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Aortic valve disease in the older adult

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1 Background

As the population continues to age, aortic stenosis remains as the most prevalent valvular disease in Western countries.[1] The number of elderly patients with aortic stenosis continues to pose both a diagnostic and therapeutic challenge. Despite new advances such as transcatheter aortic valvular replacement (TAVR), there is still much patient-provider decision making that needs to take place given the comorbidities and complex goals of care in an elderly patient population.

The increased longevity due to advances in health care has resulted in an increase in diagnosis of aortic stenosis. While the prevalence is low in patients < 60 years of age, it increases to approximately 10% in patients > 80 years of age.[2] The severity of aortic stenosis increases with age, with one in eight people older than age 75 showing moderate to severe aortic stenosis.[3]

This represents a significant health care burden that is projected to increase as the population progressively ages. Age related, or degenerative valvular heart disease, represents the most common etiology of aortic stenosis in the elderly population. Degenerative aortic valve disease affects over 25% of all patients over the age of 65. Most patients have only mild thickening and normal valve function, called aortic sclerosis. However, 2%–5% of these patients have significant aortic stenosis with obstruction of left ventricular outflow.[4]

Clinical risk factors for degenerative aortic valve stenosis mirror those associated with coronary atherosclerosis. Traditional cardiovascular risk factors such as age, male gender, smoking, elevated LDL cholesterol, hypertension, and metabolic syndrome have been associated with development and progression of aortic stenosis.[5,6] Elderly patients with aortic stenosis typically have concomitant coronary or peripheral vascular disease. Risk factors associated with disease initiation may differ from those that promote disease progression, but disease progresses more rapidly at elderly age.

Aortic valve disease constitutes a chronic, progressive disease over time. Mild fibro calcific leaflet changes progress to active bone formation on the aortic valve apparatus, causing significant obstruction to left ventricular outflow. Otto, *et al.*[7] noted initial aortic lesions containing disorganized collagen fibers, chronic inflammatory cells, proteins of extracellular bone matrix and bone minerals, suggesting that this is a chronic inflammatory process. Hemodynamic stress initiates endothelial activity, contributing to aortic valvular damage. Increased calcification of the valve cusps causes increased valvular stiffness and narrowing. Over time, an increased aortic gradient causes a pressure overload resulting in left ventricular (LV) wall thickening and hypertrophy. Sustained hypertrophy and pressure over time contribute to LV diastolic dysfunction and left ventricular strain, leading to left ventricular failure.[7]

Given the similarity of both coronary atherosclerosis and aortic stenosis it was hoped that prevention and treatment with cardiovascular drugs would prevent progression of aortic stenosis. Treatment with medications such as beta blockers or statins have not proved of benefit in reducing or halting progression of aortic stenosis. The use of statins to reduce aortic calcification in hope that it could prevent progression of aortic stenosis has been disappointing. While initial studies showed some benefit,[8–10] a recent meta-analysis showed that statins had no effect on aortic valve

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structure, function, calcification, and clinical outcomes.[11] Similarly, bisphosphonates had been posited to ameliorate aortic stenosis progression but have not been proven helpful in prospective studies. There is some promise for other medications such as angiotensin converting enzyme inhibitors (ACEI) — some studies have shown changes in hemodynamics due to improved left ventricular unloading, although this requires further investigation.[10]

When evaluating the elderly patient for aortic stenosis, clinicians often have a myopic focus on the valve as the main cause of the patients' complaints. The presence of comorbidities, which are often severe, should be taken into account. Medical comorbidities can affect the outcome of procedures and full evaluation is warranted. In elderly patients with significant lung disease such as pulmonary hypertension or chronic obstructive pulmonary disease, it can be difficult to discern whether symptoms are due to a cardiovascular or lung pathology. Replacement of the valve might not improve clinical symptoms or outcomes. In patients who underwent TAVR, 60% had significant lung disease, with up to 30% having oxygen dependence.[12] In patients undergoing aortic valve replacement, significant lung disease has been associated with an increase in morbidity and mortality.[13] Another small cohort study found a prevalence of 77% of significant sleep-related breathing disorders.[14] Chronic kidney disease, liver disease, and anemia have been independently associated with increased mortality after aortic valve replacement.[15]

