

AORTIC STENOSIS

Epidemiology

Calcific aortic valve disease (CAVD) is the most common valvular heart disease in high-income countries, encompassing a disease spectrum ranging from aortic valve (AV) sclerosis (i.e. fibro-calcific leaflet remodelling without significant impairment in leaflet motion and aortic orifice narrowing) to severe left ventricular (LV) outflow obstruction by calcific AV stenosis (AS).¹ It affects about 5% of the population at age 65 years with increasing prevalence as age advances.² Aortic stenosis (AS) is one of the most prevalent forms of cardiovascular disease in the Western world after hypertension, coronary artery disease and mitral regurgitation. The estimated prevalence of severe AS is 0.4%, and in patients ≥ 75 years old is 2.8%.^{3, 4} It is the most common form of valvular heart disease needing surgery in Europe.³ In the US, approximately 652,000 patients were subjected to aortic valve surgical replacement in 2010, mainly for AS. Aortic sclerosis, defined as irregular valve thickening without obstruction to LV outflow, is present in about 25% of adults over 65 years of age, and is associated with clinical factors such as age, sex, hypertension, smoking, serum low-density lipoprotein and lipoprotein(a) levels, and diabetes mellitus.⁵ Approximately 1.8% of individuals with aortic sclerosis progress to AS annually.⁶ The burden of disease attributable to calcific aortic valve disease is increasing. In 2017, there were an estimated 12.6 million cases of calcific aortic valve disease, and an estimated 102,700 calcific aortic valve disease deaths, with higher rates among men.⁷

Aetiology

The most common cause of AS in adults is calcification of a normal trileaflet or congenital bicuspid valve. The disease process characterized by lipid accumulation, inflammation, and calcification, with many similarities to atherosclerosis, although the pathophysiological processes in calcific AS are locally determined and regulated.⁵ Lipoprotein(a) and familial hypercholesterolemia, and high LDL and triglycerides have been associated with calcific aortic valve disease.⁸⁻¹¹ Metabolic syndrome is an independent predictor of AS progression, especially in younger patients,¹² and obesity is associated with an increased risk of AS.¹³ Rheumatic AS due to fusion of the commissures with scarring and eventual calcification of the cusps is less common in developed countries, and is invariably accompanied by MV disease. Progression of aortic valve stenosis is associated with bone remodelling and secondary hyperparathyroidism in elderly patients.¹⁴ In the young, AS is due to congenital malformations such as bicuspid aortic valve, the presence of which significantly increases the risk of AS, or discrete subvalvular obstruction or supra-valvular stenosis. Long-term exposure

to elevated BP is associated with increased risk of AS and AR.¹⁵ Chronic kidney disease, even in moderate to severe stages, is associated with an increased risk of AS.¹⁶ Calcific valvular disease is known to cluster within families, and single nucleotide polymorphisms in the lipoprotein(a) locus have been associated with aortic valve calcification.^{17,18} It is estimated that $\leq 15\%$ of the AS population and $\leq 30\%$ of the subset with low-flow, low-gradient pattern may have transthyretin cardiac amyloidosis.^{19,20}

Pathophysiology and Natural History

Inflammation, fibrosis and calcification contribute to the development of AS.²¹ The trilayered structure of the AV matrix may be disrupted because of an imbalance in the expression of matrix metalloproteinases and their inhibitors, and eventually, the expression of bone-related proteins increases and results in osteoblastic differentiation of the valve interstitial cells.^{5,22} The calcific disease progresses gradually over many years from the base of the cusps to the leaflets with formation of hydroxyapatite nodules, cartilage and bone tissue, eventually causing a reduction in leaflet motion and effective valve area without commissural fusion. The LV adapts to the obstruction by increasing wall thickness while maintaining normal chamber size. The consequent concentric hypertrophy is a compensatory mechanism to normalize the LV wall stress. As a result of increased wall thickness and diminished compliance of the chamber, LV end-diastolic pressure increases without chamber dilatation. LV systolic function is usually preserved, and cardiac output is maintained for many years. If LV systolic dysfunction is present, it usually improves after aortic valve replacement (AVR). Irreversible LV dysfunction is possible but may not be easily diagnosed by preoperative imaging. Decreased levels of Von Willebrand factor develop with high shear stress associated with severe disease and predispose to epistaxis and ecchymosis, cerebral microbleeds, and gastrointestinal bleeding in the presence of latent intestinal angiodysplasia (**Heyde syndrome**).²³ Total creatine kinase (CK) activity is reduced in severe aortic stenosis with preserved systolic function and is lowest in AS with systolic failure.²⁴

The narrowed AV orifice and restricted leaflet opening create and acceleration of blood through the valve, from a low velocity ($V < 1$ m/s) in the LVOT to the maximum velocity at the vena contracta (VC) of the jet (Figure 1). The area formed by the free edges of the AV leaflets is known as the geometric orifice area (GOA) of the valve, whereas the area of the flow jet at the VC is known as the effective orifice area (EOA). GOA is greater than EOA, or equal when GOA and LVOT area are equal, and it is measured at peak systole with planimetric methods at echocardiography or CT scanning. EOA is probably the most important parameter because it represents the work-load imposed on the LV, but some uncertainty still exists.²⁵ ΔP_{rec} is the pressure difference as measured between LVOT and

ascending aorta during cardiac catheterization, especially when it is done with pullback of one catheter), and is usually less than the $\Delta P_{\max}$ measured between LVOT and EOA at the vena contracta measured by Doppler echocardiography. This is because the blood flow contracts to pass through the stenotic orifice, and a portion of the potential energy of the blood (ie pressure) is converted into kinetic energy (ie velocity). Downstream of the vena contracta, a part of the kinetic energy is irreversibly dissipated as heat because of flow turbulences. The remaining portion of the kinetic energy is recovered back to potential energy and represents the so-called “pressure recovery” (Figure 2).²⁵ Thus, Doppler derived gradients may be theoretically more accurate in the absence of conditions that violate the assumptions of the modified Bernoulli (continuity) equation, such as aortic regurgitation or anemia/fever/thyreotoxocosis where flow velocity in LVOT is $>1\text{m/s}$. They are subject to error, however, because echocardiography may underestimate the LV outflow tract diameter, an integral component of the continuity equation, that is not circular but oval. The combination of CT with Doppler assessment has been proposed, but clinical experience is limited.²⁶

