Transcatheter aortic valve implantation

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GRADUATE THESIS

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This graduation paper was made at the Division for Cardiovascular diseases; Department of Internal Medicine, Clinical Hospital "Dubrava", School of Medicine, University of Zagreb, under the supervision of Boris Starčević, MD, PhD, and it was submitted for evaluation in the academic year of 2014/2015.

ABBREVIATIONS

AR - Aortic Regurgitation

AS - Aortic Stenosis

AVA- Aortic Valve Area

AVR - Aortic Valve Replacement

CAD - Coronary Artery Disease

CBC - Complete Blood Cell

CHF - Congestive Heart Failure

CI - Confidence Interval

CK - Creatine Kinase

CPB - Cardiopulmonary Bypass

CT - Computed Tomography

CVD - Cardiovascular Disease

ECG - Electrocardiography

EuroSCORE - European System for Cardiac Operative Risk Assessment Score

INR - International Normalised Ratio

IQR - Interquartile Range

LBBB - Left Bundle Branch Block

LDL - Low Density Lipoprotein

LVEF - Left Ventricular Ejection Fraction

MDCT - Multidetector Computed Tomography

NYHA - New York Heart Association

PAVR - Percutaneous Aortic Valve Replacement

PTT - Partial Thromboplastin Time

PVL - Paravalvular Leak

RBBB - Right Bundle Branch Block

SAVR - Surgical Aortic Valve Replacement

STS - Society of Thoracic Surgeons Score

TAVI - Transcatheter Aortic Valve Implantation

TAVR - Transcatheter Aortic Valve Replacement

THV - Transcatheter Heart Valve

TOE - Trans-Oesophageal Echocardiography

TTE - Trans-Thoracic Echocardiography

TABLE OF CONTENTS

SUMMARY

Title: Transcatheter Aortic Valve Implantation

Keywords: Transcatheter Aortic Valve Implantation, Aortic Valve Stenosis, Heart Team

Author: Jamal Ahel

Aortic stenosis is the most common valvular heart disease, with it's incidence growing in developed countries, as the population ages. When it becomes symptomatic it tends to take a rapidly progressive course and soon requires intervention in the form of aortic valve replacement. If left untreated, mortality rates are as high as 50% within 2 years of symptom onset. Surgical replacement of the aortic valve can significantly increase survival in such patients and reduce symptoms of the disease. Unfortunately, the existence of many comorbidities are often found in such patients and may severely influence the operative risk and outcome of the aortic valve replacement surgical procedure, thence many patients are doomed inoperable and unfit for surgery.

This category of inoperable patients comprises up to 30% of cases of severe symptomatic AS. Up until 2002, this group of patients did not have a viable alternative treatment. In 2002, however, the first transcatheter aortic valve implantation procedure was performed where the valve was introduced to the appropriate position by means of a catheter.

Transcatheter aortic valve implantation is now the treatment of choice for high risk and inoperable patients with severe symptomatic aortic stenosis. Despite increasing advantages of transcatheter aortic valve implantation, however, several important setbacks and complications still exist and many improvements to the procedure are possible and necessary.

1. AORTIC STENOSIS

Aortic stenosis is defined as narrowing of the aortic valve. This narrowing impedes the delivery of blood to the aorta with consequent deleterious effects on the heart, both structurally and functionally. Aortic stenosis is the most common valvular heart disease, with it's incidence growing in developed countries, as the population ages (1). The most important etiopathogenic factor is the age-related progressive calcification of the valve, with this group of patients comprising more than 50% of patients with aortic stenosis. Remaining cases mostly consist of patients with calcification of a congenital bicuspid aortic valve (30 - 40 %) (2). Rheumatic fever, as a cause of aortic stenosis, is nowadays rarely seen in the developed world.

Aortic stenosis usually take a prolonged, latent course, with years to take before the appearance of symptoms. The rate of the appearance of symptoms usually correlates with the degree of stenosis, with mild and moderate stenosis usually being asymptomatic. Severe aortic stenosis is usually symptomatic, with the cardinal symptoms comprising a triad of exertion syncope, anginal chest pain and shortness of breath due to congestive heart failure. If left untreated, mortality rates are as high as 50% within 2 years of symptom onset (3).

