Chapter 13

Current Treatment Options in Aortic Stenosis

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1. Introduction

There is a trend towards a worldwide aging in the last decades and diseases which are common in the elderly people would take important place in clinical practice. Although patients with aortic stenosis (AS) usually remain asymptomatic for a long time, once the classic triad of angina, syncope, and exertional dyspnea develop, the prognosis becomes dramatically worse. Accurate diagnosis and efficient treatment are getting more important as aortic valve replacement is the treatment of choice for severe AS.

We present a detailed description of the different therapeutic procedures that are being developed and increasingly used as an alternative to standard surgical treatment. However special surgical techniques as low-profile mechanical prosthesis, biological prosthesis (both stented and stentless), homograft and Ross technique (pulmonary autograft in aortic position and homograft in pulmonary position) will also be discussed in this chapter. We would also like to mention special considerations about treatment in special groups such as elderly.

2. Medical treatment

The standard therapy for symptomatic patients with severe aortic stenosis (AS) due to any cause is replacement of the valve. Since the prognosis dramatically worsens once the symptoms of AS develop, this is a late stage for an effective medical treatment. Patient education regarding the disease course and typical symptoms is an important priority. Current management of patients with AS comprises monitoring disease progression. Unfortunately, in patients with AS medical therapy may not prolong life nor improve progression and has limited utility in alleviating symptoms. Severe AS is adversely affected by changes in preload

and afterload. In patients with severe AS, drugs that reduce preload or afterload should be used with caution because any medical treatment option used in these patients may worsen the patients' conditions. Meanwhile, there is a growing body of evidence about TAVI which is currently used mainly in patients with multi-morbidity and high surgical risk. In patients with rheumatic valve disease, rheumatic fever prophylaxis is strongly recommended to prevent repetitive valve scarring [1]. It has been hypothesized that some of the risk factors and pathophysiologic mechanisms in atherosclerosis play an important role in the development of calcific AS. Therefore theoretically, anti-inflammatory and anti-proliferative agents might slow or prevent disease progression. Because patients with severe AS are mostly older adults, some important and common issues like kidney insufficiency (KI), autonomic dysfunction, conduction disturbances, propensity to falls, and osteoporosis should always be kept in mind in the medical management of these patients.

2.1. Hypertension

Hypertension is not uncommon in patients with AS and approximately 40 percent of patients have hypertension [2]. In patients with concomitant hypertension and AS, left ventricular afterload is elevated as result of the "double-load" of increased systemic vascular resistance and valve stenosis [3]. For this reason reducing afterload may improve the degree of valvular opening and stroke volume. Therefore treatment of hypertension is recommended in patients with asymptomatic AS by many clinicians. There are a few studies assessing the safety of anti-hypertensive treatment in patients with AS [4]. Angiotensin converting enzyme (ACE) inhibitors seem to be well tolerated both in patients with mild-to-moderate and severe AS [5, 6]. Recently, ACE inhibitors and angiotensin receptor blockers (ARBs) were reported to be associated with improved survival and reduced cardiovascular (CV) events [7]. On the other hand, the recently published Simvastatin and Ezetimibe in Aortic Stenosis (SEAS) study reported an increased risk of CV events associated with antihypertensive treatment. However, this study was not a dedicated study on HT in AS and the only type of anti-hypertensive drug group associated with increased CV events was alpha-blockers [4]. This finding is in accordance with the results of Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial [8]. Blood pressure lowering agents should be initiated at low doses and gradually titrated with frequent monitoring, especially in older patients with increased risk of falls and osteoporotic fractures. Especially older patients given alpha blockers or diuretics should be informed about orthostatic hypotension to avoid falls.

2.2. Coronary artery disease

Coronary artery disease (CAD) is rather common in patients with AS and evaluation regarding conventional atherosclerotic risk factors is recommended in these patients. Tobacco use should be discouraged. The current US Preventive Services Task Force recommends usage of low dose aspirin for primary prevention when CV risk outweighs the risk of gastrointestinal hemorrhage in men between 45-79 years and when the risk of ischemic stroke outweighs the risk of gastrointestinal hemorrhage in women between 55-79 years [9]. It is also stated that the current evidence is insufficient to assess the balance of benefits and harms of aspirin in patients 80

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years or older [9]. A recently published article reported the outcomes of percutaneous coronary intervention (PCI) in patients with concomitant severe AS and CAD [10]. In this well-matched trial, 30-day mortality after PCI was similar in patients with and without severe AS. In this study AS patients with low EF (≤30) and high Society of Thoracic Surgeons score (≥10) were associated with significantly increased 30-day mortality after PCI. Patients with mild AS should not be restricted from physical activity. Patients with severe AS should avoid competitive or vigorous activities that involve high dynamic and static muscular demands, although other forms of exercise are safe. Exercise may also improve functional capacity and may prevent skeletal muscle mass loss (i.e. sarcopenia).

2.3. Atrial fibrillation

Valvular heart disease, particularly left-sided valvular lesions precipitate the development of atrial fibrillation (AF). Although it has been less well studied in AS compared to mitral valve disorders, AF often complicates uncorrected aortic valve disorders [11]. In the recently published SEAS study, baseline or prior was present in approximately 9% of patients with mild-to-moderate AS [12]. The study excluded the patients with baseline and prior AF and sought the effect of simvastatin plus ezetimibe on new-onset AF. During an average of 4.3±0.8 years of follow up, 6% of the patients developed AF and the rate was similar between the simvastatin plus ezetimibe and placebo groups. In this study, increased age and left ventricular mass index were independent predictors of new onset AF. New-onset AF was associated with two-fold higher risk of AF related outcomes and four-fold higher risk of nonfatal nonhemorrhagic stroke. In a previously asymptomatic patient, new onset AF may cause overt heart failure symptoms due to the noncompliant left ventricle which is associated with a relative shift of left ventricular filling to the later part of diastole with a greater dependence upon atrial contraction. Similar treatment approaches for AF in patients with AS can be used as in patients without AS. Heart rate control is important to enable an adequate diastolic filling time. Although guidelines generally recommend rate control over rhythm control in patients with AS, there is a trend towards preference of rhythm control with the benefits of early rhythm control and options of left atrial catheter ablation and new anti-arrhythmic drugs [13, 14]. Within the current ECS guidelines on AF, severe AS is stated as a contraindication for verkalant usage [14]. It is also important to screen for coronary disease in patients with AS before the initiation of class Ic anti-arrhythmic drugs for rhythm control for AF [11]. Significant ventricular hypertrophy or dysfunction increases the risk of proarrhythmia associated with class Ic and most class III anti-arrhythmic drugs. In such patients amidodarone is the preferred agent [11]. However, when medications for heart rate control such as beta blockers and non-dihydropridine calcium channel blockers are used, their potential to depress LV systolic function and cause clinical deterioration should be kept in mind. Specific considerations about drug choices to control heart-rate are depicted in the following specific drug classes section. Specific considerations about warfarin treatment are depicted in the following specific drug classes section.

