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Geriatric Aspects of 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. Aortic stenosis (AS) is a common and important condition among the elderly.

2. Etiology and prevalence

Currently, AS is the most frequent heart valve disease in industrialized countries and its prevalence sharply increases with age (Iung et al., 2003; Nkomo et al., 2006). Thus with the prolongation of life expectancy, the population of old patients with AS is expected to grow in the future. In elderly patients AS is most frequently caused by progressive calcification and degeneration of the tricuspid aortic cusps (Otto et al., 1997; Lindroos et al., 1994). The commissures are not fused as in rheumatic AS. Traditionally, AS has been thought of as a passive degenerative "wear and tear" disease associated with aging. Certain clinical factors like coronary artery disease (CAD), hypertension, obesity, diabetes mellitus, smoking, hyperlipidemia and chronic kidney disease (CKD) are associated with AS. However, the studies of Otto CM et al. support that the histopathological property of calcific aortic valve disease represents an active process with some similarities to atherosclerosis, including lipid deposition, macrophage and T cell infiltration, basement membrane disruption and microscopic calcification (Otto et al., 1994). Both AS and atherosclerosis have many clinical risk factors in common such as diabetes mellitus, hypertension, dyslipidemia, CKD, and tobacco use. (Peltier et al., 2003). Ortlepp JR et al observed that genetic factors may be important in the development of valve calcification (Ortlepp et al., 2001). They showed that patients with AS had significant difference in vitamin D receptor genotypes compared to individuals without AS.

The research of Stewart Bf et al. revealed that in 5201 men and women older than 65 years, 26% of study participants had frank aortic sclerosis (thickening of or calcific deposits on the aortic valve cusps with a peak velocity across the aortic valve of <1.5 msn) (Stewart et al., 1997). In the initial stages, aortic sclerosis is present without stenosis, but as the disease advances the valve leaflets which become less mobile eventually fuse together and cause left ventricular outflow tract (LVOT) obstruction. The study by Cosmi JE et al., in which more than 2000 patients with aortic sclerosis were examined, %16 developed AS (Cosmi et al., 2002). Of these patients mild, moderate and severe AS developed in 10.5, 3, and 2.5%

respectively. This cohort study showed that the average time interval of aortic sclerosis to AS was 8 years.

Other causes of AS in the elderly include rheumatic aortic valve disease (always occurs in conjunction with mitral valve involvement) and late degeneration of congenital bicuspid valves (Beppu et al., 1993; Pachulski et al., 1993). Congenital bicuspid valve anomaly accounts for about one fourth of AS in patients older 70 than years (Passik et al., 1987).

3. Pathophysiology

Regardless of the etiology, AS results in obstruction of LVOT. Obstruction of the LVOT leads to concentric hypertrophy (increase in LV wall thickness and mass) which normalizes systolic wall stress and maintains normal LV ejection fraction (LVEF) and cardiac output (Kennedy et al., 1968; Hood et al., 1968). Although hypertrophy helps to preserve ejection performance, it leads to abnormal LV compliance, LV diastolic dysfunction with reduced LV diastolic filling, increased LV end diastolic pressure and is associated with increased mortality (Levy et al., 1990; Zile et al., 2002). As the left ventricle becomes less compliant, atrial systole becomes more important for maintaining cardiac output, and onset of atrial fibrillation (AF) may result in clinical worsening and ventricular decompensation. The increases in systolic blood pressure, ventricular mass and ejection time lead to increased consumption of oxygen by the myocardium. Increased oxygen demand by the hypertrophic myocardium and abnormal patterns of coronary flow lead to angina pectoris in AS (Gould et al., 1997; Julius et al., 1997; Villari et al., 1992). Coexisting coronary disease is common with significant coronary narrowing in about 50% of elderly patients with AS (Georeeson et al., 1990). The increase in oxygen consumption and its contribution to decreased myocardial ischemia cause further deterioration of LV function. The stroke volume and cardiac output decrease and the mean left atrial and pulmonary capillary pressures increase and pulmonary hypertension occurs. This stage usually coincides with the occurrence of severe stenosis and the onset of symptoms. Several mechanisms have been postulated to explain the third cardinal symptom of AS, syncope. Although ventricular arrhythmias, bradyarrhythmias and left ventricular systolic dysfunction have been proposed, most of the data suggests that an acute drop in blood pressure caused by inappropriate LV baroreceptor response because of increased LV pressures (Johnson et al., 1971; Richards et al., 1984).

4. Natural history

The patient with AS is generally asymptomatic for a prolonged period despite the obstruction and increased pressure load on the heart. Adults with asymptomatic AS have an excellent clinical outcome, indistinguishable from age-matched controls without aortic valve disease. It was estimated that sudden cardiac death accounted for 3-5% of all deaths in patients with asymptomatic AS (Braunwald, 1990). Hemodynamic progression in patients with AS has an average rate of increase in aortic jet velocity of 0.3 m/s per year, with an increase in mean transaortic pressure gradient of 7 mmHg per year and decrease in aortic valve area (AVA) of 0.1 cm² per year (Otto et al., 1989; Faggiano et al., 1996). However there is a wide range of hemodynamic progression among the patients with AS. Predictors of symptom onset in two studies included baseline jet velocity, the rate of change in jet velocity over time, the extent of valvular calcification, and functional status (Otto et al., 1997;

Rosenhek et al., 2000). The prognosis changes dramatically with the onset of symptoms of angina, syncope, or heart failure (HF) after a long latent period. The development of symptoms is a critical point in the natural history of AS. Older adults, who typically have decreased activity levels, experience delayed onset of clinical symptoms or they tend to relate their symptoms to other coexisting conditions. Ross and Braunwald found that the average survival after the onset of angina pectoris, syncope and HF was 3, 3 and 1.5-2 years respectively (Ross & Braunwald, 1968). In the study of Bouma et al., non-operated elderly patients with severe AS had a wide range of survival rates (Bouma et al., 1999). In this study, the three poor prognostic factors were a New York Heart Association (NYHA) functional class of III-IV, coexisting mitral regurgitation, and left ventricular systolic dysfunction. Survival was particularly poor (20% at 3 years) in the presence of NYHA III-IV symptoms and impaired left ventricle systolic function. The presence of AS in older adults increases their risk of having myocardial infarction and cardiovascular death (Aronow et al., 1998). Additional comorbidities which also affect survival are frequent in elderly patients with AS.

5. Symptoms

The cardinal manifestations of acquired AS are angina pectoris, syncope, and ultimately HF. Aronow et al. observed that in elderly patients, HF, syncope, or angina pectoris was present in 90%, 69% and 27% of patients with severe, moderate and mild AS respectively (Aronow et al., 1998). In the elderly, a clear description of the symptoms and their onset may be difficult to obtain. Most common initial symptom in the elderly is impaired exercise tolerance, exertional dyspnea and dizziness. In elderly symptoms of chest pain, shortness of breath, exercise intolerance, and dizziness are common and have many other potential causes, so that AS is generally not considered in the differential diagnosis. Symptoms may be absent in inactive elderly patient or may not be elicited from a patient with memory impairment. Establishment of symptomatic status and the severity of valvular disease can be troublesome because of subjectivity of symptom assessment and ambiguity of individual functional capacity in elderly (Sciomer et al., 2004). Concordantly, significant AS is underdiagnosed in the elderly.