1.1. The Aortic Valve

The aortic valve is a semilunar, trileaflet heart valve situated between the left ventricle and the aorta. In it's normal anatomy, it consists of three cusps; namely the left posterior valve, right posterior valve and the anterior valve. In 1-2 % of the population, however, the aortic valve is found to be consisted of only two leaflets, a condition named congenital bicuspid aortic valve.

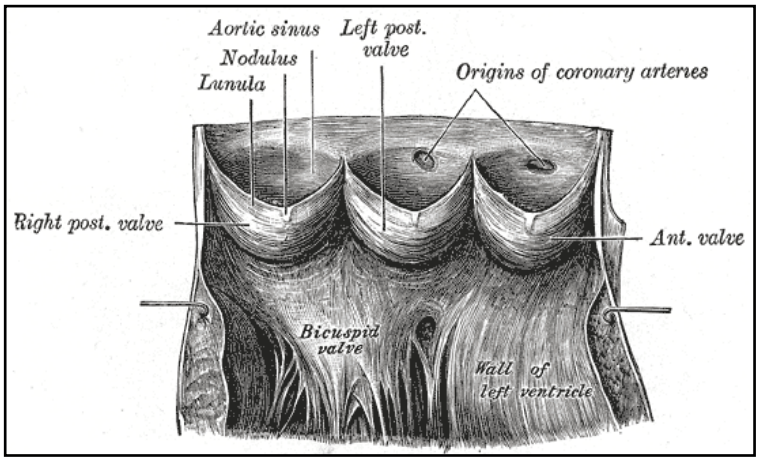


Figure 1. Anatomy of the Aortic Valve

The aortic valve, like the remaining heart valves, functions as a pressure valve, meaning that the state of the valve being opened or closed will depend on the pressure gradient between the left ventricle and the aorta. As the pressure within the left ventricle rises during the systole, it overcomes the pressure present in the aorta and the valves will shut open to allow the blood to flow from the left ventricle into the aorta. During diastole, the pressure gradient reverses, and the valve will shut close. The main purpose of the aortic valve is to prevent the back-flow of blood from the aorta to the left ventricle during diastole, thus ensuring the unidirectional flow of blood. Additionally, the valve contains openings for the origins of the coronary arteries to nourish the myocardium.

Physiologic values of the surface area of the valve is in the range of 3.0-4.0 cm^2.

1.2. Stenosis

Degenerative aortic stenosis, the most common variety, as well as the bicuspid aortic stenosis, have a common beginning - damage to endothelial cells from increased mechanical stress. In calcific AS, the valve cusps become progressively thickened, fibrosed, and calcified.

Inflammation is thought to be involved in earlier stages of the pathogenesis of AS and its associated risk factors are known to promote the deposition of LDL cholesterol and Lipoprotein(A) into the aortic valve resulting in significant damage and stenosis over time (3,4).