2.4. Heart failure

In patients with severe AS, aortic valve replacement (AVR) is indicated when symptomatic heart failure develops. Even when severe AS is present, transvalvular pressure gradients may not be found high because of left ventricular systolic dysfunction. Reduced EF is associated with worse clinical outcome. A recent study compared the outcomes of severe AS patients with an EF of ≤30 or >30 who was followed with medical treatment or underwent TAVI [15]. While an EF of ≤30 was associated with worse prognosis in the medically treatment group, TAVI was associated with an improvement in EF and functional class and patients who underwent TAVI had better prognoses irrespective of their baseline EF. When patients with mild or moderate AS have HF, there is generally other causes of HF like coronary heart disease and medical therapy of HF is preferable to AVR. Vasodilator therapy and beta blockers may be started with careful dose titration and closely monitoring. Volume status of patients should also be determined and followed up carefully [3, 16].

Invasive hemodynamic monitoring in the intensive care unit should be considered for decompensated patients with severe AS [3]. Nitroprusside rapidly and markedly improves cardiac function in patients with decompensated HF due to severe left ventricular systolic dysfunction and severe AS. It provides a safe and effective bridge to AVR or oral vasodilator therapy in these critically ill patients [17].

Phosphodiesterase type 5 inhibition had beneficial effects on pressure overload in preclinical models and a preliminary study of oral sildenafil in 20 patients with severe symptomatic AS showed that it was associated a reduction in systemic and pulmonary vascular resistance and pulmonary artery and wedge pressures [18]. Although sildenafil was also resulted in 11% decrease in mean systemic arterial pressure, it was not associated with any episodes of symptomatic hypotension.

2.5. Metabolic syndrome

Metabolic syndrome (MS) is a worldwide problem with increased risk of CV events. The results of Multi-Ethnic Study of Atherosclerosis (MESA) and another recent prospective trial suggest that MS is independently associated with progression of AS, particularly in younger individuals [19, 20]. Although these findings need to be confirmed in larger studies, studies assessing the effects of lifestyle modification and reduction of insulin resistance on the incidence and progression rate of AS could be of value.

2.6. Malnutrition

Malnutrition is a common and important health problem in the older adults and being underweight is associated with a worse prognosis than being overweight in this population [21]. Association of malnutrition and heart valve disorders is rarely reported in the literature. Otto et al reported increased long-term mortality independently associated with cachexia in 674 elderly patients who underwent balloon aortic valvuloplasty for AS [22]. Another observational study showed association of heart valve calcification with malnutrition in patients on hemodialysis [23]. In this study evaluation of malnutrition was done only with albumin level

which is not specific for malnutrition. Wang et al demonstrated the correlation of fetuin-A, which has recently been identified as an important circulating inhibitor of calcification, with the presence and degree of malnutrition in patients on peritoneal dialysis [24].

There is also data indicating undernutrition is associated with worse outcomes after cardiac valve surgery. In a retrospective study, impact of BMI and albumin levels on morbidity and mortality after cardiac surgery was assessed in 5168 patients undergoing coronary artery bypass or valve operations [25]. Preoperative low albumin (<2.5 g/dl) and low BMI (<20 kg/m2) were independently associated with increased postoperative mortality. Tepsuwan et al. assessed the impact of cardiac cachexia retrospectively in 353 patients who underwent cardiac valve surgery [26]. The study population was relatively young and mitral stenosis and mitral regurgitation were the most frequent valve disorders. They found significant association between cachexia and worse New York Heart Association functional class and worse postoperative outcomes. Thourani et al investigated the impact of body mass index (BMI) on outcomes after cardiac valve surgery in 4247 patients [27]. Most of the procedures were isolated AVR (47.2%). They showed increased in-hospital and all-cause long-term mortality in patients with a BMI of less than 25 compared to patients with a BMI of 25-35 or higher than 35. In this study, no laboratory or clinical data about nutritional status was reported.

Patients with AS may suffer from dietary restriction due to reduced physical capacity and depressive mood. When concomitant mesenteric vessel atherosclerosis is present, abdominal angina may cause avoidance from eating. All these factors may render these patients susceptible to infectious diseases, osteoporosis, skeletal muscle loss (i.e. sarcopenia) and fall related fractures. Unfortunately, there is no study evaluating the role of nutritional intervention, which may potentially improve muscle and bone mass, muscle functions, and functional capacity, on clinical outcomes in patients with AS.

2.7. Depression

Later-life depression (LLD) is associated with disability and poor outcomes [28]. Among various chronic medical conditions, cardiac disease and arthritis are the most commonly ones associated with depression [29]. Underlying medical problems may affect the prognosis of depression and depression may decrease compliance to medical treatment thus delay recovery from medical illnesses [28]. The importance of screening for depression in patients with heart disease is well established, but identifying patients with depression may be difficult. Organic somatic symptoms possibly unrelated to mood may increase the score on depression scales and patients with depression may deny and do not report their depressive symptoms [28]. Furthermore, there are many shared symptoms of heart disease and depression like insomnia, fatigue, shortness of breath, weight loss, palpitations, and exercise intolerance. Vascular depression is associated with late onset, treatment-resistant symptoms, vascular disease, vascular risk factors, and extensive cerebrovascular lesions [28]. Although there is no specific data about the association of vascular depression and AS in the elderly, atherosclerosis has pivotal role in the pathogenesis of both.

Beta blocker treatment, which is being used commonly in patients with heart disease, may potentially precipitate depression. Although there is conflicting data about the association of

beta blockers and depression, and individual susceptibility to depression may be important, patients with risk factors for depression should be followed up in terms of development of depression [30]. Lipophilic beta blockers like propranolol, timolol, pindolol, metoprolol, carvedilol and nebivolol are more strongly associated with depression than hydrophilic beta blockers like atenolol, nadolol, practolol and sotalol [30]. When there are strong indications like CAD and CHF for beta blocker treatment are present, depression should not be considered as an absolute contraindication. SSRI are among the most commonly used medications in the treatment of depression. There is some data that indicate use of SSRI in patients with CAD and depression may improve CV outcomes [31]. Because treatment with SSRI may reduce platelet functions as severe AS do, bleeding complications of surgical procedures may be increased in patients with severe AS under SSRI treatment. Sodium levels should be monitored in older patients under SSRI treatment, especially if concomitant diuretic use is present because both of them may be associated with hyponatremia.

