JMS 2024;Vol 7(3): 87-94
UDC: 616.132-007.271-073.763.5
doi.org/10.55302/JMS2473087a

AORTIC VALVULAR STENOSIS IN ELDERLY POPULATION

Emilija Antova[1], Anita Hristova Dimceva[2], Biljana Stojanoska Bojadzieva[3], Biljana Trpkovska[3], Biljana Zafirova[3], Emilija Lazarova Trajkovska[1], Valentina Andova[1]
[1]University Clinic of Cardiology, Skopje, Faculty of Medicine, Ss. Cyril and Methodius University in Skopje, Republic of North Macedonia
[2]Institute of Transfusion Medicine, Skopje, Faculty of Medicine, Ss. Cyril and Methodius University in Skopje, Republic of North Macedonia
[3]Institute of Anatomy, Faculty of Medicine, Ss. Cyril and Methodius University in Skopje, Republic of North Macedonia

Abstract

Aortic valve stenosis(AS) is the most common degenerative valvular disease with an increasing prevalence as a result of prolonged life expectancy.The hemodynamic disturbances that occur in the heart depend on the degree of narrowing of the aortic orifice. AS often remains undiagnosed due to its prolonged asymptomatic period. By the time significant symptoms appear, the disease is usually in an advanced stage, leading to a rapid and steep decline in survival.

Echocardiography is the most important diagnostic method, used to analyze the cusps, evaluate the degree of valve calcification, and assess the severity of AS(mild, moderate, or severe) as well as its consequences. A decrease in global longitudinal myocardial strain(GLS) below -16% signifies worsening and predicts future adverse events. Computed tomography(CT) is frequently necessary to determine calcium score of the aortic valve. Cardiac magnetic resonance imaging(MRI) is valuable for detecting and quantifying myocardial fibrosis.

Patients with severe AS and symptoms should be promptly referred for either an interventional percutaneous procedure, such as **transcatheter aortic valve implantation (TAVI)**, or **surgical aortic valve replacement (SAVR)**, when the valve is replaced with either a biological or mechanical prosthesis. The study findings highlight the evolving role of TAVI as a comparable or superior alternative to surgical AVR, particularly in **high-and intermediate-risk patients**, and suggest similar efficacy in **low-risk patients** with procedural advantages for TAVI.

Medical management focuses on addressing all cardiovascular risk factors. If an intervention or surgery is not feasible, patients remain on palliative care. Palliative care plays a crucial role in the management of patients with AS or other valvular heart diseases, particularly when the surgery or interventional procedures are not performed on time.

Key words: aortic valve stenosis, TAVI, surgical aortic valve replacement

Introduction

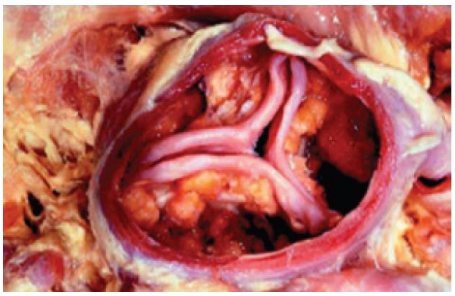
Aortic valve stenosis (AS) is the most common degenerative valvular disease with an increasing prevalence as a result of prolonged life expectancy. In individuals aged 65-74 years, the prevalence is approximately 2-3%. For those aged 85 years and older, the prevalence exceeds 8-10%. Severe aortic stenosis affects roughly 2-4% of individuals aged ≥75 years. The progression from aortic sclerosis to severe aortic valve stenosis occurs in about 10% of patients over a period of 5 years. [1,2]

Contributing factors to the rising prevalence of AS include aging-related calcification and degeneration of the aortic valve as primary causes in the elderly, as well as accompanying risk factors such as hypertension, hyperlipidemia, smoking, renal diseases, and diabetes, which contribute to both atherosclerosis and valve calcification. Chronic inflammation, lipid deposition, and endothelial dysfunction contribute to the progression of AS and coronary artery disease (CAD) simultaneously. The prevalence of AS (mild, moderate, and severe) is 25-30% in patients with coronary artery disease (CAD), with higher

rates observed in individuals aged >70 years. Aortic valve stenosis (AS) is the third most common cardiovascular disease, following hypertension and coronary artery disease.