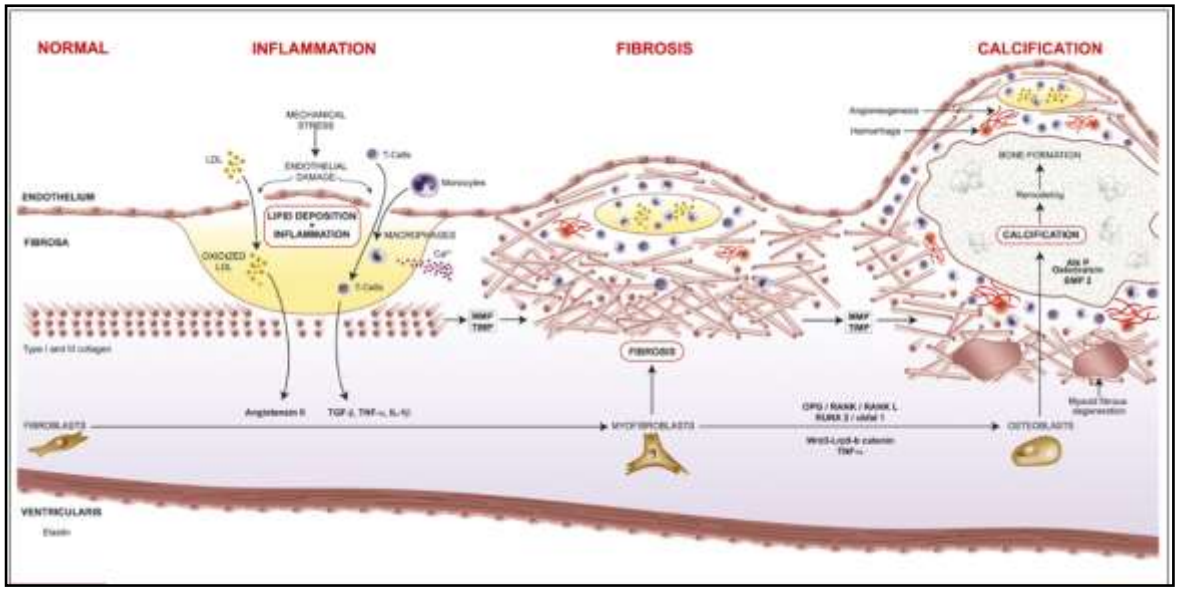


Figure 2. Pathophysiology of Aortic Stenosis

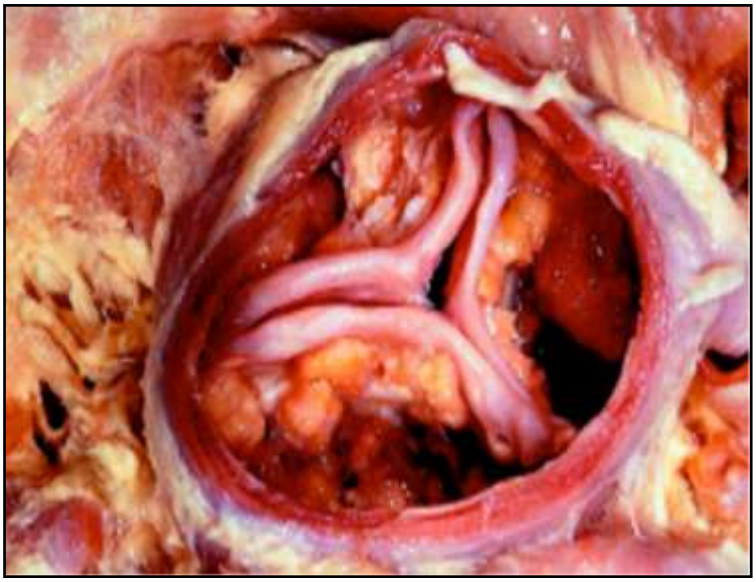


Figure 3. Calcified Aortic Valve in a Patient With Aortic Stenosis

The normal aortic valve usually has an opening with the cross-sectional surface area of approximately 3.0-4.0 cm^2. With progression of AS, this surface area diminishes.

Surface area of less than 1.0 cmm^2 is associated with symptomatic aortic stenosis with increasing severity (5).

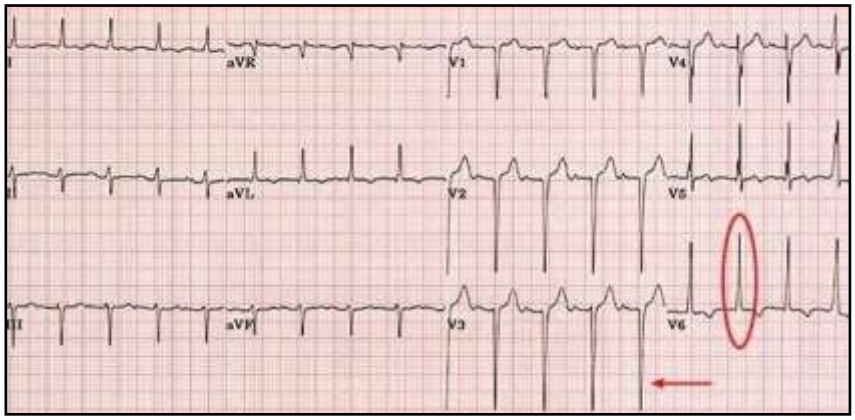
Continuos heart action against increasing resistance exerted by the stenotic valve will progressively lead to structural and functional changes within the heart itself. AS causes an increase in pressure afterload and ventricular wall stress that stimulates hypertrophy of the left ventricular myocardium. Myocytes enlarge and wall thickness increases in a response that initially restores wall stress and preserves left ventricular function (6,7). However, evidence is accumulating that increasing levels of hypertrophy may in fact be maladaptive. The landmark Framingham studies first linked increasing hypertrophy with the progression to heart failure, and left ventricular hypertrophy is now considered a marker of an adverse prognosis across a number of cardiac conditions, including AS (8).

