women

Several studies have shown that AS in women is often diagnosed late in their disease trajectory with a more significant risk profile, such as advanced age, more symptomatic burden, frailty, renal insufficiency, and a higher rate of symptomatic heart failure (HF) (1). Additionally, on presentation, women are more likely to have concomitant moderate to severe mitral regurgitation than their male counterparts (15).

One of the potential reasons for this delayed diagnosis is the lack of awareness about the disease. A European Heart Health survey [2019] indicated that people (both men and women) have a low level of concern for valvular heart diseases, including AS, compared to diseases like cancer, Alzheimer's disease or stroke. Only 26.2% were aware of AS, in which women demonstrated better knowledge than men (16). Additionally, younger people (60–64 years of age) appear to be better informed about AS than older people (≥80 years of age). However, patients (both male and female) with typical symptoms like fatigue, reduced physical activity, and feelings of premature ageing did not seek medical care, and older patients (≥60 years of age) rarely received regular check-ups with a stethoscope by their general practitioner (GP). In addition, males (31.3%) were more likely to undergo regular check-ups at every visit to their GP than female patients (24.2%, P<0.001) (16). Similar study findings were reported by Gaede *et al.* in their public survey on awareness of AS in 8,860 people aged ≥60 years of age (17), and Hengstenberg *et al.* (18) in an AS awareness survey in 1,001 participants of age more than 60 years, underscoring the limited awareness and treatment disparities concerning AS between sexes.

Another reason for the underdiagnosis and undertreatment of women is a disparity in specialist referrals. According to data gathered from the United States administrative claim databases, women with AS received fewer referrals for specialist care and underwent fewer diagnostic tests compared to male patients. Consequently, approximately half the number of female patients underwent SAVR (19). It was suggested that the lower

referral rate to SAVR in women was due to unfavourable preoperative baseline characteristics (19). Furthermore, a retrospective study on the Spanish hospital discharge database [2016–2019] on elderly patients (≥80 years of age) also revealed that women were less likely to get admitted to speciality departments such as cardiology [odds ratio (OR) =0.82; 95% confidence interval (CI): 0.77–0.87] and cardiac surgery (OR =0.82; 95% CI: 0.76–0.87), but more often admitted to internal medicine (OR =1.01; 95% CI: 0.95–1.08), despite having higher prevalence of severe AS than males (14.8% *vs.* 11.3%, P<0.001) and having a higher prevalence of congestive HF. Moreover, female patients were less likely to undergo echocardiogram (OR =0.96; 95% CI: 0.94–0.98) and coronary catheterization (OR =0.81; 95% CI: 0.77–0.87) than males and, and their referral rate for SAVR (but not TAVR) was lower, despite having less frequent elective admissions (20). Similar lower referral rates to SAVR in women were reported by Bienjonetti *et al.* (21) and other studies (22-24). Bienjonetti *et al.* observed this disparity, particularly in female patients showing discordant low-gradient AS (discordance between small AVA indexed and low mean gradient/V_{Peak}) and higher mortality (21). Some factors known to be accountable for the diagnostic delay and few specialist referrals were more prolonged duration of initial medical management in women, physical frailty, advanced age, underestimation of AS severity, patient's hesitancy in undergoing the diagnostic procedure, and unfavourable preoperative baseline characteristics (21,23,25). Although TAVR is as common in women as men (12), they experience longer workup and procedural waiting, leading to higher 30-day mortality and HF hospitalization compared to men (23,26). Therefore, it is paramount that awareness amongst physicians of the sex-related disparities in treating severe AS is raised to abolish the current healthcare gap between the sexes.

Clinical presentation and comorbidities of AS: women *vs.* men

Compared to men, women with severe AS are more symptomatic, older, frailer, have lower body mass index (BMI), exhibit higher operative risk [higher Society of Thoracic Surgeons (STS) scores], and often belong to New York Heart Association (NYHA) class III/IV (1,21,23,27). Cardiac symptoms, such as chest pain, shortness of breath, dizziness, or syncope, were found common in both sexes but more pronounced in women (1,21,23). The heightened likelihood of symptomatic manifestation in women can be attributed to advanced age (over 80 years), diverse underlying pathophysiological profiles, diminished exercise tolerance, and higher frequency of concomitant mitral or tricuspid valve disease (1,21). In addition, the increased symptomatic burden experienced by women is attributed to several pathophysiological changes arising from chronic pressure overload due to AS, resulting in concentrically remodelled LV hypertrophy (LVH). Consequently, women experience higher relative wall thickness, higher filling pressure, lower wall stress, and a smaller LV cavity volume and dimensions than men (4,25). Also, in a study by Tribouilloy *et al.*, non-invasive Doppler echocardiographic assessment revealed higher left atrial volumes (indexed) and pulmonary artery systolic pressures in women (23).