Some patients may experience severe gastrointestinal bleeding secondary to angiodysplasia in association with AS (Heyde Syndrome, Bhutani et al., 1995). Infective endocarditis is less common in elderly patients with severe AS than in younger patients because endocardial surface is more calcific in the elderly. Endocarditic vegetations, AF and aortic atheromas represent important causes of systemic embolism including stroke in the elderly patients (Furberg et al., 1994; Tunick et al., 1994). Rarely, fragments of the calcific valve may embolize into the systemic circulation. Sudden death rarely occurs in asymptomatic patients. In the presurgical era, the incidence of sudden death in patients with symptomatic AS was estimated to be as high as 15-20% (Ross, 1968). Nowadays these rates decreased due to early surgical intervention in patients with symptomatic AS.

6. Signs

AS is often diagnosed after a systolic murmur elicited on physical examination necessitates an echocardiographic examination. Signs of AS include systolic ejection crescendo-decrescendo murmur that radiates to the neck and is often accompanied by a thrill. However, the murmur may radiate to the apex instead of the carotid in elderly patients

with AS (Gallavardin phenomenon). A prominent fourth heart sound (S_4) follows atrial systole in patients with sinus rhythm and noncompliant left ventricle. In the elderly, S_4 is less specific for AS, because hypertension, CAD, and other disorders which are common in older individuals can diminish left ventricular compliance (Lombard et al., 1987). In this setting, the physical examination findings of a soft murmur with an early peak, an upstroke of carotid impulse with normal timing, and a split second heart sound (S_2) suggest that mild or moderate AS is present. In a prospective study, carotid upstroke delay and amplitude, systolic murmur grade and peak, and a single S_2 predicted AS severity and clinical outcomes of death and symptom onset (Munt et al., 1999). On multivariate Cox regression analysis, the only physical examination finding which predicted the outcome was carotid upstroke amplitude. But most elderly patients with severe valve obstruction have only grade 2 or grade 3 murmur and some have an even softer murmur despite severe disease because of presence of concomitant HF or chronic lung disease (Lombard et al., 1987; Otto et al., 1997). The pulse pressure may be normal, or even wide, and the carotid upstroke may be rapid in the elderly with severe stenosis due to concomitant atherosclerosis of the arterial tree (Otto et al., 1997). So a slow rising, low amplitude carotid pulse has a relatively high specificity, but a low sensitivity, for the presence of severe AS in the elderly. No single physical examination finding or a combination of findings has both a high sensitivity and specificity for detection of severe AS. Older adults have an absent A_2 component of the S_2 due to aortic valve leaflet calcification which predominates with increasing age. Elderly patients with severe AS and aortic regurgitation have an A_2 component of the S_2 , and in this situation, a soft diastolic murmur of aortic regurgitation may be heard.

7. Diagnostic tests

7.1 Electrocardiography

The ECG in patients with AS is not diagnostic. Findings of LVH are the most common findings on ECG in patients with severe AS. In the elderly patients, findings of LVH on ECG were seen in about two thirds of patients (Aronow et al., 1991). The voltage of the QRS complex may be markedly increased and ST-T wave changes which reflect chronic subendocardial ischemia are common. Other nonspecific signs include, left atrial enlargement, left axis deviation and left bundle branch block. AF can be seen at late stages and may otherwise suggest coexisting mitral valve disease or CAD.

7.2 Chest radiography

The chest radiography in AS is nonspecific. It is usually normal when AS is mild to moderate. Calcification the region of the aortic valve represents relevant chest radiography findings in the elderly, since calcific degeneration is the hallmark of AS in this age group. The radiographic features of compensated AS include concentric hypertrophy of the LV without cardiomegaly and poststenotic dilatation of the aorta. Of equal importance, the presence of cardiomegaly in a normotensive patient with isolated AS indicates decompensated AS.

7.3 Echocardiography

Doppler echocardiography is a cost-effective and accurate strategy to diagnose AS in the elderly (Otto et al., 1997). Echocardiography allows for the noninvasive assessment of the

valvular structures and the real time evaluation of its hemodynamic consequences. It assesses left-ventricular functions, extent of hypertrophy, and amount of valve calcification. Standard evaluation of AS severity includes measurement of aortic velocity, mean transaortic pressure gradient, and continuity equation valve area (Figure 1). Anatomic images show the etiology of AS, level of obstruction, valve calcification, leaflet motion and aortic root anatomy. Echocardiography is also used to determine diastolic dysfunction by the presence of abnormal left ventricular relaxation. The velocity of blood flow increases as the stenotic orifice area decreases. Velocity measurements can be translated into pressure gradients across the aortic valve by using the Bernoulli equation. Aortic velocity allows classification of stenosis as mild (2.6-3 m/s), moderate (3 to 4 m/s), or severe (>4m/s). In case of leaflet thickening and calcification, presence of adequate leaflet motion and a velocity of <2.5 m/s defines aortic sclerosis. A mean aortic valve gradient greater than 40 mmHg on Doppler echocardiography is indicative of severe AS.

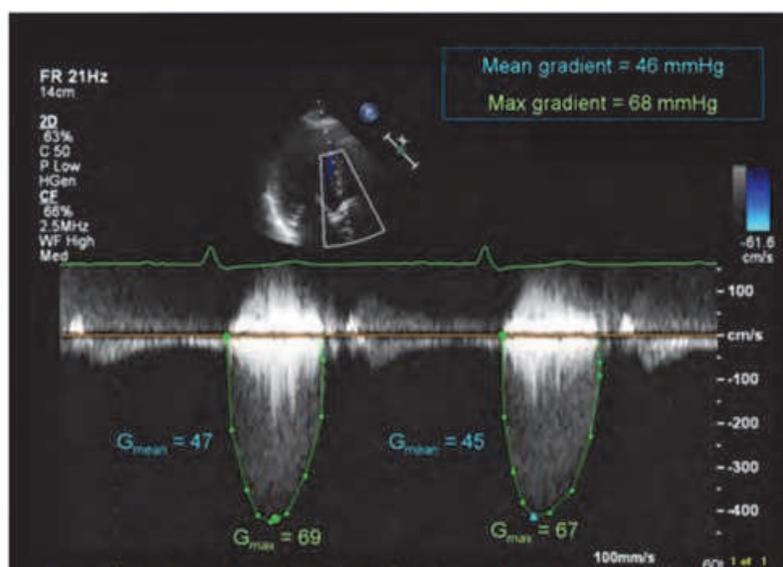


Fig. 1. To obtain the mean gradient, "trace" is used to trace the envelope of the aortic outflow. A mean aortic valve gradient greater than 40 mm Hg on Doppler echocardiography is indicative of severe AS.