Severe aortic stenosis is defined as an effective orifice area $\leq 1\text{cm}^2$ ($0.6\text{ cm}^2/\text{m}^2$ BSA) in the context of a mean transvalvular gradient $\geq 40\text{ mm Hg}$ (Tables 1 and 2, and Figure 3). It should be noted that the value of 40 mm Hg may represent an inconsistency, since in the context of normal cardiac output, an EOA of 1 cm^2 corresponds to a gradient of $30\text{--}35\text{ mm Hg}$.²⁵ However, gradients are a squared function of flow as expressed by the stroke volume, and even a modest decrease in flow may lead to an important reduction in gradient even in the presence of severe stenosis. A mean pressure gradient $\geq 40\text{ mm Hg}$ conveys a poor prognosis, even in the presence of a valve area 1cm^2 (discordant high-gradient AS) and regardless of the severity of concomitant AR.²⁷ Thus, there has been a tendency to characterise severe aortic stenosis in terms of gradient and flow, as assessed by the stroke volume index (SVi), and which is of prognostic significance as a marker of reduced cardiac pump function.²⁸

Low gradient aortic stenosis is seen in up to 50% of patients with AS who have a small aortic valve area (AVA $<1.0\text{ cm}^2$) consistent with severe AS but a low mean transvalvular gradient ($<40\text{ mmHg}$) consistent with non-severe AS.^{29,30} Three subtypes have been described. **Classical low flow-low gradient AS** is defined as an AVA $<1.0\text{ cm}^2$, a mean gradient $<40\text{ mmHg}$, and an LVEF $<50\%$. In these patients (5-10% of the AS population), the low-flow state is predominantly due to depressed LV systolic dysfunction, which may be related to the presence of severe AS and ensuing LV afterload mismatch and/or to the presence of concomitant cardiomyopathy, most frequently from ischaemic origin. This entity is associated with worse outcomes compared with patients with high-gradient AS and/or preserved LVEF. Approximately 20-30% of these patients have **pseudosevere AS** due to

intrinsic cardiomyopathy unrelated to the valve disease. Pseudosevere AS is diagnosed by dobutamine infusion that increases the valve area without significantly affecting the gradient (see Diagnosis). **Paradoxical low flow-low gradient AS** is defined as an AVA $<1.0 \text{ cm}^2$, indexed AVA $<0.6 \text{ cm}^2/\text{m}^2$, mean gradient $<40 \text{ mmHg}$, LVEF $\geq 50\%$, presence of low flow (stroke volume index $<35 \text{ mL}/\text{m}^2$), and mean transvalvular flow rate is $<200 \text{ mL/s}$. In particular, stroke volume index $<30 \text{ mL}/\text{min}^2$, and stroke volume $<55 \text{ mL}$, identify a subgroup at high risk of death under medical and surgical management.³¹ In patients with paradoxical AS (25-30% of patients with AS and usually of older age, female sex, and systemic hypertension), the reduced stroke volume is generally related to pronounced LV concentric remodelling with small LV cavity, impaired LV diastolic filling, and reduced LV systolic longitudinal function. Conditions such as atrial fibrillation, mitral and tricuspid valve disease, and RV dysfunction may also lead to a decrease in LV stroke volume and transvalvular flow rate. **Normal flow- low gradient AS** is defined as an AVA $<1.0 \text{ cm}^2$, indexed AVA $<0.6 \text{ cm}^2/\text{m}^2$, mean gradient $<40 \text{ mmHg}$, LVEF $\geq 50\%$, but normal flow, i.e. stroke volume index $>35 \text{ mL}/\text{m}^2$. This entity is relatively frequent (15–40%). The discrepancy between LVEF and stroke volume has been confirmed by invasive haemodynamics,³² and is attributed to high global afterload due to reduced aortic compliance and restricted physiology with pronounced concentric remodeling and myocardial fibrosis that are mainly reflected in impaired longitudinal function.^{33,34}

Discordant high-gradient AS is the combination of a mean pressure gradient $\geq 40 \text{ mm Hg}$ and an AVA $>1 \text{ cm}^2$. AVA has prognostic value in patients with low-gradient aortic stenosis, but a high systolic pressure gradient ($>40 \text{ mm Hg}$) is associated with reduced survival, irrespective of AVA or the severity of concomitant aortic regurgitation.³⁵

Aortic sclerosis is characterized by focal areas of valve thickening, typically located in the leaflet center with commissural sparing and normal leaflet mobility. Jet velocity in aortic sclerosis is $< 2.5 \text{ m/s}$. Diffuse leaflet thickening is not seen in aortic sclerosis, being suggestive of normal aging changes, significant AS, or imaging artifact. In significant AS, the aortic valve is usually thickened and calcified, with limited excursion and a reduced aortic valve area. Its prevalence increase with age (up to 40% in patients >80 years), there is a low (1.9% per year) rate of progression to clinical AS, but an independent increase of coronary events, stroke and mortality in these patients.³⁶

Hemodynamic progression of AS eventually leading to symptom onset occurs in nearly all asymptomatic patients with AS once the aortic velocity reaches $\geq 2 \text{ m/s}$. Although the average rate of hemodynamic progression for calcific stenosis of a trileaflet valve is an increase in aortic velocity of about 0.3 m/s per year, an increase in mean gradient of 7 to 8 mmHg per year, and a decrease in valve area of 0.15 cm^2 per year, there is marked variability between patients in disease progression.³⁷ Predictors of rapid disease progression include

older age, more severe valve calcification, and a faster rate of hemodynamic progression on serial studies. An annual increase in jet velocity >0.32 m/s indicates rapid hemodynamic progression.³⁸ Most patients with AV velocity of 4 m/s become symptomatic within the next 5 years and carry a 1% risk of sudden death per year.³⁹ Asymptomatic patients with very severe aortic stenosis (jet velocity >5 m/s) have a poor prognosis with a high event rate (mortality up to 50% at 1 year and $>90\%$ at 5 years) and a risk of rapid functional deterioration.⁴⁰ Patients with moderate/severe mixed aortic valve disease have event rates comparable to patients with isolated severe aortic stenosis.⁴¹ Native aortic valve thrombosis is rare. The most common presentation is myocardial infarction in 36%, and the most common underlying aetiology is hypercoagulable state in 30%.⁴²

Mitral stenosis severity should be carefully assessed in the setting of severe aortic stenosis, since it can be overestimated. Mitral valve area ≤ 1.5 cm², mitral annulus diameter ≤ 1 mm or extension of calcification to both anterior and posterior mitral leaflets suggest the presence of true MS.⁴³

Presentation

Almost half of patients with severe AS may be asymptomatic.⁴⁴ Usually with progression of stenosis severity SOB or heart failure (50%), angina (35%), and syncope (15%) appear. Once symptoms develop, AVR is needed because the average survival is only 2 to 3 years with an increased risk of sudden death. A clinical classification has been proposed.⁴⁵

Physical Examination

Slow arterial pulse (pulsus parvus et tardus) in severe AS. May not be present with AR, in hypertension or in the elderly due to rigid vasculature.