The rheumatic etiology of the disease, characterized by fibrotic changes of the valve leaflets, is becoming increasingly rare, while degenerative or calcific AS is very common, predominantly present in the elderly population, and is characterized by degenerative and calcific changes in the valve leaflets. [1,2,3]

Figure 1. Depiction of a degenerated and calcified tricuspid aortic valve (Adapted from Amedeo Anselmi. https://doi.org/10.1016/B978-0-12-816861-5.00001-0) [4]



Pathophysiology and main symptoms in aortic stenosis

The narrowing of the aortic valve due to significant changes in the valve leaflets leads to considerable difficulty in the ejection of blood from the left ventricle (LV) into the aorta. The hemodynamic disturbances that occur in the heart depend on the degree of narrowing of the aortic orifice.

Over time, there is a progressive increase in systolic pressure in the LV, which gradually leads to more pronounced hypertrophy of the LV walls as a primary compensatory mechanism countering the pressure overload. Additionally, the strong contraction of the left atrium, when the patient is in normal sinus rhythm, enhances LV contraction and improves LV emptying as a secondary compensatory mechanism.

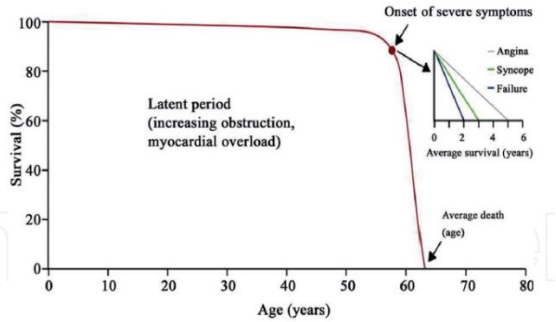
These compensatory mechanisms allow for an adequate stroke volume of the heart and explain the prolonged asymptomatic period in this valve disease.

The hypertrophied LV muscle requires increased oxygen consumption, and the mismatch between oxygen supply and demand is the primary cause of chest pain in AS. Also, reduced coronary perfusion during diastole due to elevated LV pressure contributes to ischemia. Blood flow to other organs is also reduced, especially during physical exertion. In untreated AS, there is a gradual progression to replacement fibrosis in the myocardium, LV dilatation, worsening of diastolic and systolic LV function, reduced stroke volume, decreased cardiac output, and manifest heart failure.

Aortic stenosis often remains undiagnosed due to its prolonged asymptomatic period. By the time significant symptoms appear, the disease is usually in an advanced stage, leading to a rapid and steep decline in survival. This underscores the importance of timely detection of the disease.

Common symptoms reported by patients include: dyspnea and chest pain, which occur even with minor exertion or at rest; paroxysmal nocturnal dyspnea; pulmonary edema (sometimes as the first symptom); sudden loss of consciousness (syncope) due to reduced blood flow to the brain; dizziness; and blurred vision. In advanced stages of the disease, symptoms and signs of heart failure are present. Occasionally, the first manifestation of the disease is a stroke.[5,6]

Figure 2. Natural history of AS. The prolonged latent asymptomatic period is shown. With the onset of symptoms such as angina pectoris, syncope, and heart failure in patients with severe AS, there is a rapid and steep decline in survival. (Adapted from: Susan Kwon et al. *DOI: http://dx.doi.org/10.5772/intechopen.86707*) [6]



Diagnosis

During auscultation in a *physical examination*, a clear ejection systolic murmur is heard over the aortic valve region and Erb's point, with supraclavicular propagation, often audible across the entire precordium. In more severe cases of AS, a characteristic low systolic blood pressure with a small amplitude is present. As heart failure develops, blood pressure may decrease further, leading to more frequent dizziness, fainting, and syncope. The pulse is highly characteristic of aortic stenosis: it is weak (low amplitude) and slow.

On *electrocardiography*, signs of pressure overload are seen, such as left ventricular (LV) hypertrophy with asymmetrical negative T waves. In some cases, particularly in elderly individuals or severe forms of the disease, left bundle branch block or atrioventricular block of the second or third degree may occur, necessitating prompt intervention with pacemaker implantation.