The AVA can be estimated with the use of the continuity equation which depends on the principle of the law of continuity of flow (Carabello et al., 2003). Currently AS is graded as mild, moderate, and severe when the AVA is >1.5 cm², 1-1.5 cm², and <1 cm² respectively (Table 1). The most frequent error in measuring the AVA is due to the inaccuracy of LVOT diameter measurement. This is especially difficult in older adults in whom accumulation of calcium is present on the annulus. In order to avoid these errors some authorities suggest the use of dimensionless ratio for the assessment of AS. This index is simply the ratio of the velocity across the LVOT to the velocity across the aortic valve and completely eliminates the area of the LVOT from the equation (Otto et al., 2006). A ratio of 0.9-1 is accepted normal and a ratio of <0.25 indicates a valve area 25% of expected, corresponding to severe stenosis. Transesophageal echocardiography provides excellent short-axis images of the aortic valve, thus allows for direct measurement of the AVA by planimetry in many patients (Naqvi et al., 1999). Real time three dimensional transthoracic echocardiography offers an increased

confidence level in the direct measurement of AVA (Vengala et al., 2004). Dobutamine stress echocardiography is often useful to estimate AVA and gradient at a higher cardiac output. It is particularly useful in patients with moderate to severe AS with low gradient and depressed LVEF. Truly severe AS shows only small changes (an increase of $<0.2 \text{ cm}^2$) in AVA which remains $<1 \text{ cm}^2$ with increasing flow rate but significant increase in gradients (mean gradient $> 40 \text{ mmHg}$), whereas pseudosevere AS shows a marked increase in AVA with a final value of $> 1 \text{ cm}^2$ but only minor changes in gradients. Dobutamine stress echocardiography also provides evidence of myocardial contractile reserve (increase of $>20\%$ of stroke volume during low dose dobutamine administration) (Vahanian et al., 2007; Bonow et al., 2006). Echocardiography is recommended to be performed yearly in patients with severe AS, every 2 years in patients with moderate AS, and every 5 years in patients with mild AS.

	Mild	Moderate	Severe
AoV _{max} (m/s)	2.5-3.0	3.0-4.0	>4.0
Peak gradient (mmHg)	<40	40-65	>65
Mean gradient (mmHg)	<20	20-40 (50)*	>40 (50)*
EOA (cont eq) (cm ²)	>1.5	1.0-1.5	<1.0
EOAi (cm ² / m ²)	>0.85	0.60-0.85	<0.60
Dimensionless index	>0.50	0.25-0.50	<0.25

Table 1. Grading of aortic stenosis. *EAE guidelines only, otherwise both EAE and ASE.

7.4 Exercise testing

Severe AS is considered a contraindication for exercise testing (Ha, 2003). Nonetheless, in elderly patients with hemodynamically significant AS and ambiguous symptoms, exercise testing may be useful and safe if performed by an experienced physician. It is reasonable to perform the exercise testing in patients over 70 years if they are still highly active. In asymptomatic patients, this test also may determine the recommended level of physical activity.

7.5 Cardiac catheterization

Its principle goal is to assess the extent of concomitant CAD (which is common in the elderly) by angiography rather than to determine the hemodynamic severity of AS. The valve should almost never be crossed, because the risk of death, stroke, or pulmonary edema is 7% if the valve is crossed and 3% for coronary angiography (Chambes, 2004). If the clinical findings are not consistent with the Doppler echocardiographic results, cardiac catheterization is recommended for further hemodynamic assessment. Cardiac catheterization should consist of the simultaneous measurement of the pressures in the left ventricle and in the aorta, enabling the calculation of the mean gradient. A "pull-back" tracing from the left ventricle to the aorta may be used in patients with normal sinus rhythm but it is not accurate in patients with rhythm disturbances or low-output states. In elderly patients with tortuous vessels the pull back technique may be preferred to a second femoral puncture needed to obtain a proper LV and proximal aortic pressure recording.

7.6 Computer tomography (CT)

Electron beam CT has the ability to detect and quantify calcification in AS (Pohle, 2004). It also allows detection of calcifications in coronary vessels and assessment of the ascending aorta (Pohle et al., 2004; Bouma et al., 1999). CT has shown high accuracy and reproducibility in quantifying aortic valve calcification and its progression. In patients with inadequate and inconclusive echocardiogram, CT may be as an alternative to obtain AVA.

7.7 Magnetic Resonance Imaging (MRI)

Cardiac MRI may be used to assess LV volume, function and mass. MR planimetry is reported to be highly reproducible and well tolerated and the results correlate very well with TEE results (Anna et al., 2003). Cardiac MRI is useful when acoustic windows in the echocardiogram are poor or when there is discordant imaging and catheterization results. It may also be an alternative to CT in patients with increased risk of contrast nephropathy because of older age and diminished baseline glomerular filtration rate (GFR).

8. Medical treatment

When symptoms of angina, syncope, or HF develop in patients with AS, the prognosis dramatically worsens. AVR represents the only proven treatment modality for symptomatic and hemodynamically significant AS. Other treatments such as medical therapy and TAVI are still controversial and researches are on way. There is no effective medical treatment for AS. Although medical therapy is unlikely to prolong survival, it may provide limited symptomatic relief. Hemodynamically significant AS is adversely affected by changes in preload and afterload. Potentially, all drugs used in symptomatic patients may cause worsening of the patients' conditions. Therefore, in patients with severe AS, drugs that reduce preload or afterload should be used with caution. In addition, due to the fact that chronic renal failure, autonomic dysfunction, and rhythm and conduction disturbances are more frequently seen in the elderly, side effects of drugs may be more dangerous.

8.1 Statins

Lipids are known to have important role in development of fibrosis and calcification seen in AS. Therefore, the use of lipid lowering drugs, especially the statins are recommended. Various studies suggested that the use of statins may reduce or prevent the worsening of fibrosis and calcification in patients with AS especially when used in the early periods. However, the results of the studies are conflicting and the effects of statins on the course of disease are not clear. Findings of several retrospective studies and at least one prospective trial show that patients receiving statins have slower progression of stenosis severity than do individuals not receiving them.(Rajamannan & Otto, 2004; Novaro et al., 2001). However, in a randomized trial of patients with moderate AS, Cowell and colleagues failed to show a benefit of high dose statin use in terms of halting the progression of valvular stenosis or inducing its regression (Cowell et al., 2005). Although the use of statins in patients with valvular AS is controversial, statins should be used in patients with AS and atherosclerotic vascular disease (Rossebø et al., 2008).

8.2 Angiotensin converting enzyme inhibitors (ACEI)

When patients with severe AS who can not tolerate AVR develop left HF symptoms, the use of ACEI may provide improvement in symptoms. Similar to statins, ACEI have been suggested to slow the progression of calcific valvular stenosis, but this suggestion has not been confirmed by findings of prospective studies (Rosenhek et al., 2004). On the other hand, the use of ACEI in patients with severe AS may increase the transvalvular gradient by reducing afterload or preload and may cause sudden deterioration of the patients' status. ACEI treatment should be initiated at low doses and gradually increased, avoidance of hypotension is crucial especially in the elderly patients.

8.3 Beta blockers

Beta blockers are not recommended for routine use. Patients with symptoms and signs of HF are not good candidates for beta blocker treatment because beta blockers may aggravate the symptoms of HF. Beta blockers are recommended for patients who experience angina pectoris or have AF with rapid ventricular response.