Prominent **a waves** in JVP in severe AS (reduced RV compliance due to hypertrophy of the interventricular septum. The v wave may be prominent if there is RV failure.

Soft S₁ and **single S₂** (late or absent A₂)

S₄ (vigorous atrial contraction) indicates severe AS.

A **thrill** may be present.

Hyperdynamic LV suggest concomitant MR or AR

Crescendo-decrescendo systolic murmur along the left sternal border that radiates to the upper right sternal border and the carotids. It may also radiate to the LV apex (the Gallavardin phenomenon) and may be mistaken for MR. The intensity of the murmur does not correspond to the severity of AS.

Diastolic murmur if AR is also present

Systolic ejection click in young patients with bicuspid valve.

Investigations

ECG. LV hypertrophy. The additional presence of ECG strain (≥ 1 -mm concave down-sloping ST-segment depression with asymmetrical T-wave inversion in the lateral leads), indicates myocardial fibrosis and adverse clinical outcome.⁴⁶ Left-atrial enlargement in severe AS and AF in less than 15% of patients. Various degrees of AV and intraventricular block may be seen, as well as arrhythmias, especially in the elderly (up to 20%), mainly AF, NSVT and AV block.⁴⁷

Chest radiography. Usually normal. Cardiomegaly is a late feature in AS and calcification is a universal finding but rarely visible on chest X-ray. The proximal ascending aorta may be dilated, particularly in patients with bicuspid valves.

Echocardiography is the standard imaging procedure. Two-dimensional echocardiography puts the diagnosis and may identify a bicuspid valve. Doming of the aortic leaflets due to asymmetry and restriction is often seen in young patients with bicuspid aortic valves. Planimetric systolic geometric orifice areas can also be obtained, but they may not accurately represent AS severity.²⁵ Doppler echocardiography allows quantification of jet velocity, pressure gradient derived as $4 \times (\text{jet velocity})^2$, and valve area (Table 3). In patients with mixed AS and AR, peak aortic jet velocity reflects both stenosis and regurgitation and represents a useful predictive parameter.⁴⁸ Doppler-derived gradients tend to be higher and effective orifice area lower compared to those derived by cardiac catheterization due to the pressure recovery effect (Figures 1 and 2). This can be accounted for by calculating the Energy Loss Index (ELI). ($\text{ELI} = [\text{EOA} \times A_A / A_A - \text{EOA}] / \text{BSA}$, where EOA=effective orifice area by conventional echocardiography, A_A = the cross sectional area of the aorta measured at 1cm downstream of the sinotunular junction, and BSA the body surface area). In asymptomatic patients with inconsistent grading of stenosis obtained by catheterization, it provides additional prognostic information independently of aortic gradient.⁴⁹ Flow rate (ratio of stroke volume to ejection time-ml/) is also important since a valve area measured with a flow rate < 210 ml/s does not reliably identify severe AS.⁵⁰

Low-dose dobutamine hemodynamic measurements or exercise echocardiography is useful in cases of ***low-flow/low- gradient severe AS with reduced LVEF*** in order to differentiate patients with anatomically severe AS from those with pseudo-severe AS. Dobutamine (5-20 mcg/kg/min) in AS with LV dysfunction and gradient < 40 mm Hg produces an increment in stroke volume ($> 20\%$) and valve area ($> 1 \text{ cm}^2$ and/or an increase $\geq 0.3 \text{ cm}^2$) but no change in gradient in hemodynamically non-significant stenosis (pseudosevere AS). In significant AS, the valve area remains unchanged (or increases $< 0.2 \text{ cm}^2$ but remains $< 1 \text{ cm}^2$) whereas the gradient and stroke volume increase. In ambiguous response, calculation of the projected orifice area (AVA_{proj}) that would have occurred at a

standardized flow rate of 250 ml/s may be more useful than the combination of $MG \geq 40$ mm Hg and $AVA \leq 1.0$ cm² (TOPAS trial).⁵¹ An $AVA_{proj} \leq 1$ cm² has been found to more accurately identify patients with truly severe AS and predict mortality under medical management in these patients.⁵²

In ***paradoxical low-flow, low-gradient severe AS with preserved LVEF***, detailed echocardiographic examination to avoid miscalculation of the stroke volume, evaluation of the systemic arterial compliance and valvulo-arterial impedance (Z_{VA}), and interpretation of findings in the context of peripheral blood pressure are recommended.⁵³ It has been proposed that for the measure of Doppler stroke volume, the LV outflow tract diameter should be measured preferably at the insertion of the aortic valve cusps rather than at 5-10 mm below the aortic annulus as proposed by the European Society of Echocardiography/American Society of Echocardiography.⁵⁴ Impaired longitudinal function, ie lower basal longitudinal strain and tissue velocities and mitral plane excursion, as assessed by speckle-tracking echocardiography are markers of worse prognosis.⁵⁵ The aortic valve calcification load, as assessed by multidetector computed tomography may also be of value in this case.

A high value of **plasma BNP** (>550 pg/ml) is powerful predictor of mortality in patients with low-flow/low-low gradient AS regardless of medical or surgical treatment or the presence and/or absence of flow reserve.⁵⁶

Treadmill exercise testing is useful for risk stratification of asymptomatic patients with severe AS (Table 4).^{37,44} Development of symptoms or a hypotensive response are predictors of sudden death and indicate the need of valve replacement. Truly severe AS shows only small changes in valve area (increase <0.2 cm² and remaining <1 cm²) with increasing flow rate, but a significant increase in gradients (mean gradient >40 mmHg), whereas pseudo-severe AS shows a marked increase in valve area but only minor changes in gradients. In addition, this test may detect the presence of contractile or flow reserve (increase >20% of stroke volume), which has favorable prognostic implications. Exercise testing is avoided in symptomatic patients with severe AS (Stage D1, aortic velocity ≥ 4.0 m/s or mean pressure gradient ≥ 40 mm Hg, ACC/AHA 2020 GL on HVD, III-B-NR) due to the risk of severe haemodynamic compromise.

Multidetector computed tomography is useful for the assessment of aortic root dilatation and assessment of calcification. Severe calcification detected by multi-slice tomography is useful in establishing the diagnosis of paradoxical low-flow, low-gradient AS. Aortic valve calcification $\geq 1,274$ AU in women and 2,065 AU in men or with AVC density (indexed to annulus cross-sectional area) ≥ 292 AU/cm² in women and 476 AU/cm² in men.⁵⁷ CT is also useful for valve sizing and prediction of paravalvular leakage with TAVR procedures.