2.8. Perioperative medical treatment

Careful manipulation of hemodynamics in the perioperative period is crucial in patients with AS [32]. Maintaining sinus rhythm, a relatively slow heart rate, and adequate preload and afterload are important goals to minimize the perioperative CV risk [32]. Ideal heart rate is between 60 and 70 beats per minute and bradicardia should be avoided. Careful assessment of hydration status and providing adequate hydration is also important to maintain preload which these patients are dependent upon. Careful monitoring of the arterial blood and central venous pressures is also important. Hypotension should be controlled with pure α agonists because they do not cause tachycardia. Routine antibiotic prophylaxis is not recommended unless the patient has a previous history of infective endocarditis [33]. Severe AS may be associated with markedly reduced platelet functions. One recent double-blind placebo controlled trial investigated effects of infusion of desmopressin (0.3 μg/kg) on platelet functions and postoperative blood loss [34]. The authors recommend assessing of platelet functions in the preoperative period in patients with severe AS and usage of desmopressin to avoid increased blood loss in patients with reduced platelet functions.

Delirium is rather common after cardiac valve surgery and is independently associated with increased risk of short and long term morbidity and mortality [35, 36]. Hyperactive delirium is easily recognized because of agitation, hallucinations and delusions. Routine assessment of attention and orientation is crucial to detect hypoactive delirium because it is easily and frequently overlooked. Providing adequate volume status, following up of renal functions and electrolyte levels, controlling postoperative pain and rational selection of medications may reduce the risk of delirium. Many drugs like anticholinergics, antihistaminics, narcotics and central acting drugs may precipitate delirium. Maldonado et al. investigated the effects of postoperative sedation on the development of delirium in patients undergoing cardiac valve surgery [35]. In this open label study, dexmedetomidine was associated with a significantly decreased rate of delirium with compared to propofol and midazolam (rates of delirium 3%, 50% and 50% respectively).

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2.9. Perioperative medical treatment for non-cardiac surgery

Beta blocker treatment is recommended in patients with CAD or more than one of the cardiac risk factors which are listed in Table 1 [37]. However, the multicenter POISE trial showed an increased rate of death associated with perioperative beta blocker treatment despite a significant reduction in the primary composite endpoint of CV death, nonfatal MI or nonfatal cardiac arrest [38]. This trial resulted in the following recommendation in the current guidelines: "Routine administration of high-dose beta blockers in the absence of dose titration is not useful and may be harmful to patients not currently taking beta blockers who are undergoing noncardiac surgery" [37]. Titration of beta blockers to heart rate and blood pressure is recommended if the patient will undergo high- or intermediate-risk surgery [37]. Like it is recommended for many drug classes, starting beta blockers in low doses and careful titration is important in elderly patients who are at increased risk for bradycardia and hypotension. The role of beta blockers in intermediate- and low-risk patients is not well known. Optimal type, dose, timing, duration, and titration of beta blockers are also lacking [37]. Withdrawal of beta blockers in the preoperative period may be associated with adverse events and should not be performed unless necessary. Metformin and renin-angiotensin-aldosterone system (RAS) blockers increase the risk of postoperative lactic acidosis and KI respectively and it is recommended to stop them before the surgery.

History of ischemic heart disease
History of compensated or prior heart failure
History of cerebrovascular disease
Diabetes Mellitus
Renal insufficiency (defined as a preoperative serum creatinine of greater than 2 mg/dL)

Table 1. Clinical risk factors for perioperative cardiovascular complications

2.10. Specific drug classes

2.10.1. Statins

It has been considered that the valve lesion in calcific AS might share similar pathogenetic mechanisms with atherosclerosis and progression may be related to known atherosclerotic risk factors [39]. Statins are now well established in the primary and secondary prevention of CAD. Several studies have suggested that statins may cause regression of CAD and reduce the calcific volume of coronary plaques [40]. In accordance with this finding, presence and progression of aortic valve calcification are reported to be increased in patients with a serum LDL cholesterol >130 mg/dL [41].

While some earlier studies indicate that statin therapy is associated with a slower rate of hemodynamic progression of AS [42-45], some more recent trials have inconsistent results of different statin preparations on the progression of AS [46-49]. SALTIRE (Scottish aortic stenosis

and lipid lowering therapy, impact on regression) trial was the first double blind randomized controlled trial of lipid lowering treatment in patients with calcific AS. This trial of 155 adults with calcific AS showed that, although atorvastatin 80 mg daily, more than halved serum LDL cholesterol concentrations, there was no difference in the rate of increase in aortic jet velocity or of progression of aortic valve calcification as measured by Doppler echocardiography or helical computed tomography [46]. The prospective open-label RAAVE study (The Rosuvastatin Affecting Aortic Valve Endothelium) comprised of 121 consecutive patients with moderate to severe AS. Treatment with rosuvastatin 20 mg was given when LDL-cholesterol was greater than 130 mg/dL and no statin therapy was given when LDL-cholesterol was less than 130 mg/dL. Patients treated with rosuvastatin had significantly attenuated rates of deterioration in mean aortic valve area and aortic jet velocity compared to patients who did not receive rosuvastatin [47]. The prospective and placebo controlled SEAS trial sought the effect of statins on calcific AS. In this study, 1873 adults (mean age 68) with mild-to-moderate AS were enrolled and randomly assigned to treatment with simvastatin plus ezetimibe or placebo [48]. At median follow-up of 52 months there were no differences in the peak aortic jet velocity or valve area noted between the 2 groups. There was also no difference in CV death, aortic valve replacement, non-fatal myocardial infarction, hospitalized unstable angina pectoris, and heart failure due to progression of AS, coronary artery bypass grafting, percutaneous coronary interventions, or non-hemorrhagic stroke. Although there were fewer ischemic events in the treatment group, this difference was only due to a lower rate of coronary bypass grafting at the time of aortic valve surgery so the clinical relevance of this finding is unclear. SEAS study results show that the effect of statin therapy on disease process does not provide convincing evidence [48]. The investigators of SEAS study recently reported the results of simvastatin plus ezetimibe on new-onset AF in 1421 patients with asymptomatic mild-to-moderate AS [6]. The rate of new-onset AF was similar in the simvastatin plus ezetimibe group compared to placebo group. Aortic Stenosis Progression Observation (ASTRONOMER) is the most recently published trial regarding effect of statins on AS. This double-blind prospective trial randomized 269 younger asymptomatic patients with mild to-moderate AS with no indications for lipid-lowering agents to rosuvastatin 40 mg daily (134 patients) or placebo (135 patients). Unlike earlier trials in which bicuspid aortic valve was rare, a bicuspid valve was present in nearly half of the subjects in this study. After a mean follow-up of 3.5 years, there were no significant differences in the transaortic gradient or aortic valve area in the rosuvastatin group compared to placebo [49].

At present, if atherosclerotic vascular disease or other indications do not coexist, statin therapy solely for AS cannot be recommended. It should be noted that effect of therapy has not been evaluated in earlier stages of the disease.