8.4 Diuretics

Diuretics are recommended in patients with lung congestion, ascites and edema. Diuretics provide improvement in HF symptoms by reducing left ventricular end-diastolic pressure. Diuretics should be used with caution because a low preload may exacerbate symptoms due to low cardiac output. Elderly patients may not excrete free water as efficiently as younger people do, and they may be more prone to develop hyponatremia after diuretic treatment (Clark et al., 1994). Thiazide diuretics are more commonly associated with hyponatremia than loop diuretics (Hwang & Kim, 2010). Nocturia is frequently seen in elderly patients and disruption of normal circadian rhythm of antidiuretic hormone may be an important factor in this issue (Moon et al., 2004). Elderly patients are also more prone to diuretic induced hyponatremia, because concomitant use of other medications like selective serotonin reuptake inhibitors (SSRI), which may precipitate hyponatremia, is common. Diuretics also lead to orthostatic hypotension by inducing volume depletion. Because falls are more frequent and are associated with greater morbidity and mortality in the elderly patients, monitoring of blood pressure at home and avoidance of hypotension is crucial. Evening and night doses of diuretics are also associated with more frequent nocturia and may increase the risk of falls during night. Thus, administration of diuretics in earlier hours may be safer.

8.5 Nitrates

Nitrates may be used in patients with severe AS who experience angina pectoris. Because it may cause sudden hypotension, it should be initiated at low doses and gradually increased. Concomitant use of nitrates with phosphodiesterase inhibitors, which are commonly used in the elderly patients with erectile dysfunction, should be avoided to prevent substantial hypotension.

8.6 Digoxin

Digoxin has a narrow therapeutic index and elderly patients may be more prone to side effects associated with its use (Cheng & Nayar, 2009). Digoxin is eliminated by the kidneys and impairment of kidney functions with aging is an important issue in this context. The recent ACC/AHA guideline recommends an initial dose of 0.125 mg daily or every other

day if the patient is more than 70 years old, has impaired kidney function, or has a low lean body mass (Hunt et al., 2009). Using a target drug concentration of 0.5-1 ng/ml is recommended despite conventional therapeutic serum concentration is defined as 0.8-2 ng/ml (Hunt et al., 2009). A digoxin concentration above 1 ng/ml may not be more effective in terms of symptomatic relief and may potentially be associated with increased morbidity and mortality (Cheng & Nayar, 2009; Hunt et al., 2009). When hypokalemia, hypomagnesemia or hypothyroidism coexists, digoxin toxicity may occur with lower digoxin concentrations (Hunt et al., 2009). Elderly patients may also be more prone to develop adverse effects of digoxin like anorexia, nausea, vomiting, confusion, visual problems, and rhythm and conduction disturbances (Cheng & Nayar, 2009). Concomitant use of drugs which may interact with digoxin may also be common in the elderly. In this context, clarithromycin, erythromycin, amiodarone, itraconazole, cyclosporine, verapamil, and quinidine can increase serum digoxin concentrations (Hunt et al., 2009). The use of digoxin is contraindicated in patients with severe AS and sinus rhythm. When AF with rapid ventricular response and hemodynamic deterioration is present, digoxin may be used to reduce the ventricular rate. Because beta blockers improve survival in patients with HF and may effectively control heart rate alone, digoxin which is associated with aforementioned potential harms, should be used with caution as an adjunctive agent for heart rate control.

9. Perioperative evaluation and management

9.1 Evaluation and management

Decision to identify patients who are at high risk for cardiac surgery is cumbersome. This issue may be further complicated in the elderly. 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 (Ambler et al., 2005). 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 (Nashef et al., 1999). An online calculator is available in their official website (<http://www.euroscore.org/>). 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/>). Recent data indicates that these scores may also predict hospital charges and resource use (Arnaoutakis et al., 2011). These risk score algorithms are widely used and validated, but they are not perfect and have many limitations (Rosenhek et al., 2011). Elderly patients above 75 years old constituted a small proportion of the cohorts used in these risk scores, thus extrapolation of these results to frail elderly patients who are generally above 75 years old may not give accurate results. In this context, a recent study which involved 1245 elderly patients (mean age 77.2 years)

who underwent AVR with or without additional bypass surgery, suggested that among these three risk scores, only STS-PROM was correlated with operative mortality (Frilling et al., 2010). The authors emphasized that risk scores aimed specifically at geriatric patients might be necessary to accurately identify patients with high surgical risk. These scores have mainly been validated in patients undergoing CABG surgery, compromising their accuracy in patients undergoing heart valve replacement surgery (Rosenhek et al., 2011). Comorbidities not included in these algorithms may increase the risk of surgery. Rosenhek et al suggest necessity of including additional variables like cognitive and functional capacity to the risk assessment tools (Rosenhek et al., 2011). Moreover, the weighting of the risk factors are variable between these algorithms. For example, EuroSCORE includes a cutoff point for creatinine (200 $\mu\text{mol/L}$), which means a creatinine level above this level increases the risk, whereas a lower level does not increase the risk. This suggestion has two limitations. First, a creatinine level above this threshold in a 65 year old male who weights 90 kg may suggest a better renal function than a creatinine level below this level in an 85 year old female who weights 50 kg. Furthermore, the creatinine level may not reflect glomerular filtration rate (GFR) accurately in a slim and sarcopenic elderly patient. Pulmonary arterial systolic pressure is also categorized in a binary fashion, thus decreasing the value of this important risk factor in this scoring system. STS-PROM does not use a cutoff for creatinine level and utilizes creatinine level as a continuous variable. However, the muscle mass is an important determinant of creatinine levels. A low muscle mass may actually represent a poor prognostic factor while it would be associated with a lower creatinine level, thus decreasing the STS-PROM risk score. Using more accurate estimations of GFR like Cockcroft-Gault formula may give more important prognostic information. Cystatin C which is not influenced by muscle mass may potentially reflect GFR more accurately and its level increase in earlier stages of kidney insufficiency compared to creatinine. However, there are limitations with measurement techniques of cystatin C and estimation of GFR by cystatin C levels is not standardized because there are many cystatin C based formulas to estimate GFR. The physiologic changes associated with aging should always be considered. A comprehensive geriatric assessment would also provide invaluable information in the preoperative evaluation and postoperative follow up of the elderly patients.

Morbidity and mortality rates may also be influenced by other factors like experience of the surgeon and the center (Rosenhek et al., 2011). Thus it would be logical to compare local outcomes with those predicted by the risk scores. Nonetheless, the decision of an experienced physician or of a specialized team may be more accurate than the risk scores. A recent trial which utilized STS-PROM, presence of pulmonary hypertension, presence of porcelain aorta and the decision of the medical team that the patient is frail as the criteria to decide a patient is inoperable and to enroll them to TAVI procedures (Rodés-Cabau et al., 2010). They suggested that frail patients even with a low STS-PROM score had increased risk. Although the decision of an experienced medical team that a patient is frail may be accurate, usage of widely used criteria to identify frailty may be more accurate and enable utilization of frailty as a risk factor in the preoperative evaluation in a standardized manner.

Brain natriuretic peptide (BNP) is widely used for prognostic prediction in heart diseases. BNP is higher in symptomatic patients compared to asymptomatic patients (Carabello & Paulus, 2009). BNP may also predict onset of symptoms when elevated values are found in

an asymptomatic patient and facilitate advising surgery to an asymptomatic patient with AS (Carabello & Paulus, 2009). Recently Monin et al. followed up 107 asymptomatic patients with moderate to severe AS to predict death or need for AVR and to build a continuous risk score using the independent predictors of this outcome (Monin et al., 2009). One of the most powerful predictors of outcome was BNP in this study. BNP levels were shown to predict postoperative survival and complications (Bergler-Klein et al., 2004; Nozohoor et al., 2009; Pedrazzini et al., 2008). Limitations of utilizing BNP include absence of a standardized cutoff for prediction of outcome in AS, interference of the predictive value of BNP with presence of renal dysfunction, pulmonary hypertension and obesity (Carabello & Paulus, 2009). Unlike BNP, amino terminal-proBNP levels may increase significantly when renal dysfunction exists, thus it seems more suitable to use BNP levels in patients with renal dysfunction (Tagore et al., 2008). Bernstein et al. suggest adjustment of proBNP levels with a formula utilizing estimated GFR level and age (Bernstein et al., 2009).