Cardiac magnetic resonance allows anatomic measurement of the valve area and estimation of jet velocity and stroke volume (especially in paradoxical low flow, low gradient AS). It has

lower spatial resolution than CT.²⁵ In severe aortic stenosis, late gadolinium enhancement appears to be a useful biomarker of left ventricular remodeling, with myocardial scar present in over 50% of patients, that denotes worse long-term outcomes following aortic valve intervention.⁵⁸

Cardiac catheterization may be necessary for assessment of the gradient in the case of inconclusive noninvasive tests results. Simultaneous pressure measurements across the valve (and not pull back) are necessary. Dobutamine can also be used to identify low-flow/low-gradient AS during cardiac catheterization.

Coronary angiography is necessary before surgery in patients with risk factors or clinical suspicion of coronary artery disease (see General Principles), and occasionally before a Ross procedure to identify the origins of the coronaries.

Therapy

Medical therapy

Medical therapy consists of exercise restriction and cautious use of diuretics and ACE/ARB, for symptomatic relief (Table 5). Vasodilators can cause an increase in cardiac output that helps offset the drop in systemic vascular resistance even in severe AS.⁵⁹ Systemic hypertension in low-gradient severe aortic stenosis with preserved ejection fraction is associated with elevated LV filling pressures and pulmonary hypertension, and vasodilator therapy in this setting appears to be beneficial.⁶⁰ In patients without coronary disease or diabetes, optimal blood pressure is systolic 130-139 mm Hg and diastolic 70-90 mm Hg.⁶¹ There are no studies addressing specific antihypertensive medications in patients with AS, but diuretics may reduce stroke volume, particularly if the LV chamber is small at baseline. In theory, ACE inhibitors may be advantageous because of the potential beneficial effects on LV fibrosis, in addition to control of hypertension.³⁷

So far, no medical therapy has been convincingly shown to reduce AS progression.⁶² Statins are not recommended in the absence of CAD.⁶³ Antihypertensive drugs, and drugs targeting phosphate and calcium metabolism have also failed to demonstrate significant benefits in subclinical AS,²¹ and antiresorptive agents such as denosumab and alendronate, inhibit bone resorption but no effect was seen on progression of aortic valve calcification or function even after 2 years.⁶⁴ Medical therapy of co-existing amyloidosis improves prognosis following aortic valve replacement.⁶⁵ Multiple other potential targets for treatment are considered.^{1,66}

Surgical Therapy

(Surgical aortic valve replacement-SAVR)

Indications for AVR are presented in Tables 6 and 7 and Figures 4-6. AVR is indicated in **symptomatic patients with severe AS** even in the presence of LVEF<35% unless if this is due to previous myocardial infarctions.^{37,67} Symptom onset within 2 to 5 years is likely when aortic velocity is ≥ 4.0 m/s or mean pressure gradient is ≥ 40 mmHg. The additive risk of AVR at the time of other cardiac surgery is less than the risk of reoperation within 5 years.³⁷ AVR with or without CABG may also offer a survival benefit in patients with moderate AS (mean AoV gradient ≥ 25 and < 40 mmHg) and severe AS in the context of a reduced LVEF ($< 50\%$).^{68 69} AVR should also be considered in patients with coexistent AS undergoing CABG. However, in the current era of rapid developments in transcatheter valve implantation technologies, a decision regarding replacement of the aortic valve for moderate stenosis/regurgitation should be carefully considered on a case-by-case basis in discussion with the HeartTeam.⁷⁰

In the 2016 report of the US STS/ACC Registry on surgical replacement with various types of valves, 30-day mortality was 4.6% (in-hospital mortality 2.9%), 1-year mortality 21.6%, stroke rate 1.9%, and permanent pacing need 12%.⁷¹ The 30-day mortality is up to 6% for AVR plus CABG.⁴⁰ Mortality for isolated AVR octogenarians it is now $< 6\%$,⁴⁰ and long-term survival after surgical aortic valve replacement in the elderly is excellent, although patients with a high (≥ 10) STS perioperative risk of mortality and those with certain comorbidities (lung disease and renal failure, particularly dialysis-dependent renal failure) carry a particularly poor long-term prognosis.⁷² Survival is substantial (16.2 years), in younger (< 64 years), low risk patients.⁷³ Post-surgical AV block requiring permanent pacing 6-13 days following AVR varies from 3.0% to 11.8%,⁷⁴ with an average 1-year permanent pacemaker implantation rate 6.6% after AVR, 9.3% after AVR plus MV repair, and 13.3% after AVR plus MV replacement.⁷⁵ New-onset left bundle-branch block after surgical aortic valve replacement is associated with an increased all-cause mortality during follow-up.⁷⁶ Despite the younger age and lower prevalence of cardiovascular risk factors, bicuspid aortic valve aortic stenosis patients have a markedly elevated risk of permanent pacemaker implantation and new-onset left bundle-branch block compared with tricuspid aortic valve aortic stenosis patients, in particular bicuspid aortic valve aortic stenosis patients with fusion of the right- and non-coronary cusps.⁷⁶

Hemodynamic deterioration of bioprosthetic aortic valves, defined as the indexed effective orifice area < 0.85 cm²/m², is often echocardiographically evident approximately 7 years post-operatively. Leaflet calcification identified by multidetector computed tomography is an early and sensitive marker of structural deterioration of bioprosthetic heart valves.⁷⁷

Most patients undergoing catheter ablation for **VT after AVR** have VT from substrate unrelated to AVR. However, periaortic scar is universally present and bundle branch re-entry can be the VT mechanism. This condition is usually curable with catheter ablation.⁷⁸ Electrophysiology studies are recommended in these patients (ESC 2022 GL on VA and SCD, I C).⁷⁹

In truly **asymptomatic patients with severe AS**, exercise testing is useful to identify whether patients are truly asymptomatic.⁶⁹ Although these patients might be managed conservatively with close monitoring to detect new onset of symptoms, increasing AS severity, or deterioration in LV function,⁶⁹ AVR is preferable. Observational, non-randomized studies in these patients have reported 3-year mortality rates of approximately 3-10% with AVR compared with 30-54% without surgery.⁸⁰⁻⁸² In the RECOVERY randomized trial on patients with severe AS (aortic-valve area of ≤ 0.75 cm² with either an aortic jet velocity of ≥ 4.5 m per second or a mean transaortic gradient of ≥ 50 mm Hg), the incidence of the composite of operative mortality or death from cardiovascular causes during the follow-up period was significantly lower among those who underwent early AVR, but, of note, there was no operational mortality. These benefits persisted over 8 years, and the number needed to treat to prevent one death from cardiovascular causes within 4 years was 20 patients.⁸³ In the AVATAR randomized trial in asymptomatic patients with severe AS (valve area ≤ 1 cm² with aortic jet velocity >4 m/s or a mean transaortic gradient ≥ 40 mm Hg), and with normal left ventricular function, early surgery reduced a primary composite of all-cause death, acute myocardial infarction, stroke, or unplanned hospitalization for heart failure compared with conservative treatment.⁸⁴ The same outcome was observed at 5 years follow-up.⁸⁵ Acquired Von Willebrand deficiency and gastrointestinal bleeding may also resolve following valve replacement.²³ In a meta-analysis of 4 RCTs, early AVR was associated with a significant reduction in unplanned cardiovascular or HF hospitalization and stroke and no differences in all-cause and cardiovascular mortality compared with clinical surveillance.⁸⁶