2.10.2. Angiotensin converting enzyme inhibitors

Although expression of angiotensin II has not been shown the in normal valves, sclerotic aortic valve tissues demonstrably express angiotensin II and angiotensin converting enzyme (ACE). Therefore it may contribute to valve inflammation, calcification, and disease progression [50]. It has been shown that ACE inhibitors suppress ventricular fibrosis and inhibit angiotensin II

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type 1 receptor in the cardiomyocytes and therefore decrease systolic and diastolic dysfunction in patients with left ventricular hypertrophy and AS [51]. For these reasons ACE inhibitors may have a role in the management of patients with AS. Two preliminary observational studies examined the effect of ACE inhibitors in patients with AS in preventing further changes in the valve leaflets. Rosenhek et al showed that hemodynamic progression of AS did not occur in 211 patients with moderate AS after at least 6 months of treatment with the ACE inhibitors. Furthermore, the presence of hypertension did not appear to influence the outcome [44]. Another retrospective study by Obrien et al of 123 patients evaluated the aortic valve calcium score by electron beam computed tomographic scans. The study showed that ACE inhibitor treatment was associated with a 71% reduction in the progression of aortic valve calcification in 123 patients with AS [52]. At the present, there are no published randomized prospective studies using ACE inhibitors to delay the progression of calcific AS. Some potential targets for therapy in AS such as the pathways involved in inflammation and tissue calcification have not yet been studied. ACE inhibitors have beneficial effects on ventricular systolic and diastolic functions and are well tolerated, increase exercise capacity, and reduce dyspnea in symptomatic patients with mild to moderate AS [6]. ACE inhibitors may provide symptomatic relief when patients with severe AS who are not good candidates for surgery develop symptoms of left heart failure. It should also be kept in mind that ACE inhibitors may increase the transvalvular gradient by reducing afterload or preload and cause sudden clinical deterioration in patients with severe AS. In older adults, ACE inhibitors should be initiated at low doses and gradually increased to avoid hypotension and fall related fractures. Because elderly patients with severe AS generally have extensive atherosclerosis, before initiation of ACE inhibitors bilateral renal artery stenosis should be considered and investigated if suspected.

2.10.3. Angiotensin receptor blockers

Angiotensin receptor blockers have similar hemodynamic effects like ACE inhibitors. A recently published observational study indicates that both ACE inhibitors and ARBs are associated with lower mortality and CV events in patients with AS [7]. However, prospective and controlled studies are needed to test this finding. Although similar precautions as in ACE inhibitors should be considered when starting and maintaining ARBs, they have some benefits like less incidence of cough. Because compelling evidence does not exist for neither ACE inhibitors nor ARBs for these patients, when RAS blockage is planned ACE inhibitors may be selected in the first step and switching to ARBs may be considered if adverse effects like chronic cough develop.

2.10.4. Beta blockers

Beta blockers are a not part of routine medical treatment. Because beta blockers may aggravate the symptoms of HF, patients with symptoms and signs of HF are not good candidates for this treatment option. Beta blockers may be used in AS patients with angina pectoris or AF with rapid ventricular response. Because older adults are at increased risk for hypotension, bradycardia, conduction disturbances and diabetes, a close follow-up should be performed when patients with AS are given beta blocker treatment.

2.10.5. Diuretics

Diuretics are not indicated in patients without signs of congestion because of their potential for reducing preload, which may lead to fall in cardiac output and exacerbation in symptoms of HF. Therefore, diuretics are not first-line treatment options in hypertensive patients with severe AS without findings of congestion. Diuretics may improve symptoms of HF by reducing left ventricular end-diastolic pressure in patients with lung congestion, ascites or edema. Older patients may not excrete free water effectively, and they may more easily develop hyponatremia after diuretic treatment [53]. Thiazide diuretics cause hyponatremia more frequently than loop diuretics [54]. These older patients also have increased tendency to diuretic induced hyponatremia, because concomitant use of other medications like selective serotonin reuptake inhibitors (SSRI), which precipitate hyponatremia, is common. Because of disruption of normal circadian rhythm of antidiuretic hormone, nocturia is frequently seen in elderly patients and may be bothersome and increase the risk of falls when evening or night doses of diuretics are used [55]. Administration of diuretics in earlier hours of the day may be safer. Patients with urgency incontinence may need urinary anti-cholinergics under diuretic treatment to avoid urgency induced falls and significant physical exertion. Diuretics also lead to orthostatic hypotension by inducing volume depletion. Because falls are more frequent and are associated with great morbidity and mortality in these older patients, monitoring of blood pressure at home and avoidance of hypotension is crucial.

2.10.6. Nitrates

Nitrates may be used in symptomatic treatment of angina pectoris in patients with severe AS. They should be initiated at low doses and gradually increased to avoid sudden hypotension. Concomitant use of phosphodiesterase inhibitors for erectile dysfunction should be avoided to prevent substantial hypotension.

2.10.7. Digoxin

Digoxin has a narrow therapeutic index and the risk of adverse events associated with it may be more common in older patients [56]. Digoxin levels may be increased in older patients with impaired kidney functions. Because creatinine levels may be normal or minimally increased in older adults with impaired kidney functions when significant loss of muscle mass (i.e. sarcopenia) is present. It is recommended in the recent ACC/AHA guideline that an initial dose of 0.125 mg daily or every other day is chosen if the patient is older than 70 years old, has impaired kidney function, or has a low lean body mass [57]. Digoxin above 0.125 mg/d is also listed among the potentially inappropriate medications (PIMs) list in the recent Beers criteria [58]. Because digoxin concentrations above 1 ng/ml are not associated with better clinical outcomes and may adversely increase morbidity and mortality, a target digoxin concentration of 0.5-1 ng/ml is recommended despite conventional therapeutic serum concentration is defined as 0.8-2 ng/ml [56, 57]. When there is concomitant hypokalemia, hypomagnesemia or hypothyroidism, digoxin toxicity may occur in lower concentrations [57]. Older patients under digoxin treatment may develop adverse effects like anorexia, nausea, vomiting, confusion, visual problems, and rhythm and conduction disturbances more commonly [56]. Clarithro-

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mycin, erythromycin, amiodarone, itraconazole, cyclosporine, verapamil, and quinidine can increase serum digoxin concentrations [57]. Digoxin should not be used in patients with severe AS and sinus rhythm. Digoxin may be used to reduce the ventricular rate in patients with AF and a rapid ventricular rate especially when hemodynamic deterioration is present. When these harms are taken into consideration, should be used with caution as an adjunctive agent for heart rate control. Alternatively, beta blockers, which are associated with improved survival in patients with HF and may effectively control heart rate alone, may be used as first line agents in these patients. However, when hypotension and significant HF signs are present, digoxin may be a better agent for symptomatic treatment.

2.10.8. Calcium channel blockers

Although published data regarding anti-hypertensive drugs in patients with AS is limited, calcium channel blockers like amlodipine do not appear to depress LV function and may be safe to use in patients with AS. Non-dihydropridine agents like diltiazem and verapamil may influence left ventricular systolic functions and may cause clinical deterioration.