Several studies indicate women have high non-atherosclerotic comorbidities, such as hypertension, diabetes mellitus, renal impairment [glomerular filtration rate (GFR) ≤30 mL/min], atrial fibrillation (AF) and anaemia with a critical preoperative status, but have less overall comorbidity burden compared to men (1,24,28,29). The prevalence of atherosclerotic comorbidities such as cerebrovascular disease, coronary and peripheral arterial disease and previous sternotomies are lower in women compared to men (24,29). Researchers posit that estrogen may have protective effects that help mitigate the progression of atherosclerosis in women (30).

Sex-related disparities in cardiac CT and echocardiography

AS develops due to long-term inflammatory processes that culminate in valvular calcification, fibrotic changes and myocardial modifications due to heightened pressure overloads (4,25). Therefore, apart from clinical presentation, apparent sex-related differences are observed during cardiac imaging. A comparative study on AVC density using multidetector CT (MDCT) found that women exhibited a reduced burden of AVC, even after accounting for body surface area (BSA) and echocardiographic parameters (31). Besides, the female sex was linked to slower AVC progression, while the hemodynamic advancement of the disease remained comparable between both sexes (32). Notably, valvular calcification plays a more significant role in leveraging the progression of AS in men than in women (31,33,34). This divergence could be attributed to a more pronounced fibrotic remodelling in women, resulting in elevated levels of valvular fibrosis and dense connective tissue at the same degree of hemodynamic stenosis severity (25).

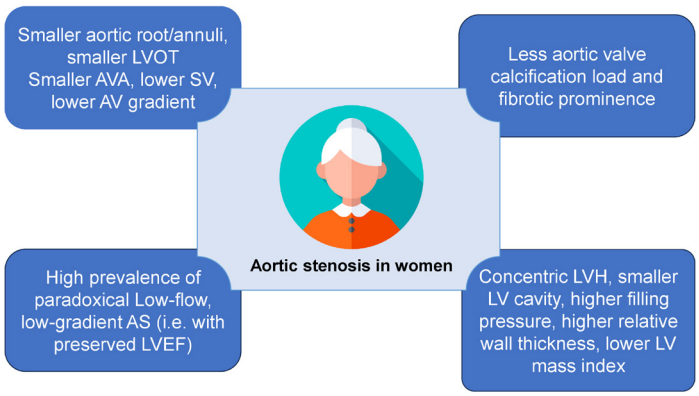

Figure 1 Difference in haemodynamics and LV characteristics in women with AS. LVOT, left ventricular outflow tract; AVA, aortic valve area; SV, stroke volume; AV, aortic valve; AS, aortic stenosis; LVEF, left ventricular ejection fraction; LVH, left ventricular hypertrophy; LV, left ventricle.

However, an 11-year study (2010 to 2021) on the influence of AVC score (AVCS) on mortality after TAVR revealed a more pronounced statistical association between increasing AVCS and elevated mortality rates in women but not in men. Precisely, an increase of 500-unit AVCS was linked with a 7% increase in mortality in women [with a hazard ratio of 1.07 (95% CI: 1.02–1.12)]; no such association was observed in men (35). Therefore, AVCS, as measured by MDCT, exhibits different threshold units: women (>1,600= highly likely; >1,200= likely) have lower sex-specific Agatston unit thresholds for diagnosis of severe AS than men (>3,000= highly likely; >2,000= likely) (36). Moreover, female patients harbour more severe mitral annular calcification and ascending aorta calcification, and men have worse AVC and coronary artery calcification. Interestingly, among all the cardiac calcification subgroups, sex is an independent predictor of the calcifying process, except for ascending aortic calcification. However, other risk factors influencing calcification include age, concurrent medications, and mitral valve disease morphology (37).