In the subsequent EVOLVED RCT, in asymptomatic patients with severe aortic stenosis and myocardial fibrosis, early aortic valve intervention (SAVR or TAVR) had no demonstrable effect on all-cause death or unplanned aortic stenosis-related hospitalization. However, the study was underpowered to allow definitive conclusions.⁸⁷ The EARLY TAVR RCT, considered transaortic valve replacement in patients with asymptomatic severe aortic stenosis. Early TAVR was superior to clinical surveillance in reducing the incidence of death, stroke, or unplanned hospitalization for cardiovascular causes.⁸⁸ In another recent RCT among asymptomatic patients with very severe aortic stenosis, early surgery led to a lower risk of a composite of operative mortality or death from cardiovascular causes than conservative care at 10 years.⁸⁹

Patients with **low-flow/low-gradient severe AS and LVEF $\leq 40\%$** have poor

prognosis, with medical therapy (survival rates <50% at 3-year follow-up).²⁸ Operative risk is 22-33% in those with no flow reserve (increase in stroke volume <20% with dobutamine-pseudosevere AS), but 5-8% in the presence of preserved contractile/flow reserve.²⁸

Patients with **pseudo-severe AS** have a 5-year survival better than patients with true severe AS under medical therapy, and similar to patients with systolic heart failure and no evidence of valve disease.⁹⁰

The prognosis of patients with **paradoxical low-flow, low-gradient severe AS and LVEF>50%** is controversial. It has been reported to be worse than those with high-gradient severe AS or those with moderate AS,^{91,92} but in other studies outcome was similar with that of patients with moderate stenosis, and did not improve with surgery.^{54 93-95} Patients with paradoxical low-flow/low-gradient severe AS can be managed medically with special attention to treating concomitant hypertension,⁶⁰ and with serial (6-12 months) clinical and echocardiographic evaluations. The SVi is a predictor of perioperative mortality in all patients with low flow/low gradient AS.⁹⁶ A flow rate >210 ml/s confers adverse prognostic significance in the context of a valve area <1 cm².⁵⁰ In two meta-analyses, SAVR or TAVR were found to improve survival in patients with paradoxical low-flow, low-gradient, and in those with normal-flow, low-gradient severe AS in the context of a preserved LVEF.^{97,98}

Indications for intervention in patients with **mixed AS and AR** valve disease and for patients with **mixed AS and MR** valve disease are presented in Table 7. In moderate mixed aortic valve disease, the presence of symptoms or LVEF < 50% is associated with increased mortality, comparable to isolated severe AS under similar conditions, and these patients may benefit from AVR.⁹⁹

The choice of a **mechanical or bioprosthetic** valve is discussed in detail in Chapter 23. Indications for **concomitant CABG** are presented in Chapter 16. Indications for pacing (may be needed in up to 6% of patients) are provided in Table 8.

Interventional Therapy

(Transcatheter aortic valve replacement (TAVI or TAVR))

Percutaneous implantation of bioprosthetic valves is now the treatment of choice in selected inoperable (STS score>10 or logistic EuroSCORE>20%) or high-risk patients as judged by dedicated heart team of surgeons and cardiologists (Figures 7 and 8, Tables 9-11).¹⁰⁰⁻¹⁰⁴ TAVI (also called TAVR) has also been found noninferior to surgery by means of mortality and stroke rates in intermediate- or low-risk patients with up to 8 years follow-up.¹⁰⁵⁻¹¹¹ In a meta-analysis of 7 studies on 8020 patients, compared with SAVR, TAVI was associated with reduction in all-cause mortality and stroke up to 2 years irrespective of baseline surgical risk and type of valve implanted.¹¹² In the low surgical risk population, TAVI may be

preferable to SAVR especially in patients with preexisting right ventricular dysfunction or significant tricuspid regurgitation, or both.¹¹³⁻¹¹⁶ It is superior to clinical surveillance in patients with asymptomatic severe AS,⁸⁸ and a safe option for patients with porcelain aorta,¹¹⁷ and failed bioprosthetic valves,^{118,119} especially in nanogenarians.¹²⁰ The valve is usually implanted by a transfemoral retrograde approach; the alternatives are a subclavian or trans-aortic approach. The transapical approach carries a higher complication rate.^{121,122} Either cardiac CT or CMR may be used for guidance.¹²³ General anaesthesia is not necessary,^{124,125} and a minimalist approach (including local anesthesia only) versus standard of care (including conscious sedation) by means of complications and mortality, albeit at higher intraprocedural anxiety and stress levels (DOUBLE-CHOICE RCT).¹²⁶

Procedural complications of TAVI depend on patients status, accumulated experience, and valve model used. In-hospital reported mortality is 0.5-3%, and 30-day mortality 2-6%, which is similar (or perhaps even lower) to that reported for surgical AVR. Other complications are stroke (0.5-3%), renal failure (1-5%), AV block requiring pacing (8-20% depending on the type of valve), AR (2-18%), vascular complications (2.5-5%), bleeding (3-13%), and myocardial infarction (1%). Several TAVR risk models have appeared. Frailty of the patient, assisted living, lung and kidney disease, anemia, hypoalbuminemia, cognitive impairment, and age >85 years predict increased mortality after TAVI.¹²⁷⁻¹³⁰ Approximately one-third of patients undergoing TAVI do not improve their exercise capacity postprocedure.¹³¹ Hospital readmission is needed in 25% of patients and is associated with increased mortality.¹³² Standardized criteria and end-point definitions have been published (VARC-3).¹³³ Multiple studies and registries, such as the BENCHMARK, have described factors associated with a cost-effective and safe procedure.¹³⁴