2.10.9. Alpha blockers

Peripheral alpha blocker use may possibly lead to hypotension or syncope, decreased coronary perfusion due to reduced afterload and should generally be avoided. Alpha blockers are listed among the PIMs in the recent Beers criteria and routine use for the treatment of hypertension is not recommended [58]. Alpha blockers are also listed among the PIMs in patients with a history of syncope [58].

2.10.10. Warfarin

Warfarin treatment is generally recommended in patients with AS and AF to decrease the incidence of stroke and systemic arterial embolism. Assessing the risk of embolism associated with AF and bleeding associated with warfarin treatment should be carefully performed. It is very important to educate the patient and his/her relatives about the benefits and risks of warfarin treatment and the details of follow-up. Integration of the patients' relatives in the treatment plan is crucial especially in older adults with significant cognitive problems. A meta-analysis which was published in 2007 indicated that aspirin was associated with a 22% reduction in the rate of stroke, while warfarin was associated with 64% reduction [59]. Because warfarin is associated with a significantly lower risk of stroke than aspirin, simply prescribing aspirin without discussing the benefits and risks of warfarin treatment with the patients and their relatives would be therapeutic nihilism. Although there are newer anticoagulant medications like dabigatran which do not require therapeutic monitoring, we need more data especially in the older individuals in order to prescribe them instead of warfarin. For instance, dabigatran is associated with greater risk of bleeding than with warfarin in patients ≥ 75 years and efficacy and safety is not known in patients with a creatinine clearance below 30 ml/min [58].

Warfarin is also the drug of choice in patients with AVR with mechanical prostheses. To date there is no alternative for warfarin for these patients and a higher international normalized ratio (2.5-3.5) is targeted. This translates into increased risk of bleeding associated with warfarin especially in the older patients. These patients may also have other bleeding risk factors like concurrent anti-platelet, SSRI or ginkgo biloba use and platelet dysfunction associated with KI or significant AS. Whether warfarin treatment is appropriate for the patient, may even determine if AVR might be performed and if a mechanical prosthesis might be used. Patients, in whom warfarin treatment is planned, should also be carefully assessed about the risk of falls which may lead to significant bleeding, most importantly to intracranial hemorrhage. If warfarin is started, ensuring precautions by educating the patients and their relatives to avoid falls is also crucial.

3. Transcathater aortic valve implantation

Surgical AVR is currently the gold-standard treatment for patients with severe symptomatic AS. Without surgery, the prognosis is extremely poor, with a 3-year survival rate of <30%.However, in the huge Euro Heart multinational registry in Europe, 33% of symptomatic patients over the age of 65 years were not referred for surgery [60]. The reasons for not planning surgery were not always the co morbidities. David Bach's series showed the same issue and 33% of symptomatic patients were not referred for surgery, some of whom had a low Euro Score risk [61]. Balloon aortic valvuloplasty, which was described in the 1980s, was the first alternative to surgical therapy [62]. Despite high rates of initial procedural success, restenosis is frequently encountered in the long term. The procedure has generally been abandoned in adult patients except as a palliative procedure often prior to surgical AVR [63]. Trans-catheter aortic valve implantation (TAVI) was first described by Andersen et al in 1992 [64]. They implanted an expandable aortic valve by a catheter technique in a closed chest pig model. The first attempt to use TAVI in man was in 2002 by Cribier et al [65]. A percutaneous bioprosthesis was successfully implanted within the diseased native aortic valve through an antegrade transseptal approach. In more recent years, the technology has developed very rapidly and, to date, more than 40,000 transcathater valves have been implanted worldwide. The results of several large multicenter registries and randomized Placement of Aortic Transcathater Valves (PARTNER) trial, TAVI is now the standard of care for extremely high risk or 'inoperable ' patients and is a valid alternative to surgery for selected high-risk but ' operable ' patients with symptomatic AS [66-68].

Patients might be considered candidates for TAVI if they fulfill the following criteria: symptomatic severe AS, a life expectancy of >1year, contraindications for surgery, high risk for surgery (clinical judgment plus Euro Score (logistic) >20%; STS Score>10%), and/or porcelain aorta, history of thoracic irradiation, severe thoracic deformity, patent coronary bypass, cachexia, recurrent pulmonary emboli, right ventricular insufficiency and cirrhosis.

Contraindications for TAVI are as follows: an aortic annulus of <18 mm or >27 mm, bicuspid valves or unicuspid or noncalcified valve, severe aortic regurgitation or mitral regurgitation,

estimated life expectancy < 12 months, evidence of an acute myocardial infarction within one month, MRI confirmed CVA within six months, ejection fraction < 20 %, heavy calcification in front of LM, presence of LV thrombus and need for CABG

Risk Estimation: Accurate estimation of the risk of SAVR performed by an experienced cardiothoracic surgeon and cardiologist is vital to appropriate evaluation of potential candidates for TAVI. Some risk score algorithms like Ambler score, logistic EuroSCORE and Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM) are widely used to identify patients at high risk for cardiac surgery. Ambler score was dedicated to predict in-hospital mortality after heart valve surgery [69]. EuroSCORE integrates increased age, female gender, chronic pulmonary disease, extracardiac arteriopathy, neurological dysfunction, previous cardiac surgery, increased serum creatinine, active endocarditis, critical perioperative state, unstable angina, LV dysfunction, recent MI, and pulmonary hypertension as patient and cardiac related factors and some operation related factors like emergency, other than isolated CABG, surgery on thoracic aorta, and postinfarct septal rupture. An online calculator is available in their official website (http://www.euroscore.org/). Logistic EuroSCORE appears to overestimate mortality risk in patients undergoing high-risk aortic valve replacement. The STS-PROM risk scoring which is more complicated integrates age, gender, race, weight, creatinine level, various chronic cardiac and non-cardiac diseases, previous cardiovascular interventions, perioperative cardiac status, hemodynamic status, and operative risk factors. This scoring estimates the rates of postoperative morbidity, mortality, permanent stroke, prolonged ventilation, renal failure, and reoperation. It is updated regularly and calculation can be performed only via the online calculator (http://www.sts.org/). However the STS-PROM model may provide more accurate risk stratification than other scores, more appropriate scoring systems are not currently available. In clinical practice, it seems reasonable that high –risk patients should be evaluated using clinical judgment and a combination of several scores [70, 71].

4. Overview of procedure

4.1. Approaches used for TAVI

Stented valves placed either transapically or percutaneously are garnering much attention. In the percutaneous approach, the valve is deployed either antegradely via the transseptal route,or retrogradely across the native aortic valve.