Sündermann et al. utilized a comprehensive assessment of frailty (CAF) score to predict outcomes after cardiac interventions (CABG, valve surgery, TAVI or combined procedures) in 400 patients aged ≥ 74 years (Sündermann et al., 2011). This score integrated weakness assessed with grip strength, self-reported exhaustion assessed with a questionnaire, slowness of gait speed measured with 4 meter usual gait speed test, activity level evaluated by instrumental activities of daily living, standing balance, body control, forced expiratory volume in 1 s, and levels of albumin, creatinine, and BNP. Although the variables were used in a binary fashion in this study CAF score was found to be correlated with EuroSCORE and STS-PROM scores and also predicted 30-day mortality.

A recent study which investigated influence of preoperative LV diastolic functions on development of postoperative LV systolic dysfunction showed that besides advanced age and prolonged myocardial ischemic time, preoperative LV diastolic dysfunction was also an important determinant of LV systolic dysfunction after AVR operation (Licker et al., 2010). Another recent study assessed presence and degree of myocardial fibrosis on the outcomes after AVR (Weidemann et al., 2009). Intraoperative myocardial biopsy and preoperative and postoperative cardiac MRI were used to assess myocardial fibrosis in this study. They found a significant correlation of myocardial fibrosis with NHYA class and markers of longitudinal systolic function but not with global ejection fraction or aortic valve area. They found significant correlations between the presence and degree of myocardial fibrosis and clinical outcomes. Another recent study evaluated the influence of preoperative illness beliefs on postoperative disability, physical functioning, psychological well being and depressive symptoms (Juergens et al., 2010). Postoperative outcomes were correlated with patients' preoperative beliefs but not with cardiac risk factors used in this study (EuroSCORE and LVEF).

Spirometric pulmonary functions were assessed preoperatively in a recent trial and percentage of predictive forced vital capacity was found to be an independent predictor of in-hospital mortality, even when adjusted for the logistic EuroSCORE (Nissinen et al., 2009). They also suggested that this parameter was an independent predictor of postoperative stroke.

Preoperative six minute walk test with a cutoff value of 300 meters was utilized in patients undergoing AVR in a recent trial (de Arenaza et al., 2010). It was indicated that six minute walk test added prognostic information to EuroSCORE and was an independent predictor of the composite outcome of death, myocardial infarction or stroke at 12 months.

Monin et al suggested that a good outcome after AVR may be seen when severe AS caused left-ventricular dysfunction, especially if inotropic reserve is present (Monin et al., 2003). They utilized dobutamine stress Doppler hemodynamics to show presence of LV contractile reserve in their study.

Aside from a high risk score, there are some other factors like patient refusal and porcelain aorta which deem some of the patients inoperable. The opinion of the experienced physician is also important to define patients at higher risk for surgery and to provide required precautions for the patients. Furthermore there are more non-invasive procedures like TAVI which may be used in patients with a high surgical risk.

Current ESC and ACC/AHA guidelines were published in 2007 and 2008 respectively. ESC guidelines emphasize that AS is increasingly observed in the elderly and AVR could prolong and improve the quality of life despite the increased risks of morbidity and mortality in this population (Vahanian et al., 2007). It is also noticed that a large percentage of suitable candidates for AVR are not referred for surgery. It is recommended that age, per se, should not be considered a contraindication for surgery and decisions should be made on an individual basis, provided that patients' wishes and cardiac and non-cardiac factors are taken into account. It is also denoted that early intervention at an asymptomatic stage should be avoided. ACC/AHA guidelines state that no effective medical treatment exists and balloon valvotomy is not a suitable alternative to surgery (Bonow et al., 2008). Among denotations about valve surgery in elderly patients in these guidelines are: CAD and LV dysfunction are associated with worse outcomes; advanced diseases like cancer, stroke and dementia render surgery inappropriate; and deconditioned and debilitated patients often do not return to an active life after surgery. Other peculiar considerations stated for the elderly are: a narrow LVOT and a small aortic annulus could require enlargement of the annulus, heavy calcification may require debridement, and a composite valve-aortic graft may be needed. Importance of recognition of marked LV hypertrophy which could be a marker of perioperative morbidity and mortality is emphasized. Absence of a perfect method to weigh all of the relevant factors and to identify high- and low-risk elderly is also noted.

Data about comparison of mechanical prostheses and bioprostheses for AVR in the elderly is scarce. One recent report suggests good outcomes of bioprostheses for AVR after more than 10 years of follow up in the elderly (Suojäranta-Ylinen et al., 2009). In the Veterans Affairs randomized trial, patients who underwent single AVR or mitral valve replacement with mechanical valve versus bioprosthesis were enrolled in a randomized fashion (Hammermeister et al., 2000). They found a better survival with mechanical valves largely because primary valve failure was virtually absent in this the mechanical valve group while it was seen in an important proportion of the bioprosthesis group. However primary valve failure was not significantly different between these groups in the elderly population. While the rate of thromboembolism was similar between the groups, bleeding complications were more common in the mechanical valve group. It is of note that lifelong warfarin treatment is required in patients who undergo AVR with mechanical valves and bleeding complications with warfarin is more common in the elderly. Further trials are needed to compare the outcomes of AVR with mechanical valves and bioprostheses in the elderly.

Patients with severe AS may have markedly reduced platelet functions and thus experience increased postoperative blood loss. One recent double-blind placebo controlled trial investigated effects of infusion of desmopressin (0.3 µg/kg) on platelet functions and postoperative blood loss (Steinlechner et al., 2011). They recommended assessing of platelet

functions and usage of desmopressin to avoid increased blood loss in patients with reduced platelet functions.

Among perioperative cautions for the patient with AS, careful manipulation of hemodynamics is crucial (Frogel & Galusca, 2010). Main goals to decrease the perioperative cardiovascular risk are to maintain sinus rhythm, a relatively slow heart rate, and adequate preload and afterload (Frogel & Galusca, 2010). In this context, a slower heart rate decreases myocardial oxygen demand and increases coronary perfusion time. Routine antibiotic prophylaxis is not recommended unless the patient has a previous history of infective endocarditis (Frogel & Galusca, 2010). Regarding anesthetic premedication, anticholinergics may cause tachycardia in a dose dependent manner and careful titration of sedation is crucial because oversedation may cause hypotension and undersedation may increase the sympathetic tone (Frogel & Galusca, 2010). Because of the risk of serious arrhythmias, a defibrillator should be readily available and placed on the patient before sterile draping. Ideal heart rate is in the range of 60 to 70 beats per minute and bradycardia should be avoided especially in the elderly patients who may have predisposition to it (Frogel & Galusca, 2010). As atrial systole is necessary for maximal LV preload, maintenance of normal sinus rhythm is very important. Adequate hydration is very important as well, since patients with AS are preload dependent (Frogel & Galusca, 2010). Elderly patients and patients with central nervous system disorders affecting sensation of thirst have tendency to develop dehydration and need careful evaluation of hydration status. Regarding type of anesthesia, an epidural technique may be preferred to neuroaxial anesthesia with sympathectomy because it allows incremental dosing and does not cause sudden changes in systemic vascular resistance (Frogel & Galusca, 2010). Opioids, midazolam, etomidate and cisatracurium may be good options for general anesthesia because they offer relatively stable hemodynamic effects (Frogel & Galusca, 2010). Careful monitoring of the blood pressure is pivotal and hypotension should be avoided and once hypotension develops it should be controlled with pure α agonists since they do not cause tachycardia (Frogel & Galusca, 2010). Invasive arterial blood pressure and central venous pressure monitoring are also recommended.