1.3. Diagnosis and Classification of Aortic Stenosis

The diagnosis of aortic stenosis is most commonly established during it's mild, asymptomatic stage, as an incidental finding during a routine physical examination. Despite the lack of symptoms, certain signs can be detected by the physician, who may thereafter question the well-being of the cardiovascular system. Pulsus parvus et tardus, apical-carotid delay, ejection click with a split of the first heart sound and, most prominently, a pan-systolic ejection murmur (usually described as crescendo-decrescendo) radiating to the carotid arteries are the most common abnormal findings during the physical examination that will cause the physician to order additional work-up and try to reveal the root of these abnormalities.

Even though electrocardiography does not contain pathognomonic signs of AS, it does show some changes that are characteristic but not specific for the disease, if they are present. The changes that are more likely to be seen are those indicating left ventricular

hypertrophy, a consequence of the increased workload on the left ventricle. Additionally, in cases where the calcification progresses and affects the conducting system of the heart, these changes can also be detected by ECG in the form of heart blocks such as the left bundle branch block. Again, the aforementioned changes are not specific for AS, hence additional, more detailed examination of the heart, and visualisation of the chambers,



valves and heart walls is necessary (5).

Figure 4. ECG Showing Signs of Left Ventricular Hypertrophy in a Patient With Aortic Stenosis

Echocardiography is used as a non-invasive method for the assessment of the heart valves. By determining the velocity of the blood through the valve, the pressure gradient across the valve can be calculated by the continuity equation or using the modified Bernoulli's equation. The stenotic aortic valve will significantly elevate the pressure gradient and aortic jet velocity. Both trans-thoracic and trans-oesophageal echocardiography can be used in the assessment.

Heart catheterisation provides a definite diagnosis, but due to it's invasiveness, it is reserved only for those patients where the severity of the stenosis cannot be determined by any other means with satisfactory accuracy to guide clinical decision for the choice of treatment. When there are discrepancies between the clinical picture presented by the patient and echocardiographic findings obtained by the physician, heart catheterisation offers means to directly measure the pressures in the left ventricle and the aorta for more

precise assessment of the degree of stenosis. Since the values obtained by these method are a result of a direct measurement, as opposed to calculated values derived by echocardiography, they are used as a basis for further treatment plans and options.

The severity of aortic stenosis is assessed by echocardiography. There are three main parameters that are used to classify AS into mild, moderate and severe: aortic jet velocity, mean pressure gradient across the aortic valve and the aortic valve surface area.

	Aortic Jet Velocity (m/s)	Mean Gradient (mmHg)	Valve Area (cm^2)
Normal	≤2.0	<5	3.0–4.0
Mild	<3.0	<25	>1.5
Moderate	3.0–4.0	25–40	1.0–1.5
Severe	>4.0	>40	<1.0

Table 1. Classification of Aortic Stenosis

1.4. Treatment

In general, pharmacological therapy has relatively poor efficacy in treating aortic stenosis (5). Pharmacological therapy is therefore mainly focused on managing and treating commonly present coexisting conditions.

Hypertension is a high priority in treatment as it is associated with higher mortality rates in patients with AS and the occurrence of left heart failure due to its additional load to the left ventricle which is already overstressed by the stenotic valve. However, extreme caution must be exercised if beta-blockers are to be administered. If angina is present, calcium channel blocker and sometimes beta-blockers are used, but nitrates are contraindicated due to the possibility of severe hypotension in patients taking nitrates in the settings of AS. Heart failure is also treated appropriately, with caution in the choice of medicaments.

The role of statins in treatment and slowing the progression of AS is still elusive, with latest trials not showing significant benefit. There are some studies, however, that are

trying to prove the benefit of *rosuvastatin* in the slowing of progression during the earlier phases of AS (9). Regardless, statins are still used for their beneficial effect in prevention of ischemic heart disease, an important sequelae of long-standing AS.

Eventually, in severe symptomatic AS, patients will require aortic valve replacement. For many decades, surgical replacement of the aortic valve was the standard of care for all patients with aortic stenosis once they became symptomatic. If left untreated, due to it's progressive nature, aortic stenosis will lead to decompensation, left heart failure and, eventually, exitus letalis.