Transfemoral Approach: The transfemoral approach is simper and quick to access the aortic valve. This route is the first choice of approach in the vast majority of centers performing TAVI procedures. Although surgical cutdown was the technique used for the transfemoral approach at the beginning of the TAVI experience, most centers are now using a fully percutaneous technique. The aortic valve is corossed and a stiff wire is placed in the LV with a large loop. Within these procedures, firstly balloon aortic valvotomy is undertaken and a stented bioprosthesis is then deployed over a balloon intothe aortic annulus. Inflation of the balloon anchors the valve in place in the annulus,effectively achieving AVR. Some specific contrain-

dications for transfemoral approach are; narrow peripheral arteries (diameter < 8-9 mm), severe tortuousity or calcification, history of aorto-femoral by pass, aneurysm of abdominal aorta with thrombosis, and severe atheroma of the arch.

Transapical approach: Transapical approach necessitates a thoracotomy but the valve is deployed into the beating heart and extracorporeal circulation is not performed. This approach is particularly suited to patients with severe peripheral artery disease and heavily calcified ascending aorta and arch. The transapical approach includes the following other benefit: no stored tension in the delivery system, more reliable device control and feedback and no size limitations. The main disadvanteges are the need for thoracotomy; a greater degree of myocardial injury and the potentially life threating bleeding complications associated with the surgical repair.

Subclavian Approach: A subclavian approach allows patient with unfavorable iliofemoral artery anatomy or extensive disease to be treated with TAVI. A surgical cutdown is needed to isolate the subclavian artery. However no specific complications for subclavian access reported, any injury of the subclavian artery would translate into a major intrathoracic bleeding that might be difficult control.

Transaortic approach: In 2009 and 2010, transaortic approach with direct access to the ascending aorta though an anterior minithorocatomy has been advocated. Altough requiring sternotomy, avoidance of LV apical injury and avoidance of the use of large cathaters are potential advantages of this novel approach.

4.2. TAVI systems and placement

Currently two valve systems are approved for TAVI: the balloon expandable Edwards valve-the first generation Cribier-Edwards, second generation Edwards SAPİEN, and the third generation Edwards SAPIEN XT versions and the self expandable CoreValve (Medtronic CV) system.

The EdwardsSAPİEN System consists of a trileaflet pericardial bovine valve mounted in a stainless steel,and it is available in three sizes: 23 mm, 26 mm and 29 mm for transfemoral, transapical and subclavian approaches [Fig1]. The third generation SAPİEN XT calve is available in 20 mm, 23 mm, and 29 mm sizes and is introduced via an 18 F sheath.

The CoreValve ReValving System consist of three porcine pericardial leaflets mounted in a self expandable nitinol frame housed within a percutaneus delivery catheter. This system is available two sizes, 26 mm and 29 mm. The valve is introduced via an 18 F sheath [Fig 2].

Balloon aortic valvuloplasty is systematically performed before valve implantation to facilitate passage of the prosthesis through the stenotic native valve. Although, Grube at al. have suggested direct implantation of the CoreValve system with no prior balloon valvuloplasty [72]. The balloon expandable valve is positioned using fluoroscopy and echocardiography, and ventricular burst pacing is used at balloon inflation to decrease transvalvular flow and avoid expulsion of the system toward the aorta. The self-expandable valve is deployed without burst pacing, by the retracting the outer sheath of the delivery catheter.

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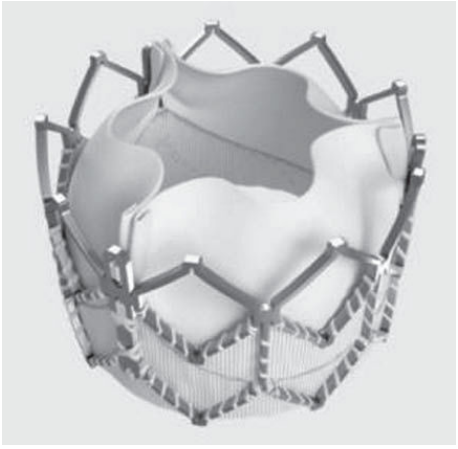

Figure 1. The EDWARS SAPİEN system

Figure 2. The CoreValve ReValving System

5. Outcomes

Overall, the procedural success rate was >90% in all studies. Valve embolization or conversion to open heart surgery occurred in ~1% of the patients (0.3–3.0% for valve embolization; 0.5–2.3% for conversion to open heart surgery) [73].

5.1. Mortality

In the multicenter registries and series, mortality was systematically <10% in patients treated using the transfemoral approach and ranged from 11.3% to 16.9% in patients treated using the transapical approach, probably owing to the higher risk profile of the patients treated via the latter route [73-74].At 1-year follow-up, the survival rates were ~80% (75–85%) for the transfemoral approach and ~70% (63–78%) for the transapical approach.

As the first of two parallel trials was completed, the results of PARTNER IB showed that TF TAVI was superior to standard therapy in patients not deemed candidates for surgery [73]. The primary endpoint of all-cause mortality was markedly reduced by 46% (P, 0.001). Recently reported 2-year outcomes showed continued encouraging results. At 2 years, the primary endpoint of all-cause mortality was reduced from 67.6% in the standard treatment arm to 43.3% in the TAVI arm (P, 0.001). The PARTNER cohort IA compared TAVI with SAVR and met its non-inferiority endpoint: the all-cause 1-year mortality in the TAVI group was non-inferior to the SAVR group (24.2 vs. 26.8%;P: 0.44; P: 0.001 for non-inferiority) [74]. Some concerns were raised with regard to neurologic events that were somewhat higher with TAVI than SAVR at 30 days (5.5 vs. 2.4%; P: 0.04) and 1 year (8.3 vs. 4.3%; P: 0.04). Although the recently published 2-year results showed that stroke rates were similar for TAVI and SAVR during 1 and 2 years with a hazard ratio of 1.22 (95% CI 0.67–2.23, P: 0.52), the issue of stroke warrants further investigation and should not be underestimated The rate of the composite of all-cause death and stroke was encouragingly nearly identical after TAVI (37.1%) and SAVR (36.4%) at 2 years (P: 0.85)[73-74]

Predictors of mortality — Risk factors for early and late mortality were identified in a study of 663 patients undergoing TAVR with CoreValve. Intraprocedural mortality was 0.9 percent. Mortality was 5.4 percent at 30 days and 15 percent at one year. Independent predictors of mortality at 30 days included certain procedural complications (conversion to open heart surgery, cardiac tamponade, major vascular or access site complications) as well as baseline characteristics (left ventricular ejection fraction <40 percent, prior balloon valvuloplasty, and diabetes mellitus). Independent predictors of mortality between 30 days and one year included prior stroke, postprocedural paravalvular leak ≥2+, prior acute pulmonary edema, and chronic kidney disease.

Indeed, in the past few years, 1-year survival rates from some registries have been reported to be ≥80%, and we can expect better survival rates at the 2-year and 3-year follow-ups in the coming years. Importantly, no structural failures of the transcatheter valves have been seen in studies with a follow-up of more than 1 year [73-74].