2 Diagnosis

In evaluating elderly patients with aortic stenosis, it is important to elicit a comprehensive and meticulous history. The three cardinal symptoms of aortic stenosis that prompt urgent valve replacement include angina, syncope, and heart failure symptoms (including orthopnea, edema, and paroxysmal nocturnal dyspnea). In the elderly population, it can be difficult to elicit these symptoms as many patients have significantly decreased mobility or might not complain of these symptoms. It is integral to involve family members or caretakers who might notice a change in activity, appetite, or overall health. While carefully supervised exercise testing can help evaluate those who are truly asymptomatic, other procedures such as a gait evaluation can help the clinician determine if hemodynamically significant aortic stenosis is the culprit. While patients might be categorized asymptomatic due to lack of functional impairment, a very high event rate can be expected with echocardiographic evidence of significant aortic stenosis and warrants clinical follow up.[16]

It is important to determine whether symptoms are related to aortic stenosis. Patients with limited mobility, deconditioning, or oxygen dependent lung disease may have dyspnea unrelated to their valvular pathology such that treatment with valve replacement would not produce benefit.

The physical examination can further provide clues on the severity of the aortic stenosis and burden on the cardiovascular system. Presence of a delayed carotid upstroke, a sustained point of maximal impulse due to LV hypertrophy, and a harsh, late peaking systolic murmur best heard in the right or left upper sternal border are compatible with severe aortic stenosis. However, vascular stiffness may mask the delayed aortic upstroke and dorsal kyphosis may lessen murmur intensity. In the elderly, the murmur intensity may even decrease as stroke volume declines. In severe aortic stenosis, the aortic component of S2 is either soft or absent. While the physical examination can point the clinician toward aortic stenosis, further evaluation with echocardiography is warranted.

Transthoracic echocardiography (TTE) remains the gold standard for evaluating aortic stenosis. Evaluation of LV wall thickness, systolic function, and aortic valve morphology can be assessed with two dimensional imaging. Doppler echocardiography provides hemodynamic measurement, severity of valvular stenosis and regurgitation, and pulmonary pressures.[17] Aortic stenosis is considered severe when the peak velocity is greater than 4 m/s, peak gradient is greater than 64 mmHg, mean gradient is greater than 40 mmHg, or aortic valve area is less than 1.0 cm^2.[18] Further testing with submaximal stress testing can be useful in evaluation if the patient is asymptomatic.[18]

Clinicians should not depend solely on the echocardiogram for clinical decision-making. It is imperative that the clinician is able to connect the history, physical findings, and imaging results. This will allow to the clinician to be aware of any discrepancies which might warrant further investigation. Other imaging modalities for further evaluation include transesophageal echocardiogram, computed tomography, cardiac catheterization and cardiac magnetic resonance. Once the decision is made for aortic valve replacement, coronary artery anatomy must be assessed re need for concomitant coronary revascularization.

3 Treatment

Aortic stenosis has high morbidity and mortality after the occurrence of symptoms, where the two year mortality risk is higher than 50%.[16] Aortic valve replacement with either open heart surgery or TAVR are the only treatment modali-

ties that reduce morbidity and mortality with significant aortic stenosis. Prior to the advent of TAVR, over one third of patients were unsuitable to undergo valve replacement due to age-related comorbidities.[19] TAVR has emerged as an alternative in those who cannot undergo or who are high risk for surgical valve replacement.[12,20] The AHA/ACC valvular guidelines recommend valve replacement in symptomatic patients with evidence of left ventricular dysfunction, in the presence of severe aortic stenosis.[18] More importantly, they recommend a multidisciplinary heart valve team approach when deciding on individualized treatment. This is paramount in patients who are elderly and have nontraditional risk factors that are not seen in younger cohorts. When evaluating risk, it is important to evaluate frailty, disability, mobility, cognitive impairment, malnutrition, and fall risk. Equally important is shared clinician-patient decision-making.