In progressive AS, sex-related differences are also noted in LV structure, function, and hemodynamics, necessitating differential diagnostic criteria defining the AS severity during echocardiography in both sexes. Women generally exhibit smaller BSA than men, leading to smaller cavity size, smaller AVA, restricted LV filling, lower stroke volume (SV) and decreased AV gradient (38-40) and exhibit a higher prevalence of paradoxical low-flow low-gradient AS than men (4) (*Figure 1*). Women have smaller aortic size, aortic root/annuli and LV outflow tract (LVOT) than men (7). Therefore, these inherent differences related to haemodynamics in women prompt the usage of echocardiographic parameters indexed by BSA, such as using AVA index ≤0.6 cm^2/m^2 to define the severity of AS in women. Additionally, defining sex-specific thresholds or cut-off valves for lower SV helps to achieve precise severity grading in women (40). A study by Guzzetti *et al.* indicates the use of sex-specific thresholds <40 mL/m^2 for men and <32 mL/m^2 for women to define low SV outperforms the guideline-indicated threshold (35 mL/m^2) and improves severity assessment and risk stratification after AV replacement (AVR) (41). Furthermore, the difference in the adaptive physiological response such that the concentric hypertrophic LV remodelling in women results in greater relative wall thickness, smaller LV cavity, smaller LV mass index, LV ejection fraction (LVEF), and higher filling pressure than men who develop an eccentric remodelling pattern and cavity dilation (4,7). In a study by Treibel *et al.*, cardiovascular magnetic resonance findings revealed that normal LV geometry and predominant concentric remodelling were observed among women. In contrast, men displayed a higher prevalence of eccentric hypertrophy. However, transthoracic echocardiography did not reveal significant differences in LV remodelling patterns based on sex (42).

Treatment outcomes of AVR in women *vs.* men

Replacement of the AV via SAVR or TAVR is the well-known treatment option for treating severe symptomatic AS (43). Current treatment guidelines recommend TAVR as the most appropriate treatment for patients with advanced

age or high surgical risk and severe symptomatic AS (44). According to worldwide registries, women are still less in number undergoing AVR than men (45,46). In women, SAVR may be technically more demanding and complicated due to sex-specific pathophysiological differences, such as smaller annular sizes and LVOT dimensions linked to concentric LVH (47). Besides, a higher prevalence of paradoxical low-flow, low-gradient AS is linked to unfavourable outcomes and increased mortality rate with SAVR in women compared with high-gradient AS in men (48). Besides, old age and advanced disease stages with greater frailty during surgical referral are thought to be contributing factors (47). Also, according to the STS score and EuroSCORE, the female sex itself is an independent risk factor for SAVR (49,50). Therefore, in recent years, less invasive TAVR has been more common in treating female patients with severe AS. Older patients with very high surgical risk have markedly improved outcomes with procedural success that seems to be comparable between both sexes (44).

Despite significant advancements in TAVR procedures, disparities in outcomes, including mortality rates between male and female patients, exist. Studies have indicated that TAVR is linked to lower 30-day and 1-year mortality risks in women (51). Various studies assessing the differential impact of sexes on long-term outcomes after TAVR show that women have a significantly lower re-operation rate and better long-term survival rate (1 and 3 years) compared to men (28), and it is less complicated and safer than SAVR (14,52). Tarantini *et al.*, in their multicentre observational registry (European outcome), reported a lower 4-year post-TAVR mortality in women *vs.* men (36.0% *vs.* 39.7%, P=0.0911) with no difference in cardiac mortality (24.2% *vs.* 24.7%) (53). Although women have post-procedural survival benefits compared to men, they exhibit a higher risk of post-TAVR stroke, vascular complications and bleeding blood transfusion requirement at 30 days than their male counterparts (54). Several real-world cohorts (27,28,55-60) reported similar study findings on TAVR (*Table 1*). It is hypothesized that advanced age, smaller blood vessels, and lower BSA increase the risk of procedural bleeding and vascular complications in women (54). Therefore, careful consideration and appropriate antithrombotic therapies should be employed to prevent thrombotic complications (54).

During TAVR, women often receive smaller transcatheter heart valves than men due to their smaller aortic annular size and perimeter (61), reducing the likelihood of paravalvular leaks (62). Moreover, the reduced calcification burden in women might have contributed to a more favourable stent frame expansion during the TAVR procedure, reducing the occurrence of moderate/severe aortic regurgitation after TAVR compared to men (63). These unique features might explain why women benefit more from TAVR than surgical procedures, which may be associated with a greater incidence of severe prosthetic-patient mismatch, adversely affecting clinical outcomes (30).