In addition to baseline and procedural factors, the learning-curve phenomenon and the improvements in valve prosthesis and delivery catheters have also been associated with a substantial improvement in the results obtained with TAVI.

5.2. Symptom improvement

Three-year follow-up data have been published and are consistent with lasting improvement in cardiac symptoms [72]. While 86% of patients were in NYHA class III or IV at baseline, 93%

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of surviving patients were in NYHA class I/II at 3-year follow-up. Similarly, the PARTNER trial showed that patients treated with TAVI compared with patients treated with standard medical therapy have better symptom control at 1 year. Indeed, the 1-year rate of NYHA class III or IV was 25.2% for the TAVI group compared with 58.0% for the standard medical therapy group (P, 0.001).

6. Complications

Stroke: The occurrence of stroke is one of the most –fearing complication of TAVI. The most frequent etiology of procedural stroke is likely to be atheroembolism from the ascending aorta or the aortic arh. Other several factors include manipulation of a wire, positioning of device, performance of the balloon aortic valvuloplasty, air embolism, dissection of the arc vessels and inadequate blood flow to brain during rapid pacing. Reported 30 day stroke rate was 3.5 (ranging from 1.2% to 6.7%) [76]. Additionaly Kahlert et al observed that using diffusion-weighed MRI has underlined this issue, demonstrating multiple embolic cerebral lesion in all patients after TAVI. Although most of these lesions were clinically silent, silent cerebral infarcts are associated with subtle cognitive change. Efforts have been directed towards prevention of stroke. Procedural anticoagulation to reach a target activated clotting time over 250 s is suggested. Empiric dual antiplatelet therapy is recommended for 3 to 6 months followed by long-term daily low dose aspirin. Additionally less traumatic valve delivery system and embolic protection devices (Embrella embolic deflector system) currently under devolepment might lower the risk of stroke. However some authors have suggested that stroke risk might be lower with transapical access, this has not been a universal finding.

Vascular Complication: Common vascular complication arterial dissection, closure device failure, arterial stenosis, haematoma in the accsess site. Artery avulsion, vessel perforation, annulus rupture represent more severe complications which are fatal if not rapidly treated. In the SOURCE registry, 10.6 % of patients had major vascular complication and major vascular complications were less frequent in the transapical approach (2.4 %) [73-74]. Small vessel diameter, severe atherosclerosis, bulky calcification, and tortusosity are the main determinats of vascular complications. In the future delivery catheter and sheath size will likely decrease which should be associated with reductions in the risk of vascular injury. Additionally, for patients with unsuitable access, alternatives include apical, axillar/subclavian or transaortic approaches, or treatment of iliofemoral lesion with stents or grafts.

Coronary obstruction and myocardial infarction: Coronary ostia obstruction (especially of the left main coronary artery) might occur if an obstructive portion of the valve frame or the sealing cuff is placed directly over a coronary ostium however this is very rare but potentially fatal event [77]. Some cases may require immediate coronary angioplasty or coronary artery bypass graft operation. TAVI has been associated with a variable rate of myocardial infarction, ranging from 0% to 16.3% [73-74] Myocardial infarction could be explained by myocardial tissue compression, hypotension due to rapid pacing, atheroembolism and mechanic complication such as coronary ostia obstruction. Additionally myocardial infarction was associated with an increased cardiac mortality at midterm follow up

Heart Block: High grade atrioventricular block and consecutive pacemaker implantation are frequent (especially in CoreValve) complications following TAVI. CoreValve implantation is associated with a need for permanent pacemaker in 20 % of patients compared with in 5 % of patients implanted with the balloon expandable valves [78]. Potential risk factors include aggressive over sizing, low implantation of the prosthesis, small annulus diameter, using CoreValve and the presence of preexisting infranodal block such as RBBB [79, 80].

Cardiogenic Schock and low cardiac output: This complication may be induced by ischemia, rapid pacing, volume depletion, anesthesia and interruption in cardiac output during valve implantation. Vasopresor agents and intraaortic balloon support to maintain adequate perfusion pressure are often helpful. Rarely elective femoral cardiopulmonary bypass is an option for patients at hemodynamic instability.

Paravalvuler Regurgitation: However paravalvuler aortic regurgitation is common, occurring in about 85 %, Grade > 2 + regurgitation is found in 7-24 % [72,73].Trivial, mild and even moderate degrees of regurgitation seem well tolerated, although grade > 2+ regurgitation associated with increased short and long term mortality [81]. Causes of paravalvular regurgitation include a heavily calcified annulus,large annulus size, an undersized prosthesis, device failure and inadequate balloon aortic valvuloplasty. Redilatation or implantation of a second, overlapping transcathater valve can often correct the problem.

Acute Kidney Injury: Angiographic contrast injection, hypotension, atheroembolism, periprocedural blood transfusion might contribute to acute renal failure. The incidence of acute kidney injury after TAVI has been reported with incidence of 8 %. Additionally need for hemodialysis has ranged from 1.4% to 15.7 %, respectively [82]. Predictors of acute kidney injury include hypertension, decrease baseline renal function, previous myocardial infarction, high logistic EuroSCORE and chronic obstructive pulmonary disease [83].

Other Complication: Other significant and very rare complications include aortic rupture, aortic dissection, periaortic hematoma, ventricular or aortic embolization of valve, structural valve failure, cardiac tamponade and acute mitral regurgitation due to mitral valve apparatus damage [73-74].

Valve-in-valve — A valve-in-valve procedure involves catheter-based valve implantation inside an already implanted bioprosthetic valve. This approach may provide an alternative to replacement of a degenerated surgically-implanted valve, or a means of salvaging suboptimal implantation of a catheter-based valve during the initial implantation procedure.

Conclusion: Despite continual technical advancement of TAVI devices and procedures, the combined mortality and morbidity is still high in the range of 5-10%, especially when we are facing a group of high surgical risk patients. In addition TAVR offered no survival benefit compared to standard therapy in patients with an STS score of > 15 % because of high degree of comorbid conditions in these patients. In the future when it is a safer and more reliable procedure and further refinement of the device (i.e. smaller size delivery systems and multiple valve size options) is done, utilization of the procedure in patients with lower surgical risk may be possible.

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7. Surgery

In 1912, Theodore Tuffier was the first to attempt opening AS using his finger. Russel Brock and then Bailey used dilatators for stenotic aortic valves. Today more than 1000 patients have aortic valve surgery per year and surgery for AS is more common than it is for aortic insufficiency [84]. Aortic valve surgery has been improved with the developments of new technologies in cardiopulmonary bypass techniques and valve industry. Approximately 2% to 5% of elderly individuals aged 75 years present with signs of severe AS and they are scheduled for elective AVR. AVR is the treatment of choice for patients with severe degenerative AS, offering both symptomatic relief and a potential for improved long term survival [85].