Frailty is defined as a state of vulnerability, a syndrome characterized by decreased reserve and diminished resistance to stressors.[21] This evaluation provides better insight into the "physiological age" of the patient.[22] Increasing evidence shows an increase in cardiovascular mortality in patients with frailty, independent of other comorbidities.[23,24] Traditionally, surgical risk of aortic valve replacement is estimated using two scores: the Society of Thoracic Surgery (STS)[25] and the European System for Cardiac Operative Risk Evaluation.[26] Unfortunately, neither of these scores take into consideration frailty, cognitive disorders, multimorbidity, or social support, which are of importance in this population undergoing valvular replacement. The evaluation of gait speed and comprehensive geriatric assessment is advocated for all older, complex patients with symptomatic aortic stenosis since it can predict further outcomes beyond the traditional scoring systems.[22] Other factors that should be considered when deciding for valve replacement include high STS score, impaired left ventricular systolic function, low valve gradients, reduced stroke volume, severe myocardial fibrosis, and severe pulmonary hypertension.[27]

Despite the significant comorbidities of the elderly, the outcomes for aortic valve replacement have been improving. Vasques, *et al*.[28] reviewed 48 studies with patients over the age of 80 and showed an improvement of morbidity and mortality from 7.5% to 5.8% over the past twenty years. In the era of TAVR, the postoperative mortality in octogenarians after 2000 was between 2.4% and 6.8%.[29] Postoperative complications of concern are stroke, paravalvular leaks, and vascular complications (vascular dissection perforation, hematoma, bleeding). Randomized trials have shown no significant differences in mortality between surgical valve replacement (SAVR) *vs*. TAVR in patients who are high risk. Patients undergoing SAVR have a higher risk of bleeding, kidney injury, and atrial fibrillation while those who undergo TAVR have higher vascular complication, paravalvular leak, and permanent pacemaker insertion.[12] Recent studies of TAVR in the elderly have shown that despite significant comorbidities, frailty, and high STS scores, they have an acceptable short and long term survival benefit along with improvements in function and quality of life.[30]

Elderly patients and their families must be queried and presented both the risks and benefits of SAVR and TAVR prior to allow for informed decision-making. An overlooked aspect of the decision to pursue valve replacement involves discussing expectations with patients and setting realistic goals for enhancements in quality of life and reduction of disease burden. With the help of geriatricians and primary care physicians, it appears possible to better identify frail patients with diminished physiological reserve versus patients with the potential to recover after intervention.[31] Establishing a framework to align patient goals and outcomes can aid in decisions regarding potential treatment options. If a patient is thought to have prohibitively high risk where intervention would be futile, end-of-life planning should be pursued. In all patients it is essential to delineate goals of care in advance.

4 Follow up

After valve replacement, careful monitoring and management of comorbidities is crucial. Elderly patients are at higher risk of bleeding, renal failure, arrhythmias, heart block, and cognitive decline. Patient who have severe, symptomatic aortic stenosis have significant decline in preoperative functional capacity, and often severe malnutrition, leaving patients at higher risk postoperatively. Jagielak, *et al*.[32] showed that among elderly patients undergoing aortic valve replacement, 39.4% were diagnosed preoperatively as malnourished. Hospitalization is invariably associated with functional decline and perioperative delirium may result in cognitive decline. Mobility and rehabilitation after valve replacement remains important, with some promise seen in cardiopulmonary rehabilitation in elderly patients going TAVR.[33] Close follow up with the primary care physician or geriatrician is warranted to evaluate for long term complications or changes in coexisting medical conditions.

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