Elderly patients are at increased risk for experiencing adverse events like delirium and electrolyte disorders in the postoperative period. There are many metabolic, infectious and psychological factors which predispose the frail elderly to develop delirium. It is of note that delirium is very common after cardiac surgery and is associated with increased risk of short and long term morbidity and mortality (Maldonado et al., 2009). Psychotic symptoms of delirium like hallucinations and delusions are easily recognized, but many patients do not have these symptoms and routine assessment of attention and orientation is crucial. Of note, symptoms of delirium wax and wane and make identification of it difficult. Despite its high prevalence and adverse outcomes, many physicians do not recognize delirium (Maldonado et al., 2009). Giltay et al., focused on the psychotic symptoms of delirium after cardiac surgery and suggested that they are independently associated with adverse outcomes (Giltay et al., 2006). They found higher age, renal failure, dyspnea, HF, and left ventricle hypertrophy as independent preoperative predisposing factors and hypothermia ($<33,8^{\circ}\text{C}$), hypoxemia, low hematocrit, renal failure, increased sodium, infection and stroke as independent precipitating factors. Careful monitorization of volume status, follow up of renal functions and electrolyte levels, adequate pain control and rational medication selection are of great importance. Many drugs like anticholinergics, antihistaminics,

narcotics and central acting drugs like benzodiazepines may precipitate delirium in an elderly patient with predisposing factors. When a precipitating factor for delirium is identified in a delirious patient, search of other potential causes of it should continue, because especially patients without dementia do not easily develop delirium. Maldonado et al. investigated the effects of postoperative sedation on the development of delirium in patients undergoing cardiac valve surgery (Maldonado et al., 2009). They compared dexmedetomidine, which is not a GABAergic agent, has no anticholinergic effects, promotes a more physiological sleep pattern without significant respiratory depression, and may be associated with a decreased need for opioid use, with current postoperative sedation practices (propofol or midazolam) in a prospective, randomized and open label trial. They showed a significantly decreased rate of delirium with dexmedetomidine compared to propofol and midazolam (rates of delirium 3%, 50% and 50% respectively). Because fluid and electrolyte disturbances are common in the elderly, especially in the postoperative period, avoidance of hypotonic fluid administration and monitorization of volume status and electrolytes are crucial.

9.2 Perioperative management for noncardiac surgery in patients with aortic stenosis

Regarding noncardiac operations, postponing elective surgery is recommended for patients with symptomatic severe AS or asymptomatic severe AS in whom evaluation of the valve has not been done within the last year (Fleisher et al., 2009). If AVR is not feasible because of comorbidities or patient refusal, mortality risk of noncardiac surgery is approximately 10% in patients with severe AS (Fleisher et al., 2009). Stratification of cardiac risk for noncardiac surgery reported in the current ACC/AHA guidelines is summarized in Table 2 (Fleisher et al., 2009). In patients with mild or moderate AS, no clear recommendation is present (Bonow et al., 2008). In the asymptomatic patient with severe AS, AVR is indicated if concurrent CABG operation is required; if EF is below 50%; or if likelihood of rapid progression is high (Bonow et al., 2008). If symptoms are equivocal, an exercise test can be performed and AVR may be planned if symptoms or hypotension occur during the test. Beta blocker treatment should be continued if class I indications for it exist. If the patient is not using beta blockers and has CAD or more than one cardiac risk factor, titration of beta blockers to heart rate and blood pressure is recommended if the patient will undergo high- or intermediate-risk surgery (Fleisher et al., 2009). These cardiac risk factors are listed in Table 3. Starting beta blocker treatment in low doses and careful titration is important in elderly patients who are at increased risk for bradycardia and hypotension and thus adverse events like falls. Furthermore, data about the role of beta blockers in intermediate- and low-risk patients and optimal type, dose, timing, duration, and titration of beta blockers are lacking (Fleisher et al., 2009). Withdrawal of beta blockers in the preoperative period is associated with adverse outcomes and should not be done unless necessary. Cessation of metformin and renin angiotensin system blockers, which increase the risk of postoperative lactic acidosis and renal insufficiency respectively, before the surgical procedure is essential. In a recent study by Calleja et al., elderly patients with asymptomatic severe AS had low morbidity rates that were similar to that seen in well-matched patients with mild-to-moderate AS following intermediate-to-low-risk noncardiac surgery (Calleja et al., 2010). No postoperative death or HF was observed until dismissal. However, intraoperative hypotension requiring vasopressor use was more common in patients with asymptomatic severe AS. BNP may also be used to predict postoperative poor outcomes in patients with heart disease undergoing noncardiac surgery, however data about BNP used for this purpose is scarce. Leibowitz et

al. suggest that it may be beneficial to measure BNP levels in the preoperative period for this purpose (Leibowitz et al., 2008).

Risk Stratification	Procedure Examples
Vascular (reported CR often more than 5%)	Aortic and other major vascular surgery Peripheral vascular surgery
Intermediate (reported CR generally 1% to 5%)	Intraperitoneal and intrathoracic surgery Carotid endarterectomy Head and neck surgery Orthopedic surgery Prostate surgery
Low (reported CR generally less than 1%)	Endoscopic procedures Superficial procedure Cataract surgery Breast surgery Ambulatory surgery

* Combined incidence of cardiac death and nonfatal myocardial infarction. CR: cardiac risk.

Table 2. Cardiac Risk* Stratification for Noncardiac Surgical Procedures

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 3. Clinical risk factors for perioperative cardiovascular complications

10. Surgery

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 (Heinze et al., 2010). The results of the conventional surgery for octogenarians are satisfactory and 5% to 10% of mortality is noted for isolated AVR (Heinze et al., 2010). On the other hand, elderly patients stay longer in the hospitals and intensive care units during the postoperative period (Avery et al., 2001).

In 1912, Theodore Tuffier was the first to attempt opening AS using his finger. Russel Brock and then Bailey used dilators 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. (Barbour J.R. & Ikonimidis J.S., 2007). 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. United Kingdom heart valve registry observed 1100 elderly patients (56% women) who underwent AVR and the 30-day mortality was 6.6% (Asimakopoulos, 1997, as cited in Aronow, 2007). 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 who

becomes symptomatic. The indications for AVR in patients with AS according to the current ACC/AHA guidelines are listed in Table 4 (Bonow et al., 2006).