It's obvious that AVR is indicated in all symptomatic patients and asymptomatic patients with severe AS undergoing open heart surgery. The surgery should immediately be programmed if the patient becomes symptomatic. Despite LV dysfunction, the risk of aortic valve replacement for AS was satisfactory and related to meanaortic gradient and additional coronary artery disease, and long-term survival was related to also coronary disease and cardiac output [86].

5-year survival for adults after aortic valve replacement is 80-90%. The results of the conventional surgery for octogenarians are also satisfactory and 5% to 10% of mortality is noted for isolated AVR (2). On the other hand, elderly patients stay longer in the hospitals and intensive care units during the postoperative period [87]. United Kingdom heart valve registry observed 1100 elderly patients (56% women) who underwent AVR that the 30-day mortality was 6.6% [88]. The actuarial survival was 89% at 1 year, 79% at 3 years, 69% at 5 years, and 46% at 8 years. The mortality is rising up to 10% per year for the patient becoming symptomatic. The indications for AVR in patients with AS according to the current ACC/AHA guidelines are listed in Table 2 [89]. Although the surgery for the asymptomatic patients is preferred due to sudden death, surgery for asymptomatic octogenarians is controversial. The complex cardiac procedures have high risks for elderly patients.

The mortality rate of valve surgery and risk of sudden death without surgery have to be carefully considered. Postoperatively symptoms diminish and quality of life is improved in the majority of patients ≥75 years who had undergone aortic valve surgery, but long term survival was not affected [90].

AVR usually performed under general anesthesia using conventional techniques of open heart surgery with median sternotomy. Minimally invasive surgery has continued to be an evolving concept after the first publication of Cosgrove in 1996 [91] Minimally invasive procedures are associated with acceptable mortality and morbidity rates even in high risk patients. 30-day in-hospital mortality was 0.8% for 1,103 minimally invasive aortic valve procedures [92].

The major advantages of minimally access surgeries are improved cosmesis with reduced insicion size, decreased surgical trauma, less pain, better respiratory function and early return to work [92].

These procedures can be performed through different approaches. These are upper mini sternotomy, transverse sternotomy and right parasternal or anterolateral mini thoracotomy,

Class I
AVR is indicated for symptomatic patients with severeAS.* *(Level of Evidence: B)*
AVR is indicated for patientswith severe AS* undergoing coronaryartery bypass graft surgery(CABG). *(Level of Evidence: C)*
AVR is indicated for patientswith severe AS* undergoing surgeryon the aorta or other heartvalves. *(Level of Evidence: C)*
AVR is recommended for patientswith severe AS* and LV systolicdysfunction (ejection fractionless than 0.50). *(Level of Evidence: C)*
Class IIa
AVR is reasonable for patients with moderate AS*undergoingCABG or surgery on the aorta or other heart valves(see Section3.7 on combined multiple valve disease and Section10.4 on AVRin patients undergoing CABG). *(Level of Evidence: B)*
Class IIb
AVR may be considered for asymptomatic patientswith severeAS* and abnormal response to exercise (e.g., developmentofsymptoms or asymptomatic hypotension). *(Level of Evidence: C)*
AVR may be considered for adults with severe asymptomaticAS* if there is a high likelihood of rapid progression (age,calcification, and CAD) or if surgery might be delayed at thetime of symptom onset. *(Level of Evidence: C)*
AVR may beconsidered in patients undergoing CABG who havemild AS* whenthere is evidence, such as moderate to severevalve calcification,that progression may be rapid. *(Level of Evidence: C)*
AVRmay be considered for asymptomatic patients with extremelysevereAS (aortic valve area less than 0.6 cm^2, mean gradientgreaterthan 60 mm Hg, and jet velocity greater than 5.0 m persecond)when the patient's expected operative mortalityis 1.0%or less. *(Level of Evidence: C)*
Class III
AVR is not useful for the prevention of sudden deathin asymptomaticpatients with AS who have none of the findingslisted underthe class IIa/IIb recommendations. *(Level of Evidence: B)*

Table 2. Indications for Aortic Valve Replacement.

using port access technique or not. Although mini sternotomy is the most common approach, the outcomes after right anterior thoracotomy have satisfactory results [93]. The arterial cannulation sites are either aorta or femoral artery. The venous cannulation sites are right atrium, femoral vein or percutanous supeior vena cava with femoral vein. The incisions differ from 5 to 10 cm and small incisions may provide low infection rates [94]. This procedure has advantages such as less 1 surgical trauma, decreased pain and faster recovery. It reduces blood transfusions and shortens the length of hospital and ICU stay [95]. It is a safe operation and results lower incidence of atelectasis inthe cardiac ICU [96]. Port access aortic surgery also allows patients to be extubated earlier [97]. Avoidance of full sternotomy for patients prompts a comfortable postoperative period. Although the number of the aortic valve procedures increase worldwide, the ideal valve choice is still a debate. There are several options for valves. These are mechanical valve prosthesis, stented and stentless bioprosthetic valves, aortic homograft and pulmonary autograft. The use of these valves differs from patient to patient due to comorbidities and anticoagulant needs. The bioprosthetic valves are good alternatives

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for elderly patients and women who want to be pregnant because long term anticoagulation use is not required. The other situation for the patients undergoing AVR is the injurious effects of Cardiopulmonary bypass to the life organs. This results as a systemic inflammatory response and this may affect the post-operative course of the patients. Paroxysmal or chronic AF is a risk factor for mortality in patients with severe AS and a LVEF <35% undergoing AVR. Of 83 elderly patients with severe AS and an LVEF <35%, 29 (35%) had paroxysmal or chronic AF [86]. The perioperative mortality was 24% in the group with AF versus 5,5% in the group without AF.

The Ross procedure is another surgical technique for aortic valve replacement. This is more commonly used in pediatric cases but also good alternative for especially young adult patients and women want have child. In this operation the patient's own pulmonary valve and main pulmonary artery are used as an autograft and they are implanted to the aortic position, with reimplantation of coronary arteries.

The primary indication for the Ross procedure is to provide a permanent valve replacement among younger patients who will grow potentially. Other possible indications include complex left ventricular outflow obstructive disease, native or prosthetic valve endocarditis, and adult aortic insufficiency with a dilated aortic annulus [98].

One of the most commonly seen complications of Ross procedure is autograft regurgitation and sinus or ascending aortic dilatation, which can usually be corrected with a valve-sparing root replacement. In a study 212 patients underwent Ross aortic valve replacement; 51% were older than 19 years old. There were just 2 early deaths. At 15 years, freedom from autograft sinus or ascending aortic dilatation was 79%, autograft dysfunction, 91%. And actuarial survival was 98% [99].

Recent years aortic valve repair also become popular when valve morphology is amenable to repair. But this is a limited procedure among patients who have aortic regurgitation (AR) without aortic stenosis. Aortic valve repair is commonly indicated commonly in patients with a dilated aortic annulus without any degeneration of the leaflets [100]

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