Self-expanding or balloon-expandable valves are being used, and several models are now available. The Edwards SAPIEN valve system is a balloon-expandable trileaflet bovine pericardial valve mounted on a cobalt chromium stent frame. The CoreValve system is a trileaflet porcine pericardial valve mounted in a self-expanding nitinol stent. They are both FDA-approved now, while other devices are also under study.¹³⁵⁻¹⁴² No significant differences in mortality between the two types of valves have been described, and differences in other clinical outcomes appear to diminish with newer generation devices. In the CHOICE randomized trial (241 patients), cardiovascular mortality at 30 days was not significantly different: 4.1% in the balloon-expandable valve group and 4.3% in the self-expanding valve group ($P = 0.99$).¹⁴³ In two French registries, the use of self-expanding valves was associated with a higher risk of in-hospital and long-term mortality compared with use of balloon-expandable valves,^{144,145} but in the LYTEN RCT on patients with failed aortic bioprostheses clinical outcomes were similar.¹⁴⁶ In the CENTER-collaboration meta-analysis of 10 trials and registries, 30-day mortality rates were similar between balloon-expandable and self-

expanding valves (5.3% vs 6.2%, $P=0.1$).¹⁴⁷ In the SOLVE-TAVI randomised trial (447 patients) using the newer generation devices (Sapien 3 and Evolut R), mortality was not significantly different between balloon-expandable and self-expanding valves (2.3% vs 3.2%).¹⁴⁸

Female sex, chronic kidney disease, center experience, and new-onset atrial fibrillation are predictors of **stroke** following TAVI.^{149,150} The risk is 0.5-3%, depending on the patient risk status, but silent cerebral embolism is probably higher.¹⁵¹ Of note, stroke rates may be higher than previously thought following surgical AVR in patients ≥ 65 years. The DeNOVO study revealed a 4% incidence of moderate or severe stroke as opposed to 1.5-2.4 % provided by the STS database.¹⁵² In the SURTAVI randomised trial, the rates of early (30-day) stroke and post-procedural encephalopathy were higher after SAVR versus TAVR (5.4% vs. 3.3%; $p = 0.031$; and 7.8% vs. 1.6%; $p < 0.001$, respectively).¹⁵³ In the PARTNER 3 trial on low-risk patients, TAVI with a balloon-expandable valve was associated with a lower risk of stroke (0.6% vs 2.4%) and death or stroke (1% vs 3.3%) than surgery.¹⁰⁵ A trial on low-risk patients with a self-expanding valve also demonstrated lower stroke (0.5% vs 1.7%) or death 0.5% vs 1.3%) with TAVI.¹⁰⁶ Neuroprotection devices by means of a mesh filter used during TAVI are of no proven value.¹⁵⁴⁻¹⁵⁶ In the CHOICE trial a trend towards reduced stroke rate with the Corevalve compared to the SAPIEN was seen (2.6 vs 5.8%, $P=0.33$),¹⁴³ and in the CENTER-collaboration meta-analysis, the risk of stroke (1.3% vs 3.3%, $P<0.001$) was lower with balloon-expandable valves.¹⁴⁷ However, in the SOLVE-TAVI trial using the newer generation devices (Sapien 3 and Evolut R), stroke was significantly higher with the balloon-expandable valve (4.7% vs 0.5%, $P=0.01$).¹⁴⁸ Approximately 25% of patients has **cerebral microbleeds** before TAVI (See pathophysiology), and 25% develop new microbleeds after TAVI.¹⁵⁷

Moderate AR (grade ≥ 2) carries adverse prognostic significance.¹²⁶ The severity of the dimensionless AR index = $([\text{diastolic blood pressure} - \text{left ventricular end-diastolic pressure}]/\text{systolic blood pressure}) \times 100$ is of prognostic significance. Patients with AR index < 25 have a significantly increased 1-year mortality rate compared with patients with AR index ≥ 25 .¹⁵⁸ The loss of high-molecular-weight multimers of von Willebrand factor and a high value for a point-of-care hemostatic test (CT-ADP), are predictive of AR after TAVI and indicate higher mortality during the next year.¹⁵⁹ Residual AR is less frequent with balloon-expandable than self-expanding valves (4.1% vs 18.3%, $P < 0.001$ in the CHOICE , and 1.5% vs 3.4%, $P=0.0002$, in the SOLVE-TAVI).^{143,148}

Late valvuloplasty with balloon dilatation after TAVI is safe and may reduce paravalvular regurgitation as well as **transvalvular gradient** due to underexpansion or valve deterioration.¹⁶⁰

The incidence of **permanent pacing** used to range between 7 to 35% but is now lower with newer generation devices.^{148,161-163} Conduction disturbances, including LBBB and permanent pacemaker implantation post-TAVR, are associated with increased risk of death and heart failure hospitalization within the year following the procedure.^{164,165} Male sex, baseline conduction disturbances, mitral annular calcification, intraprocedural AV block larger profile device and deeper implantation within the LVOT (CoreValve), and prosthesis to LVOT diameter ratio (SAPIEN valve), are predictors of permanent pacing after TAVR. The presence of RBBB is a strong independent predictor for permanent pacing after TAVI (Table 11).¹⁶⁶ The prognostic significance of LBBB following TAVI is adverse, as also is a QRS duration >160 ms.¹⁶⁷⁻¹⁷⁰ ECG monitoring following TAVI should be considered for 1- 3 days after the procedure depending on the pre-existing or developed LBBB.^{171,172} Permanent pacing for 24 h is recommended in patients with post-procedural LBBB and further evaluation with telemetry or an electrophysiology study may be necessary.¹⁷² However, the development of LBBB without concomitant new AV block (PQ>200 ms) does not necessitate permanent pacing.¹⁷³ In patients with new or worsened conduction disturbance after TAVI (PR or QRS interval increase $\geq 10\%$), a 2020 ACC Expert Consensus recommends inpatient monitoring with telemetry for at least 2 days if the rhythm disturbance does not progress, and up to 7 days if ambulatory monitoring is not going to be employed. Ambulatory monitoring for 14 days should be provided to any patient with a PR or QRS interval that is new or extended by $\geq 10\%$.¹⁶⁶ Mobile cardiac telemetry at the time of hospital discharge after TAVI has revealed high-degree or complete heart block warranting permanent pacemaker implantation in 10% of patients.¹⁶² Restoration of normal conduction may occur in up to 60% of patients within weeks following TAVI,¹⁷⁴ and permanent pacing should be withheld for at least 7 days, unless complete or high-grade AV block is present (Table 12 and Figure 9). In several previous trials and registries, the need for pacemaker implantation has been reported to be less frequent with balloon-expandable than self-expanding valves (17.3% vs 37.6%, $P = 0.001$, in the CHOICE, and 7.8% vs 20.3%, $P < 0.001$, in the CENTER meta-analysis) was lower with balloon-expandable valves.^{143,147} However, in the SOLVE-TAVI trial using the newer generation devices (Sapien 3 and Evolut R), pacemaker need were not significantly different between balloon-expandable and self-expanding valves (19.2% vs 23.0%, respectively).¹⁴⁸ No difference between various types of valves was also detected in the VIVID Registry (range 3.7% to 10.5%).¹⁶³ In the most recent **low-risk** randomized trials comparing TAVI with SAVR, the rates of permanent pacemaker implantation were 6.6% with the balloon-expandable Sapien platform (vs 4.0% with SAVR),¹⁰⁵ and 17.4% with the self-expanding Evolut platform (vs 6.1% with SAVR).¹⁰⁶