The impact and outcomes of female-specific factors, such as frailty, osteoporosis, pregnancy history, hormonal influence, and menopause age on TAVR, have not been thoroughly explored. Current research indicates that frailty and osteoporosis can result in poorer post-procedure recovery. Osteoporosis and vertebral fractures can potentially impair cardiac rotation during the TAVR procedure, impacting device positioning and implantation (64). Besides, hormonal influences in women's bodies can play a role in arterial stiffness and diastole dysfunction that affect AS progression and post-TAVR outcomes. However, more research is necessary to fully comprehend the interplay of these female-specific factors and their implication on the efficiency of TAVR in women.

Sex difference in quality of care

Until now, evaluating the quality of care in AS patients has mainly focused on procedural and post-procedural outcomes. However, evidence indicates symptomatic severe AS patients may not receive adequate AVR treatment on time, thus significantly affecting patient outcomes (65). A study by Bienjonetti *et al.* revealed that long waiting times or low referral rates to AVR procedures in symptomatic female patients result in higher mortality in females compared to males. In particular, women with discordant low gradient AS were less referred to AVR (neither SAVR nor TAVR) and were at higher mortality risk (21). At the same time, male and female patients with concordant severe AS were referred similarly to the AVR procedure and exhibited similar survival rates after the intervention (21). Furthermore, research indicates women after AVR had lower 5-year survival than expected compared to males, despite a longer life expectancy, even after matching with age: 66%±2% (expected, 75%) *vs.* 68%±2% (expected, 70%; P<0.001) (23). This reduced survival in women after AVR (TAVR or SAVR) can be attributed to the delay in AVR as women are managed conservatively (medical treatment) for

Table 1 Studies comparing clinical outcomes after TAVR in women *vs.* men

Name of study/first author, design	Total	Female (%)	Follow-up	Age (years), mean ± SD		Operative risk (STS-prom score), mean ± SD		Vascular complication (%)		Bleeding (%)		Stroke (%)		All-cause mortality at 30 days (%)		All-cause mortality at 1 year (%)	
				Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men
PARTNER II S3, randomized control trial (27)	1,661	39.5	1 year	82.5±7.2	82.0±7.1	6.8±3.0	6.3±2.8	7.2	4.2	16.7	14.6	2.1 (minor)	0.7 (minor)	2.0	1.2	9.3	10.2
Denegri *et al.*, prospective study (28)	3,821	56.2	1 year	83±6	81±6	7.8	7.1	3.9	2.4	2.5	1.4	0.8	0.4	1.1	1.1	11.5	15.0
France 2 registry, prospective observational (55)	3,972	49.5	1 year	84.0±6.6	81±6.5	21.4±13[†]	22.2±15.2[†]	4.6	1.9	4.3	1.9	3.1	2.2	9.5	9.2	19.3	23.7
Sannino *et al.*, retrospective observational (56)	910	46.5	1 year	82.0±7.6	80.9±8.4	7.9±3.7	7.1±4.0	7.8	4.1	4.0	1.6	–	–	–	–	7.0	12.7
US CoreValve trials, randomized control trial (57)	3,687	46.3	1 year	84.0±7.6	82.7±7.9	9.6±4.9	8.3±4.6	9.7	4.9	42.7	31.2	5.7	4.0	5.9	5.8	21.3	24.1
D'Ascenzo *et al.*, retrospective study (58)	377	57.2	30 days	82.9±5.4	81.6±5.3	5.6±3.1	7.6±6.2	12.9	9.8	44	25	3.1	1.9	7.4	8.7	–	–
TVT registry, prospective study (59)	23,652	49.9	1 year	82.3±8.5	81.7±8.6	9±6	8±6	8.3	4.4	8.0	6.0	2.6	1.9	5.6	4.3	21.3	24.5
Humphries *et al.*, prospective study (60)	641	51.3	30 days	83	82	7.5	7.5	12.4	5.4	21.6	15.8	2.0	1.8	6.5	11.5	–	–

[†], logistic EuroSCORE. TAVR, transcatheter aortic valve replacement; SD, standard deviation; STS, Society of Thoracic Surgeons; TVT, transcatheter valve therapy.

a longer duration than men and less frequently referred/undergo AVR, despite being more symptomatic (23). A study assessing the temporal trend of AS therapies [2015–2021] showed a 2.7-fold increase in the frequency of TAVR among younger patients (<65 years of age) (66). This increased adoption of TAVR among individuals below 65 years was influenced by several factors, including a history of vascular disease, prior percutaneous coronary intervention, stroke or myocardial infarction, female sex, and comorbidities, such as chronic obstructive pulmonary disease (COPD) and renal impairment (66). RHEIA (Randomized researcH in womEn all comers wIth Aortic stenosis) is a prospective, multicentre trial initiative that helps to specifically comprehend the safety and efficiency of TAVR *vs.* SAVR in women with severe AS, offering crucial randomized evidence for treatment decisions in female patients (67).