Class I
AVR is indicated for symptomatic patients with severe AS.* (<i>Level of Evidence: B</i>)
AVR is indicated for patients with severe AS* undergoing coronary artery bypass graft surgery (CABG). (<i>Level of Evidence: C</i>)
AVR is indicated for patients with severe AS* undergoing surgery on the aorta or other heart valves. (<i>Level of Evidence: C</i>)
AVR is recommended for patients with severe AS* and LV systolic dysfunction (ejection fraction less than 0.50). (<i>Level of Evidence: C</i>)
Class IIa
AVR is reasonable for patients with moderate AS* undergoing CABG or surgery on the aorta or other heart valves (see Section 3.7 on combined multiple valve disease and Section 10.4 on AVR in patients undergoing CABG). (<i>Level of Evidence: B</i>)
Class IIb
AVR may be considered for asymptomatic patients with severe AS* and abnormal response to exercise (e.g., development of symptoms or asymptomatic hypotension). (<i>Level of Evidence: C</i>)
AVR may be considered for adults with severe asymptomatic AS* if there is a high likelihood of rapid progression (age, calcification, and CAD) or if surgery might be delayed at the time of symptom onset. (<i>Level of Evidence: C</i>)
AVR may be considered in patients undergoing CABG who have mild AS* when there is evidence, such as moderate to severe valve calcification, that progression may be rapid. (<i>Level of Evidence: C</i>)
AVR may be considered for asymptomatic patients with extremely severe AS (aortic valve area less than 0.6 cm ² , mean gradient greater than 60 mm Hg, and jet velocity greater than 5.0 m per second) when the patient's expected operative mortality is 1.0% or less. (<i>Level of Evidence: C</i>)
Class III
AVR is not useful for the prevention of sudden death in asymptomatic patients with AS who have none of the findings listed under the class IIa/IIb recommendations. (<i>Level of Evidence: B</i>)

Table 4. Indications for Aortic Valve Replacement.

Although the surgery for the asymptomatic patients is preferred due to risk of 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 (Petersen & Poulsen, 2010).

AVR usually performed under general anesthesia using conventional techniques of open-heart surgery with median sternotomy. Minimally invasive procedures are associated with acceptable mortality and morbidity rates even in high risk patients. Minimally invasive aortic valve surgery can be performed through three different approaches. These are upper mini sternotomy, transverse sternotomy and right parasternal mini thoracotomy, sometimes

using port-access technique. This procedure has advantages such as less surgical trauma, decreased pain and faster recovery. Small incisions may also be associated with low infection rates (Olin et al., 1999). It reduces blood transfusions and shortens the length of hospital and ICU stay (Korach et al., 2010). It is a safe operation and is associated with lower incidence of atelectasis in the cardiac ICU (Foghsgaard et al., 2009). Port access aortic surgery also allows patients to be extubated earlier (Wheatley et al., 2004). Avoidance of full sternotomy for osteoporotic elderly 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 prostheses, stented and stentless bioprosthetic valves, aortic homografts and pulmonary autografts. The use of these valves differs from patient to patient due to comorbidities and anticoagulant needs. The bioprosthetic valves are good alternatives for elderly patients because long term anticoagulation use is not required.

The other situation for the elderly patients undergoing AVR is the injurious effects of cardiopulmonarybypass to the organs. This results as a systemic inflammatory response and this may influence the post-operative course of the elderly patients adversely.

Paroxysmal or chronic AF and a LVEF <35% is a risk factor for mortality in patients with severe AS undergoing AVR. Of 83 elderly patients with severe AS and an LVEF <35%, 29 (35%) had paroxysmal or chronic AF (Levy, 2006, as cited in Aronow, 2007). The perioperative mortality was 24% in the group with AF versus 5,5% in the group without AF.

11. Transcatheter 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. (Iung et al., 2003). 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. (Bach et al., 2007). Balloon aortic valvuloplasty, which was described in the 1980s, was the first alternative to surgical therapy (Cribier et al., 1986). 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 (Eltchaninoff et al., 1995). Trans-catheter aortic valve implantation (TAVI) was first described by Andersen et al in 1992 (Andersen et al., 1992). 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. (Cribier et al., 2002). A percutaneous bioprosthesis was successfully implanted within the diseased native aortic valve through an antegrade transseptal approach. Percutaneous transcatheter implantation of the aortic valve has been utilized as an alternative to open heart surgery in high risk patients with symptomatic severe AS who are not suitable for open surgery. 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 by pass, cachexia, recurrent pulmonary emboli, right ventricular insufficiency and cirrhosis.

Stented valves placed either transapically or percutaneously are garnering much attention (Lichtenstein et al., 2006; Criber et al., 2006). Within these procedures, firstly balloon aortic valvotomy is undertaken and a stented bioprosthesis is then deployed over a balloon into the aortic annulus. Inflation of the balloon anchors the valve in place in the annulus, effectively achieving AVR. Transapical approach necessitates a thoracotomy but the valve is deployed into the beating heart and extracorporeal circulation is not performed. In the percutaneous approach, the valve is deployed either antegradely via the transseptal route, or retrogradely across the native aortic valve. Contraindications for TAVI are as follows: an aortic annulus of <18 mm or >27 mm, bicuspid valves, heavy calcification in front of LM, presence of LV thrombus and need for CABG (relative). Some specific contraindications for transfemoral approach are; narrow peripheral arteries (diameter < 8-9 mm), severe tortuosity or calcification, history of aorto-femoral by pass, aneurysm of abdominal aorta with thrombosis, and severe atheroma of the arch. TAVI has revolutionized the management of patients with severe AS, with more than 10,000 implants performed to date. Two studies corroborated the results of previous reports in a real world population of consecutive patients within their respective countries (Eltchaninoff et al., 2010; Zahn et al., 2011). They demonstrated a technical success rate of 98-99%, similar 30 day mortality rates (12%), and an incidence of stroke of 3-4%. A recently published study (Partner Trial) successfully met both primary and co-primary endpoints with a significant reduction in 1-year mortality (30.7% for TAVI versus 50.7% for standard therapy, $p < 0.001$, Leon et al., 2010). It also demonstrated there was a significant reduction in the composite endpoint of death from any cause or repeat hospitalization (42.5% for TAVI versus 71.6% for standard therapy, $p < 0.0001$). However, TAVI as compared with standard therapy, was associated with a higher incidence of major strokes (5.0% versus 1.1%, $p = 0.06$) and major vascular complications (16.2% versus 1.1%, $p < 0.001$ Leon et al., 2010). 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 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.

12. Geriatric aspects

12.1 Activities of daily living

Bemmel et al investigated the impact of valvular heart disease on the activities of daily living (ADL, assessed with Groningen Activity Restriction Scale) in eighty one 90-year old individuals (Bemmel et al., 2010). The study population consisted of individuals 78% of whom lived independently and only 35% had history of cardiovascular disease. Most common valve diseases were mitral regurgitation (73%) and aortic regurgitation (47%). AS was present in 17% (14 in 81) of the study population (9 mild, 4 moderate and 1 severe). No correlation between the presence of valve diseases and dependence in ADL was found in this population. It is not feasible to extend these results to the general population because the study population consisted of healthier and cognitively more intact individuals expected for this age. Because significant AS may cause deterioration in ADL via several mechanisms like limitation of functional capacity, depression and cognitive decline due to concomitant atherosclerosis in the central nervous system, studies assessing ADL in individuals with significant AS are needed.