Chest X-ray may reveal a relatively small heart, post-stenotic dilatation of the ascending aorta, and calcifications of the aortic valve leaflets. *Echocardiography* is the most important diagnostic method, used to analyze the cusps, evaluate the degree of valve calcification, and assess the severity of AS (mild, moderate, or severe) as well as its consequences. These include the degree of LV hypertrophy, reducing of stroke volume and cardiac output, LV function (normal or reduced), and any segmental wall motion abnormalities indicative of coronary artery disease. Additionally, it evaluates the presence of pulmonary hypertension and potential right ventricular dysfunction. A decrease in global longitudinal myocardial strain (GLS) below -16% signifies worsening of the condition and predicts future adverse events.

Associated anomalies such as aortic regurgitation or other valvular diseases, especially of the mitral valve, and/or dilation of the aortic root (post-stenotic dilatation) as a consequence of the disease are often identified. [7]

Computed tomography (CT) is frequently necessary to determine calcium score of the aortic valve. Threshold values for the calcium score are defined as 2000 Agatston Units (AU) for men and 1200 AU for women. Values above these thresholds indicate severe stenosis due to pronounced valve calcification.[1,2]

Cardiac magnetic resonance imaging (MRI) is recommended for patients with suboptimal echocardiographic quality. In addition to assessing stenosis severity, ventricular volumes, systolic function, aortic regurgitation, and ascending aortic dilatation, cardiac MRI is particularly valuable for detecting and quantifying myocardial fibrosis. Myocardial fibrosis contributes to heart decompensation and other adverse outcomes, regardless of the presence or absence of coronary artery disease.

Cardiac catheterization is indicated to assess the presence and severity of pulmonary hypertension hemodynamically.

Coronary angiography is routinely performed in men over 40 years of age and post-menopausal women when preparing for surgical or interventional treatment.

Risk Stratification and Management in Asymptomatic Patients.

For asymptomatic patients with severe AS and normal left ventricular ejection fraction (LVEF) as observed on echocardiography, risk stratification is conducted using a supine exercise test.

This test aims to unmask the asymptomatic condition by identifying the occurrence of symptoms such as chest pain or dyspnea and a drop in blood pressure during exercise, which are indications for appropriate treatment. [1,3]

Asymptomatic patients with an LVEF below 50% should be promptly referred for appropriate treatment. For those with an LVEF above 55%, treatment consideration may still be warranted if they meet the following criteria:[1,2,3]

- Very severe aortic stenosis, with a maximum trans-valvular velocity exceeding 5 m/s.
- Severe valve calcification, as determined by a high calcium score.
- Rapid annual progression, with an increase in trans-valvular velocity of more than 0.3 m/s per year.
- Elevated biomarkers, with Nt-proBNP (or BNP) levels exceeding three times the normal laboratory values.

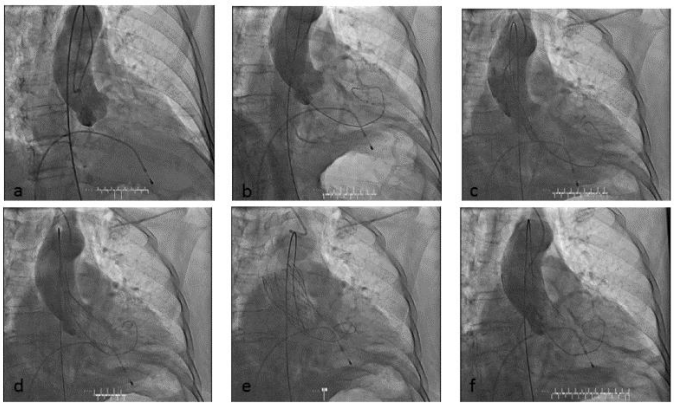
Complications

The most frequent complications in these patients include arrhythmias, heart failure, and infective endocarditis. Sudden cardiac death may sometimes be the first manifestation of the disease. In asymptomatic patients, the annual incidence of sudden cardiac death is approximately 1%, whereas it is more common in symptomatic patients.

Treatment of Aortic Valve Stenosis.