However, assessment of the quality of care for AS patients should not be limited to procedural and post-procedural outcome measurements. Since this approach does not measure the care gaps in patients not adequately diagnosed or timely referred to treatment, it becomes especially critical as healthcare observations shed light on potential disparities based on sex in AVR procedures. A systematic pathway akin to the pilot initiative of Lindman *et al.* can be established with a sole focus on continuously enhancing the quality of care for AS patients (68). This initiative should define specific metrics and guidelines (stratified by age, sex, severity of AS) to guide the entire care pathway, starting from the point of diagnosis and leading to timely treatment (SAVR or TAVR), ultimately aiming at improved long-term patient outcomes (68).

Improvement of AS management in women

To improve the AS treatment in women, a sex-specific therapeutic approach has to be established focusing on the haemodynamic differences in women to decide the best time point for intervention to produce maximal benefit. During diagnosis, using a sex-specific threshold or cut-off for various echocardiographic parameters (for example AVA index ≤0.6 cm^2/m^2 and SV <32 mL/m^2 for women) and AVC [1,200 arbitrary units (AU) by MDCT in women] helps in accurate grading and severity assessment in women. Moreover, due to the fibrotic prominence, the assessment of non-calcific leaflet thickening by contrast-enhanced CT can be proposed as a surrogate measure of valve fibrosis and combined fibrocalcific changes. This method correlates better with peak aortic velocity than the calcium score alone (69). The prospects of this modality should be further explored in the broader population. In addition, the paradoxical low-flow, low-gradient pattern exhibited in female patients should be given greater recognition in clinical practice to ensure that women have access to optimal therapeutic options even when presenting with a preserved LVEF (70). To address the under-diagnosis or treatment delay in women, a comprehensive assessment by a specialized heart team should be performed to ensure appropriate individualized decisions for selecting optimal therapy between SAVR and TAVR and urgency of intervention depending on the severity and overall risk profile. In addition, incorporating sex as a triaging criterion for intervention will improve outcomes in women as they tend to be presented later or at an advanced stage of their disease trajectory.

Strengths

This is a comprehensive review of the sex-related differences between men and women with severe AS encompassing major aspects from pathophysiological features, disease diagnosis and treatment outcomes that can guide the clinician in developing a tailored treatment approach based on better clinical care.

Limitation

This study did not focus on the genetic factors responsible for the sex-related pathophysiological differences and identified a knowledge gap. Also, it did not focus on disease prevention early phase strategies, the effectiveness of pharmacological treatment options and quality-of-life after AV intervention between sexes.

Conclusions

Enhancing our comprehension of sex-related disparities in AS can improve risk stratification strategies, optimize AVR timings, and devise tailored prevention and sex-specific treatment protocols. Delving into the elucidated sex-related differentiators summarised in *Table 2* promises an improvement in treatment among females, ultimately facilitating the development of personalized medicine approaches. However, more research should be encouraged to explore the impact of biological sex-related factors on AS prognosis in women and quality of care.