Acute **coronary obstruction** is rare (<1%) but more frequent when TAVR is performed for failed bioprostheses,¹⁷⁵ and coronary angiography may be challenging post-

TAVR.¹⁷⁶ It is more common with the SAPIEN and occurs mainly in patients with lower lying coronary ostium and shallow sinuses of Valsalva ($10.7 \pm 0.4 \text{ mm}$ vs. $13.3 \pm 0.3 \text{ mm}$, and $28.3 \pm 0.8 \text{ mm}$ vs. $31.3 \pm 0.6 \text{ mm}$, compared to matched controls, respectively),¹⁷⁷ but it may happen with any valve. Delayed coronary obstruction is very rare (0.22%) and may occur up to 60 days after TAVI, although most cases occur within 24h after the procedure.¹⁷⁸ Some degree of myocardial injury may be detected in up to two-thirds of patients, especially in those undergoing trans-apical TAVI or presenting with major procedural complications.¹⁷⁹ At present, there is no reliable way to control the transcatheter valve commissural tab orientation in relation to the coronary ostia.¹⁷⁶ However, TAVI can be performed safely in patients with untreated chronic obstructive CAD.¹⁸⁰

Complications necessitating **emergency cardiac surgery** are mainly of LV guidewire perforation, annular rupture, valve embolization/migration, and aortic dissection. Although more than half of the patients can be salvaged acutely by emergency surgery, less than 25% of patients are expected to survive at 1 year.¹⁸¹

The rate of **valve deterioration** in high-risk patients undergoing TAVI with self-expandable or balloon valves at 5 years in the FRANCE-2 Registry was 2.5% and 13.3%.¹⁸² In the UK TAVI Registry, valve deterioration occurred in 9% of patients within 5 to 10 years after implantation, without significant differences between the two types of valves.¹⁸³ In the NOTION randomised trial, rate of valve deterioration was higher for surgical AVR than TAVI with a self-expanding valve (24.0% vs. 4.8%; $p < 0.001$).¹⁰⁸ In an Italian Registry, moderate and severe deterioration of the CoreValve at 8 years after implantation were 3.0% and 1.6%.¹⁸⁴ ¹⁸ F-sodium fluoride PET is promising in the detection of bioprosthetic aortic valve degeneration and prediction of bioprosthesis failure.¹⁸⁵

The incidence of **infective endocarditis** one year after TAVI (0.3-2%) is not different than that after surgery (0.1-2.3%), and the associated mortality is approximately 50% in 2-5 years, and enterococci and staphylococci are the most common germs.¹⁸⁶⁻¹⁹⁰ Younger age, male sex, history of diabetes mellitus, and moderate to severe residual aortic regurgitation area, the use of orotracheal intubation and self-expandable valve system, have also been associated with an increased risk of infective endocarditis.¹⁸⁹ Endocarditis after TAVI is associated with high in-hospital and mid-term mortality irrespective of whether management includes antibiotics alone or is combined with surgical intervention.¹⁹¹

The reported incidence of **valve thrombosis** ranges from 0.6% to 7%.^{192,193} It presents with dyspnea and increased gradient, and responds to anticoagulant therapy. Larger valves may predispose to thrombosis whereas warfarin has a protective effect. Reduced aortic leaflet motion has also been detected by 3- or 4-dimensional volume-rendered CT (but not by transthoracic echocardiography) thus raising a concern about possible subclinical leaflet thrombosis following TAVI or surgical AVR with a bioprosthesis.¹⁹⁴⁻¹⁹⁶ Subclinical leaflet

thrombosis has been found more frequent in transcatheter compared with surgical valves at 30 days, but not at 1 year.¹⁹⁷ Following TAVR, subclinical leaflet thrombosis may be detected either by transthoracic echocardiography or by CT with specific protocols including the use of retrospective ECG gating without dose modulation (reduction of tube current to lower radiation dose for part of the cardiac cycle) permits assessment of leaflet motion in both systole and diastole, and selection of the most motion-free and artifact-free images for evaluation of hypo-attenuating leaflet thickening (HALT).^{198,199} Nonuniform expansion of transcatheter aortic valve replacement prostheses resulting in frame deformation, asymmetric leaflet, and smaller neosinus volume is related to occurrence of hypoattenuating leaflet thickening, with stronger relation than observed for other clinical variables. It happens with both balloon-expandable (SAPIEN 3 – 23%) and self-expanding (EVOLUT-16%) devices, and its presence is associated with worse survival at 1 year.²⁰⁰ Fluid mechanics analysis of the flow in the post-implantation neosinus, ie the region between the native and transcatheter aortic valve leaflets suggests that overexpansion of the SAPIEN and deeper implantation of the CoreValve are associated with increased thrombus formation.²⁰¹ Rivaroxaban is more effective than an antiplatelet therapy in preventing subclinical leaflet-motion abnormalities (GALILEO-4D trial).²⁰² However, rivaroxaban has been associated with a higher incidence of death and thrombotic or haemorrhagic complications than dual antiplatelet therapy following a successful TAVR (main GALILEO trial).²⁰³ In the ATLANTIS RCT, apixaban after a TAVI was not superior to standard antiplatelet or anticoagulant therapy, irrespectively of a concurrent indication for oral anticoagulation.²⁰⁴ In the POPular TAVI EU RCT on patients who did not have an indication for oral anticoagulation, the incidence of bleeding and the composite of bleeding or thromboembolic events at 1 year were significantly less frequent with aspirin than with aspirin plus clopidogrel administered for 3 months.²⁰⁵ Similar results were reported by the small and underpowered ARTE RCT,²⁰⁶ and aspirin alone is recommended in patients not in need for an oral anticoagulant.²⁰⁷ However, in the PARTNER 3 trial, patients with TAVI had increased valve thrombosis (2.6% compared to 0.7% after surgical replacement) over a 2 year follow-up.²⁰⁸ Thus, in patients at high ischemic risk (recent acute coronary syndrome, coronary stent implantation, coronary artery bypass grafting, peripheral artery revascularization, or stroke), dual antiplatelet therapy may be given for 1-5 months after TAVI.²⁰⁹ In high-risk patients on oral anticoagulation a single antiplatelet agent may be added for -1-6 months.²⁰⁹ In patients on anticoagulation (warfarin or DOAC) no additional aspirin is needed.²⁰⁷ In the randomized POPular TAVI trial, the incidence of serious bleeding over a period of 1 month or 1 year was lower with oral anticoagulation alone than with oral anticoagulation plus clopidogrel ²¹⁰