Asymptomatic patients with mild to moderate AS should be monitored regularly. Patients with severe AS and symptoms should be promptly referred for either an interventional percutaneous procedure, such as **transcatheter aortic valve implantation (TAVI)**, or **surgical aortic valve replacement (SAVR)**, when the valve is replaced with either a biological or mechanical prosthesis.

Figure 3. TAVI step by step. a. Preprocedural aortography, b. Crossing of the aortic valve, c. Positioning of the self expandable aortic valve (Evolut R 29mm), d. Partial deployment of the aortic valve, e. Full deployment of the aortic valve, f. Final aortography without aortic regurgitation (Adapted from: Sasko Kedev, et al. Contributions. Sec. of Med. Sci., XL 2, 2019) [8]



Risk Stratification for Intervention.

Risk stratification is essential to assess the balance between the risk of intervention/AVR and the expected natural progression of the disease, as well as to select the most appropriate type of intervention. To evaluate cardiac operative risk, the following tools are commonly used: 1. The European System for Cardiac Operative Risk Evaluation II (EuroSCORE II) Available at: EuroSCORE II Calculator; http://www.euroscore.org/calc.html and 2. The Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM) Score Available at: STS Risk Calculator; http://riskcalc.sts.org/stswebriskcalc/calculate).

These scores predicts the risk of mortality from cardiac surgery and distinguishes between high and low-risk surgical patients, providing reliable predictions for postoperative outcomes after valve surgery.

While these tools are effective for evaluating surgical patients, they have limitations for patients undergoing **TAVI**, as they do not account for major risk factors specific to this population.

Examples of these risk factors include: frailty, which is common in elderly patients, and anatomic factors influencing procedural outcomes, such as: porcelain aorta, prior chest radiation and mitral annular calcification (MAC).

To address these limitations, new risk assessment scores tailored for TAVI patients have been developed, such as TAVR Risk Assessment Tool; http://tools.acc.org/TAVRRisk/=!/content/evaluate/ [9] Additionally, **EuroSCORE III** is currently under development to improve risk stratification.

The treatment recommendations for valvular heart diseases, issued by the European and American Cardiology Societies, outline indications for referring patients to TAVI (transcatheter aortic valve implantation) or surgical aortic valve replacement (AVR).

TAVI is recommended for older patients with higher surgical risk; previous cardiac surgery; greater frailty; chest radiation therapy; porcelain aorta; high likelihood of patient-prosthesis mismatch (with an aortic valve area (AVA) < 0.65 cm^2/m^2 BSA); severe chest deformity or scoliosis.

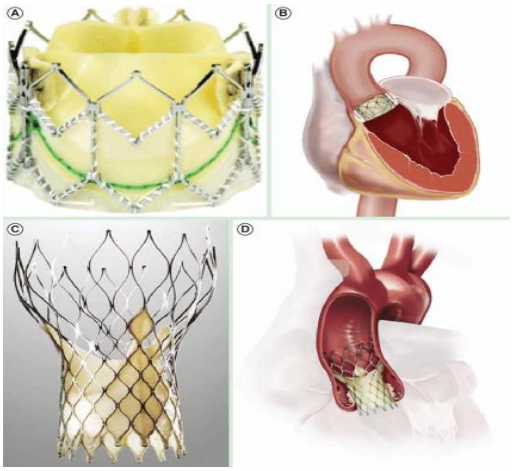
Surgical AVR is recommended for younger patients with lower surgical risk; endocarditis; left ventricular thrombus; need for simultaneous surgical intervention for: other significant valvular disease, coronary artery bypass grafting (CABG), aortic root or ascending aorta surgery or myectomy for septal hypertrophy; unsuitability for transfemoral access; low coronary ostia; inappropriate dimensions of TAVI prostheses relative to the patient's aortic annulus diameter and extensive calcification of the LV outflow tract.

The indication for treatment should be determined by a **"Heart Team"** after reviewing all examinations, discussing the options with the patient, and assessing the risks associated with the chosen treatment in terms of increased morbidity and mortality.