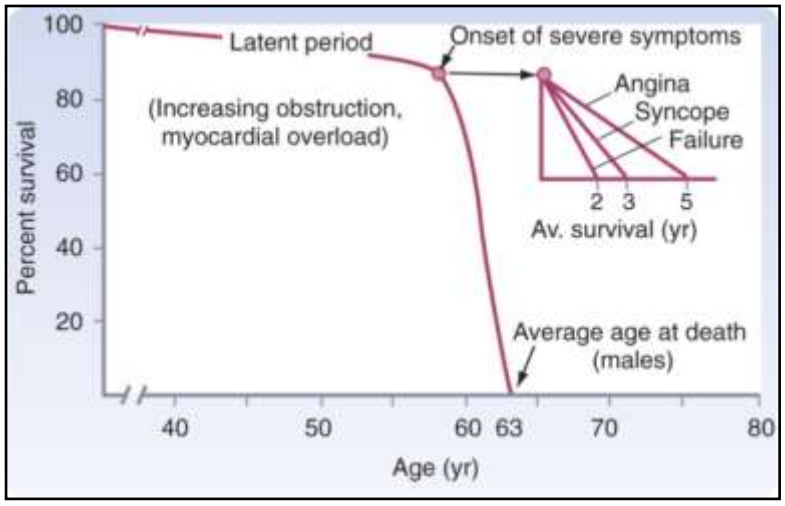


Figure 5. Natural Course of Aortic Stenosis

2. TRANSCATHETER AORTIC VALVE IMPLANTATION

Transcatheter aortic valve implantation (TAVI) is also known as percutaneous aortic valve replacement (PAVR), and transcatheter aortic valve replacement (TAVR).

In it's essence, TAVI is a novel procedure for the aortic valve replacement through a blood vessel or the chest wall with the use of a catheter to deliver the aortic valve to its appropriate position. Several different access points may be used to introduce the catheter. Trans-femoral approach uses the femoral artery as an access point for the introduction of the catheter. In the Trans-apical approach, a small incision between the ribs is made to gain access to the apex of the heart, and the valve is introduced into the ventricle transmurally. Trans-subclavian approach is an alternative retrograde pathway that has been recently explored where the catheter is introduced into the left subclavian artery and retrogradely propagated. This approach is not yet recommended formally. The trans-aortic approach involves accessing the aorta through the chest wall. The choice of the most appropriate approach depends on several factors that will be described later in this text.

In 2002, Allen Cribier performed the first human TAVI using an equine valve with a balloon-expandable frame. The need for this kind of procedure, as an alternative for surgical replacement of the valve, has been long sought, as many patients with AS (up to 30%) are deemed unfit for surgery. AS is associated with many comorbidities that increase the risk from surgery such as CVD and CHF, leading to many patients being excluded from the valve replacement program due to high risk of death. Until the introduction of TAVI, this group of patients, which represents a significant percentage of total patients with AS, did not have a viable alternative for definitive treatment of this life threatening condition. Until today, TAVI has been preformed in over 50.000 patients with high operative risk and inoperable patients.

In its essence, TAVI procedure for the treatment of advanced aortic stenosis consists of three main elements: bioprosthetic valve, a system for visualisation of the valve placement to its appropriate position, and the system for the bioprosthetic valve delivery.

Replacement of diseased valves with prosthetic heart valves reduces the morbidity and mortality associated with native valvular disease, but it comes at the expense of risking complications related to the implanted prosthetic device (10). Emergency medicine physicians must be able to rapidly identify patients at risk and begin appropriate diagnostic testing, stabilisation, and treatment. Even when promptly recognised and treated, acute prosthetic valve failure is associated with a high mortality rate. Common complications of valve replacement will be described in a later chapter.

2.1. Brief history

TAVI has been introduced to history in 2002, in Rouene, France, when Dr. Allen Cribier performed the first human transcatheter aortic valve implantation in a patient with severe aortic stenosis. In its early days, the progress made was slow, but up-to-date more than 50.000 TAVI procedures were preformed in over 40 countries worldwide.