Access-related vascular complications after TAVI remain common and significantly affect length of hospital stay, morbidity, and mortality. A combined suture-/plug-based

vascular closure device strategy appears superior to a suture-based strategy for vascular access closure.²¹¹

Atrial fibrillation is much lower with TAVR than surgical AVR due to avoidance of pericardiotomy.^{100-103,107,212,213}

Extensive LVOT calcification and aggressive annular area oversizing are associated with an increased risk of **aortic root rupture** during TAVR with balloon-expandable prostheses.²¹⁴ Transcatheter valve embolization and migration may occur in 1% of patients and are associated with increased mortality.²¹⁵

Valve compression and **late embolization** are rare complications mainly seen with the Sapien valve.²¹⁶

Thrombocytopenia (platelet count $<150 \times 10^9/L$) after the procedure is a marker of adverse prognosis.²¹⁷

The long-term **valve failure** rate is low, 3-4%, but the overall cardiac and non-cardiac mortality in these patients exceeds 50% in 3-5 years.^{216,218,219} Following TAVI, there is a mild but significant increase in transvalvular gradients over time that is associated with lack of anticoagulation therapy, a valve-in-valve procedure, a greater body mass index, and the use of a 23-mm valve.^{220 169}

VT due to **Bundle branch re-entry** may be rarely seen.⁷⁸

TAVI may be safer than surgery for **failed aortic bioprostheses**.²²¹ The rate of periprocedural permanent pacing in these patients is low, and its incidence decreased with the use of new-generation valves (<5%).¹⁶³

PCI, if indicated may be performed before TAVR to improve procedural safety (Table 13). Risk factors are LVEF $\leq$ 30% and a STS $\geq$ 10.²²² Left main stem PCI may also be performed before TAVI, despite the anatomic proximity of the aortic annulus to the left main stem.²²³

Among older adults with aortic stenosis undergoing TAVI who were at high risk for heart-failure events, dapagliflozin, an **SGLT2 inhibitor**, resulted in a significantly lower incidence of death from any cause or worsening of heart failure (DAPA TAVI RCT).²²⁴

In patients with **chronic kidney disease** (eGFR <45 mL/min/1.73 m²) and moderate to severe aortic stenosis. More frequent clinical and TTE re-evaluation (every 6–9 months) should be considered to identify optimal timing for intervention due to unreliable symptoms and fast progression rate. (ESC 2026 GL on CKD, IIa C). TAVI instead of surgical replacement should be considered in patients with severe aortic stenosis with CKD aged ≥ 70 years due to the less invasive procedure, lower risk of complications, and similar outcomes over 3–5 years (ESC 2026 GL on CKD, IIa C).²²⁵

In patients with symptomatic AS caused by **radiation for cancer** and who are considered at intermediate surgical risk, TAVI should be considered (ESC 2022 GL on cardio-oncology, IIa B).²²⁶

Surgical explantation of TAVI devices may be indicated in suitable patients in case of procedure-related failure, paravalvular leak, and the need for other cardiac surgery, and carries a 20% mortality rate.²²⁷ The most common contraindications to redo TAVI in patients undergoing TAVI-explant are the need for other cardiac surgery, unsuitable noncoronary aortic root anatomy, coronary obstruction, and endocarditis.²²⁷

Moderate or severe MR is not a contraindication and may improve following TAVI,²²⁸ but the expected benefit is smaller with respect to patients with no/mild MR.²²⁹ Mitral annular calcification is a predictor of conduction abnormalities and cardiovascular mortality following TAVI.²³⁰

Pulmonary hypertension indicates increased mortality although it may not be an absolute contraindication for TAVI.²³¹

Amyloid-related AS is not a contraindication for TAVI.²³²

Bicuspid Aortic Valve

Patients with a bicuspid aortic valve may also have an associated aortopathy consisting of aortic dilation, coarctation, or even aortic dissection. A detailed discussion on bicuspid aortic valve and associated aortopathy is provided in the relevant Chapter in ACHD. Balloon valvotomy may be the treatment of choice in **congenital (bicuspid or unicuspid) AS**. TAVI is under study, but not indicated for young, low-risk patients.²³³ TAVI may also be considered in high-risk patients,^{234,235} but at the potential risk of a higher number of cerebral ischemic lesions.²³⁶ In a registry-based study of propensity-matched patients who had undergone transcatheter aortic valve replacement for aortic stenosis, patients with bicuspid vs tricuspid aortic stenosis had no significant difference in 30-day or 1-year mortality but had increased 30-day risk for stroke.²³⁷ In an observational study, mortality and stroke rates with balloon- and self-expandable valve were similar. Balloon-expandable valve was associated with higher transvalvular mean gradient and more frequent annulus rupture, whereas self-expandable was associated with more frequent moderate to severe aortic regurgitation, additional THV implantation, and permanent pacemaker implantation.²³⁸ Calcified raphe and excess leaflet calcification are associated with increased risk of procedural complications and midterm mortality.²³⁹

Non-cardiac surgery

In patients with severe AS needing elective non-cardiac surgery, the management depends mainly on the presence of symptoms and the type of surgery. If possible, intervention should be performed before noncardiac surgery. Recommendations are presented in Table 14 and Figures 10 and 11. Even high risk non-cardiac surgery can be performed safely in patients with severe, asymptomatic AS under appropriate intraoperative and postoperative hemodynamic monitoring.²⁴⁰

Exercise

Recommendations for exercise and participation in sports are provided in Table 14.

Pregnancy

Usually, aortic stenosis in women of childbearing age is congenital. In mothers with severe AS with stable severity of stenosis, absence of symptoms of stress testing, and normal BP response, pregnancy outcomes are favorable.²⁴¹ Heart failure symptoms may develop in 10% and arrhythmias may occur in 2% to 35%, but maternal mortality is rare.²⁴² Fetal complications may also occur in up to 25% of mothers with severe stenosis, including intrauterine growth retardation, preterm birth, and low birth weight. Delivery should be planned in advance, with vaginal delivery preferred for most patients. Early delivery by Cesarean followed by urgent surgical valve replacement may be required for life-threatening symptoms if a percutaneous approach is not feasible. Recommendations for pregnancy in patients with valve disease and specifically AS are provided in Table 15 as well as in General Principles.

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