The Heart Team is a multidisciplinary group consisting of: a valvular disease expert (clinical and interventional cardiologist), a cardiac surgeon, an imaging specialist (echocardiography, computed tomography, magnetic resonance imaging), a geriatric specialist, a cardiovascular anesthesiologist.

This team presents interventional, surgical, and medical alternatives to the patient, factoring in the patient’s preferences, quality of life, and the likelihood of survival beyond one year.

Figure 4. TAVI Prostheses:
(A, B) The Edwards SAPIEN XT (Edwards Lifesciences, Irvine, CA, USA) valve.
(C, D) The CoreValve Prosthesis (Medtronic Inc, Minneapolis, MN, USA).
(Adapted from Mohamed El-Mawardy et al. Transcatheter aortic valve implantation: technique, complications and perspectives. Expert Rev. Cardiovasc. Ther. 1–20 (2014).[10]



The results of randomized controlled trials comparing TAVI and Surgical AVR, shows:

A) High-risk and Inoperable Patients with Symptomatic Severe AS

- TAVI as a superior alternative to medical therapy: TAVI proved to be a better option compared to medical treatment alone for high-risk and inoperable patients.
- TAVI demonstrated one-year survival rates exceeding 82% in patients with a mean age >80 years, in studies: PARTNER 2 and SAPIEN 3.
- New-generation TAVI devices outperformed surgical AVR in high-risk and inoperable patients.

B) Intermediate-risk Patients with Symptomatic Severe AS

Findings from PARTNER 2 and SURTAVI studies shows: lower one-year mortality rates, reduced incidence of stroke, lower rates of moderate-to-severe aortic regurgitation favoring TAVI over surgical AVR. The studies concluded that TAVI is not inferior to surgical AVR in intermediate-risk patients.[11]

C) Low-risk Patients with Symptomatic Severe AS

Four-year outcomes from the EVOLUT Low Risk trial showed a 26% relative reduction in the composite endpoint of all-cause mortality or disabling stroke in patients undergoing TAVI compared to those who received surgical AVR. Five-year outcomes from PARTNER 3 showed that the composite endpoint (death, stroke, or rehospitalization) was 22.8% for TAVI patients versus 27.2% for surgical AVR patients (p=0.07), indicating comparable efficacy between the two techniques. TAVI was associated with a lower incidence of disabling stroke and reduced rates of new-onset atrial fibrillation. Surgical AVR was associated with lower rates of moderate-to-severe aortic regurgitation.[12,13]

TAVI prostheses, like bioprostheses, have a limited lifetime, thus, TAVI in patients with previous TAVI (TAVI-in-TAVI) interventions are increased. Analyzing the safety and the outcomes of TAVI-in-TAVI interventions, the findings from a systematic review and meta-analysis present that TAVI-in-TAVI has an acceptable safety profile with relatively low in-hospital, 30-days and 1-year mortality and stroke rates, comparable to the native-valve-TAVI.[14]

Medical management focuses on addressing all cardiovascular risk factors, including: hypertension, diabetes mellitus, hyperlipidemia, renal diseases, and also, adopting a healthy diet, avoiding

smoking and maintaining a healthy body weight. For patients with heart failure, standard therapy for left ventricular systolic dysfunction should be continued. However, care must be taken with antihypertensive therapy to avoid a sudden drop in blood pressure, which can be detrimental in patients with severe AS.

If an intervention or surgery is not feasible, patients remain on **palliative care**. Palliative care plays a crucial role in the management of patients with aortic valve stenosis or other valvular heart diseases, particularly when the surgery or interventional procedures are not performed in a timely manner. So, these diseases progress to terminal phases, often presenting with severe clinical symptoms, especially in the elderly population.

Older age is frequently accompanied by worsening comorbidities, including: cardiovascular diseases, pulmonary diseases, renal dysfunction and osteo-muscular system disorders. In these cases, palliative care is essential for managing refractory symptoms, providing psycho-social support and compassionate care and alleviating suffering and pain. Geriatric specialists have the expertise to address the needs of frail elderly patients, who often face impaired functional, nutritional, or cognitive status, in terminal stages of diseases, such as aortic valve stenosis.