Table 2 Summary of sex-related disparities in AS and treatment outcomes

Characteristics/ treatment outcomes	Women	Men
Valvular pathophysiology	• Low AVC	• High AVC
	• Valvular fibrosis and dense connective tissue in AS	• Valvular calcific prominence in AS
Ventricular pathophysiology	• Concentric LV remodelling and small end-diastolic volume	• Eccentric, hypertrophic LV remodelling
	• Increased ECV	• Decreased ECV
Anatomical features	• Smaller aortic annuli/roots and LV cavity	• Larger aortic annuli/roots and LV cavity
	• More concomitant valve disease	• Less concomitant valve disease
	• Low systemic arterial compliance	• High systemic arterial compliance
	• Low LV mass	• High LV mass
	• More paradoxical low flow or low gradient AS	• Less low flow or low gradient AS
Clinical presentation	• Older	• Younger
	• Lower BMI	• Normal or higher BMI
	• Higher prevalence of hypertension	• Higher prevalence of CAD or PAD
	• More advanced LV diastolic dysfunction	• Less LV diastolic dysfunction
	• Advanced NYHA symptoms (class III/IV)	• Less advanced NYHA symptoms
	• Higher surgical risk (EuroSCORE & STS score)	• Less surgical risk profile
	• Severe shortness of breath, dizziness and syncope	• Fewer symptoms of shortness of breath, dizziness and syncope, but exhibit severe angina
	• Low GFR levels/renal impairment	• Normal GFR levels
	• Higher incidence of anaemia	• Less incidence of anaemia
	• Frailer	• Less frail
Diagnosis	• Low referral to a specialist	• Frequently referred to cardiologist
	• Low rate of echocardiography and other tests	• High rate of echocardiography and other tests
	• Often underdiagnosed or late diagnosis	• Early diagnosis
	• Delayed AV intervention	• Timely AV intervention
Outcomes of TAVR	• Lower in-hospital and 30-day mortality	• Increased in-hospital and 30-day mortality
	• Increased risk of vascular complications, bleeding, blood transfusion	• Decreased risk of vascular complications, bleeding, blood transfusion
	• Increased risk of stroke	• Decreased risk of stroke
	• Less paravalvular regurgitation	• High paravalvular regurgitation
	• Less chance of prosthesis under sizing	• Increased chance of prosthesis under sizing
	• Decreased 1- or 2-year mortality	• Increased 1- or 2-year mortality
	• Higher long-term survival benefit	• Less long-term survival benefit
Outcomes of SAVR	• Increased in-hospital and 30-day mortality	• Decreased in-hospital and 30-day mortality
	• Increased risk of vascular complications, bleeding, blood transfusion	• Increased risk of vascular complications, bleeding, blood transfusion
	• Increased risk of stroke	• Decreased risk of stroke
	• Increased risk of renal or HF	• Decreased risk of renal or HF
	• Increased prosthesis-patient mismatch	• Decreased prosthesis-patient mismatch

AS, aortic stenosis; AVC, aortic valve calcification; LV, left ventricle; ECV, extracellular volume; BMI, body mass index; CAD, coronary artery disease; PAD, peripheral artery disease; NYHA, New York Heart Association; STS, Society of Thoracic Surgeons; GFR, glomerular filtration rate; AV, aortic valve; TAVR, transcatheter aortic valve replacement; SAVR, surgical aortic valve replacement; HF, heart failure.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-406/coif). C.A. reports that she received speaker honoraria and has received travel support from Edwards Lifesciences, Medtronic and Boston. S.B. received speaker honoraria from Abbott Vascular, Boston Scientific, Edwards Lifesciences, and Medtronic. IPPMed, Cloppenburg, Germany, represented by P.B., has received honoraria (or research funding) for consultancy and medical writing from Edwards Lifesciences. V.D. received honoraria for lectures, presentations, and speakers from Abbott Vascular, Edwards Lifesciences, GE Healthcare, JenaValve, Medtronic, and Novartis Products & Features. Also, she received research grants from Philips and consultation fees from Edwards Lifesciences, Novo Nordisk, and MSD. H.E. received honoraria for lectures from Edwards Lifesciences. C.G. was supported by research grants from the Novartis Foundation, Switzerland; GE Healthcare, US; Gerresheimer AG, Switzerland; Bayer Pharmaceuticals, Switzerland; AMGEN, Switzerland; and Advisis AG, Switzerland, outside of the submitted work; has received travel support from Siemens Healthineers, Germany, and Biotronik, Switzerland; and has received speaker's fees from Sanofi Genzyme, France. C.H. received institutional grant/research support from Abbott, Boston Scientific, Edwards Lifesciences, Medtronic, and Meril; received consultant fees and honoraria from Edwards Lifesciences, Boston Scientific, and Meril. J.K. is an employee of Edwards Lifesciences and owns stocks from that company. P.M. is a scientist working for Edwards Lifesciences. T.K.R. received research support for medical writing from IPPMed, Germany. W.W. received honoraria for lectures, presentations, speakers and travel support from Abbott Vascular, Medtronic, and Edward lifesciences; received research consultancy fees and received payment for participation in data safety monitoring board or advisory board from Medtronic. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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