12.2 Frailty

Frailty is a geriatric syndrome which is associated with weakness, instability, limitation, increased vulnerability to stressors, and adverse health outcomes like falls, hospitalization, institutionalization and mortality (Evans et al., 2010). Although there are various definitions to identify individuals with frailty, the most frequently and widely used one was described by Fried and colleagues (Fried et al., 2001; Evans et al., 2010). The following five criteria are used in this definition: poor grip strength, self-reported exhaustion, unexplained weight loss, slow walking speed, and reduced physical activity. An individual having at least three of these criteria is defined as being frail. Patients with significant AS might be prone to become frail. Self-reported exhaustion, slow walking speed and reduced physical activity would be seen in a high percentage of patients with limited physical activity due to exertional dyspnea or angina pectoris associated with significant AS. They may also have weight loss and poor grip strength associated with cardiac cachexia. Assessment of patients with AS about presence of frailty would also be beneficial in perioperative risk assessment as stated in section 9.1. Further studies about the impact of frailty on presence, severity and perioperative risk of AS are needed.

12.3 Malnutrition

Malnutrition is an important health issue in the elderly. Being underweight is associated with more frequent all-cause mortality than being overweight in the elderly (Berrington de Gonzalez et al., 2010). Undernutrition is also associated with tendency to adverse health problems like pressure sores, infections and sarcopenia.

Data assessing the relationship between heart valve problems and malnutrition are very limited. Ikee et al investigated impact of malnutrition-inflammation complex on heart valve calcification in 105 patients on hemodialysis (Ikee et al., 2008). In this study mean age was 67 and aortic (77.4%) and mitral (51.3%) valve calcification rates were very high. They found some association between malnutrition and valve calcification. However, as a marker of malnutrition they used only albumin level which is not specific for malnutrition. Wang et al investigated the association of malnutrition and fetuin-A, which has recently been identified as an important circulating inhibitor of calcification, in 238 patients on peritoneal dialysis treatment (Wang et al., 2005). Nutritional assessment was done with serum albumin levels and subjective global assessment tool in this study. Cardiac valve calcification was present in 26% of the patients. They showed a significant correlation between fetuin-A levels and presence and degree of malnutrition. Otto et al reported increased long-term mortality independently associated with cachexia in 674 elderly patients who underwent balloon aortic valvuloplasty for AS (Otto et al., 1994).

Undernutrition may also influence outcomes after cardiac valve surgery. Tepsuwan et al. assessed the incidence and impact of cardiac cachexia retrospectively in 353 patients who underwent cardiac valve surgery (Tepsuwan et al., 2009). The study population was relatively young and most of them had mitral stenosis or mitral regurgitation. They used the finding of a body weight less than 80% of ideal body weight as cachexia which was present in 13% of the study population. They found significant association between presence of cachexia and worse New York Heart Association functional class, higher incidence of infective endocarditis and tricuspid regurgitation, longer postoperative hospitalization and more frequent postoperative complications and tendency to a higher mortality rate. Thourani et al investigated the impact of body mass index (BMI) on morbidity and mortality

after cardiac valve surgery in 4247 patients (Thourani et al., 2011). Most of their study population underwent isolated AVR (47.2%) or isolated mitral valve procedure (26%). 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. However they had no laboratory or clinical data about nutritional status. Engelman et al retrospectively assessed impact of BMI and albumin levels on morbidity and mortality after cardiac surgery in 5168 patients undergoing coronary artery bypass or valve operations (Engelman et al., 1999). In their study there was no correlation between albumin levels and BMI. Preoperative low albumin (<2.5 g/dl) and low BMI (<20 kg/m²) were independently associated with increased postoperative mortality. No nutritional assessment tool was utilized in this study. Potentially, significant AS may cause malnutrition via different mechanisms. Dietary restriction due to reduced physical capacity and depressive mood may enhance malnutrition. Abdominal angina may also cause avoidance from eating when concomitant systemic atherosclerosis is present in the mesenteric vessels. Further studies specifically investigating the association between malnutrition and AS are needed.

12.4 Depression

Depression is the most common psychiatric disorder in the elderly and later-life depression (LLD) is associated with disability and increased morbidity and mortality (Maixner et al., 2011). Because atypical presentations like somatic symptoms are common and LLD is generally associated with medical comorbidities, recognition is difficult. Study of Bisschop et al., suggested that cardiac disease and arthritis are the most common predisposing factors for medical illness related depression (Bischoop et al., 2004). Overall medical illness burden and degree of functional disability may be more important than specific medical illnesses alone (Maixner et al., 2011). Underlying medical illness may affect the prognosis of depression and depression may delay recovery from medical illnesses by decreasing motivation and compliance (Maixner et al., 2011). The importance of screening for depression in patients with heart disease is well established, but identifying patients with depression may be difficult because organic somatic symptoms possibly unrelated to mood may increase the score on depression ratings and many patients with depression deny a depressed mood (Maixner et al., 2011). Nonetheless, many symptoms like insomnia, fatigue, shortness of breath, weight loss, palpitations, and exercise intolerance overlap in heart disease and depression. Even when patients with depression deny sadness, they endorse anhedonia and most other depressive symptoms if further questioning is done (Maixner et al., 2011).

Vascular depression is characterized with late onset or change in course after early onset, persistent symptoms, and association of depression with vascular disease or vascular risk factors and diffuse or multifocal cerebrovascular lesions (Maixner et al., 2011). Although no specific data exist about the association of vascular depression and AS in the elderly, atherosclerosis has pivotal role in the pathogenesis of both conditions.

Among medications possibly precipitating depression are beta blockers, which is being used commonly in patients with heart disease. 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 like personal or family history of depression should be followed up in terms of development of depression (Verbeek et al., 2011). 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 (Verbeek et al., 2011). It is also important not to be reluctant to begin beta blocker treatment when strong indications like CAD exist.

SSRI are widely used in the treatment of depression. There is some data that indicate use of SSRI in patients with CAD and depression may improve cardiovascular outcomes (Kimmel et al., 2011). Because both treatment with SSRI and severe AS may reduce platelet functions, bleeding complications of surgical procedures may be increased in patients with severe AS using SSRI. Because treatment with SSRI may precipitate hyponatremia, monitorization of sodium levels is important in patients using SSRI, especially if older age and concomitant diuretic use is present.

13. Conclusion

Diagnosis and management of AS in the elderly have many differences compared to younger patients. Thus, involvement of experienced staff and utilization of comprehensive assessment in the management of these patients is crucial.

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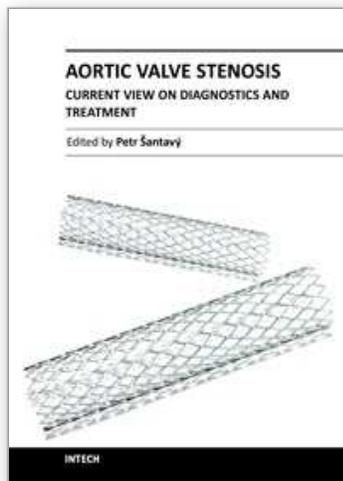
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Currently, aortic stenosis is the most frequent heart valve disease in developed countries and its prevalence increases with the aging of the population. Affecting 3-5 percent of persons older than 65 years of age, it makes a large personal and economical impact. The increasing number of elderly patients with aortic stenosis brings advances in all medical specialties dealing with this clinical entity. Patients previously considered too old or ill are now indicated for aortic valve replacement procedures. This book tries to cover current issues of aortic valve stenosis management with stress on new trends in diagnostics and treatment.

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