Conclusion

Aortic valve stenosis is the most common degenerative valvular disease. As the most of the patients are very old and fragile, they often deny surgical aortic valve replacement (SAVR). So transcatheter aortic valve implantation (TAVI) as an interventional percutaneous procedure represent a method that can prolong the life of these patients. The study findings highlight the evolving role of TAVI as a comparable or superior alternative to surgical AVR, particularly in high- and intermediate-risk patients, and suggest similar efficacy in low-risk patients with procedural advantages for TAVI.

References

1. Alec Vahanian et al. 2021 ESC/EACTS Guidelines for the Management of Valvular Heart Disease. European Heart Journal (2022) 43, 561–632 https://doi.org/10.1093/eurheartj/ehab395
2. Catherine M. Otto, Rick A. Nishimura et al. 2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2021;143:e72-e227. doi: 10.1161/CIR.0000000000000923
3. Emilija Antova. Risk stratification of the patients with severe aortic valvular stenosis with normal left ventricular function. Doctorate thesis. 2013. University Ss Cyril and Methodius, Medical faculty Skopje, R. Macedonia.
4. Amedeo Anselmi et al. Transcatheter Aortic Valve Procedures: Technology Update, Advances in Cardiovascular Technology, 2022. https://doi.org/10.1016/B978-0-12-816861-5.00001-0
5. Ross J Jr, Braunwald E. Aortic Stenosis. Circulation. 1968;38(1 Suppl):61-67
6. Susan Kwon et al. Hemodynamic Classifications of Aortic Stenosis and Relevance to Prognosis. 2019. *DOI: http://dx.doi.org/10.5772/intechopen.86707*)
7. Helmut Baumgartner MD et al. Echocardiographic Assessment of Valve Stenosis: EAE/ASE Recommendations for Clinical Practice. Journal of the American Society of Echocardiography January 2009. doi:10.1016/j.echo.2008.11.029
8. Sasko Kedev, Biljana Zafirovska, Elizabeta Srbinovska-Kostovska, Slobodan Antov, Aleksandar Nikolic, Omer Dzemali, Matjaz Bunc. Minimalistic approach for transcatheter aortic valve implantation (TAVI): open vascular vs. fully percutaneous approach. Contributions. Sec. of Med. Sci., XL 2, 2019. ISSN 1857-9345 UDC: 616.132-007.271-089.843
9. Edwards FH, Cohen DJ, O'Brien SM, Peterson ED, Mack MJ, Shahian DM, Grover FL, Tuzcu EM, Thourani VH, Carroll J, Brennan JM, Brindis RG, Rumsfeld J, Holmes DR, Jr. Transcatheter Valve Therapy R. Development and validation of a risk prediction model for in-hospital mortality after transcatheter aortic valve replacement. Steering Committee of the Society of Thoracic Surgeons/ American College of Cardiology. JAMA Cardiol 2016;1:46_52.

10. Mohamed El-Mawardy, Mohamed Abdel-Wahab, Gert Richard. Transcatheter aortic valve implantation: technique, complications and perspectives. Expert Rev. Cardiovasc. Ther. 1–20 (2014)
11. Dharam J. Kumbhani, Michael J. Reardon. Surgical Replacement and Transcatheter Aortic Valve Implantation - SURTAVI. Sep 11, 2019
12. Michael J. Reardon, MD, et al. Four-Year Outcomes from the Evolut Low Risk Trial. Journal of the American College of Cardiology. 2023
13. Martin B. Leon, MD, et al. Transcatheter Aortic-Valve Replacement in Low-Risk Patients at Five Years. PARTNER 3 Trial. The New England Journal of Medicine. 2023
14. N. Ktenopoulos, A. Apostolos, A. Karanasos, M. Drakopoulou, O. Katsaros, C. Simopoulou, G. Oikonomou, I. Kachrimanidis, L Koliastasis, G. Benetos, S. Tsalamandris, A. Synetos, G. Latsios, C. Tsioufis, K. Toutouzas. Safety and efficacy of transcatheter aortic valve implantation (TAVI) in patients with previous TAVI; a systematic review and meta-analysis. European Heart Journal (2024) 45 (Suppl 1). Interventional Cardiology - Noncoronary Cardiac Intervention, Aortic Valve Intervention