Ten years after the initial implantation by Dr. Alain Cribier, TAVI has become an established therapy for patients with symptomatic severe aortic stenosis, who are deemed to be at too high risk for surgical aortic valve replacement (SAVR). Many reviews have described the evolution of the technology and clinical practice over the past decade and several key concepts have emerged consequent to data gathered: a collaborative heart team, careful patient selection including risk scoring and frailty assessment, and development of professional guidelines on clinical practice and outcomes reporting (10,11).

The requirement of a “heart team” for successful outcomes is highlighted by the recent multi-society expert consensus document. The goal is to use a patient-centred

approach to determine the optimal treatment method for patients with symptomatic severe aortic stenosis. (12,13,14). A heart team usually consist of some or all of the following:

- Cardiologist
- Interventional cardiologist
- Cardiac surgeon
- Anaesthesiologist
- Radiologist

The PARTNER trial published in 2011 played a pivotal role in the revolution of TAVI, as it was the world's first randomised, controlled study to test the safety and effectiveness of the procedure in people with severe aortic stenosis. Convincing benefits of TAVI were proven and since, TAVI became the standard of care for patients contraindicated for SAVR (15).

Nowadays TAVI is an exciting and rapidly expanding field and offers both clinical and quality of life benefits to patients who are considered too sick or at high risk for surgery. However, important issues that adversely affect TAVI outcomes remain, and careful patient selection and device improvement may help address current challenges. A multidisciplinary patient-centred team approach will likely bring a sustained positive impact in this population.

2.2. Surgical Risk Assessment

The precise evaluation of surgical risk in a specific patient is a complex procedure requiring an individualised approach to statistical data from databases containing large numbers of procedures. The most widely accepted and validated algorithms available today are the EuroSCORE and the STS (Society of Thoracic Score) scores.

The aforementioned algorithms are used to asses the surgical risk by evaluating various factors that affect the clinical outcome by assigning values to these factors and formulating a final score. Naturally, such algorithms are sometimes prone to overestimation or underestimation of the surgical risk, especially in patients that greatly deviate from standard representatives.

EuroSCORE stands for European System for Cardiac Operative Risk Assessment. It is a predictive method for calculating operative mortality rate during or shortly after undergoing heart surgery. It was originally presented in Brussels in 1998, and has since undergone several reviews. Recently, the national British database was used to test EuroSCORE; it outperformed other simple scoring systems and approached Bayesian models in discrimination power (16).

One of the main advantages of EuroSCORE is its simplicity. If a risk factor is present in a patient, a weight or number is assigned. The weights are added to give an approximate percent predicted mortality (16).

In total, it uses 18 different variables to calculate a final score that is presented as a percentage, indicating the probability of lethal outcome during or shortly after the surgery. Some of these variables include age, gender, NYHA class, previous cardiac surgery, mobility, the presence of chronic lung disease or pulmonary hypertension and others.

Patient related factors			Cardiac related factors		
Age [1] (years)	0	0	NYHA	select	0
Gender	select	0	CCS class 4 angina [8]	no	0
Renal impairment [2] *See calculator below for creatinine clearance*	normal (CC >85ml/min)	0	LV function	select	0
Extracardiac arteriopathy [3]	no	0	Recent MI [9]	no	0
Poor mobility [4]	no	0	Pulmonary hypertension [10]	no	0
Previous cardiac surgery	no	0	**Operation related factors**		
Chronic lung disease [5]	no	0	Urgency [11]	elective	0
Active endocarditis [6]	no	0	Weight of the intervention [12]	isolated CABG	0
Critical preoperative state [7]	no	0	Surgery on thoracic aorta	no	0
Diabetes on insulin	no	0			

Figure 6. EuroSCORE Calculator

In the context of TAVI, if the EuroSCORE predicted mortality rate for surgical replacement of the aortic valve is 20% or higher, the patient is considered eligible for TAVI if no absolute contradictions for TAVI are present. In such patients, it is up to the Heart Team to do a detailed assessment of the patient and make clinical decisions concerning the treatment plan for that particular patient.

The STS Risk Calculator, developed by the Society of Thoracic Surgeons, allows the calculation a patients' risk of mortality. Unlike the EuroSCORE, however, the STS score additionally allows for prediction of other morbidities, such as long length of stay and renal failure. The Risk Calculator incorporates the STS risk models that are designed to serve as statistical tools to account for the impact of patient risk factors on operative mortality and morbidity.

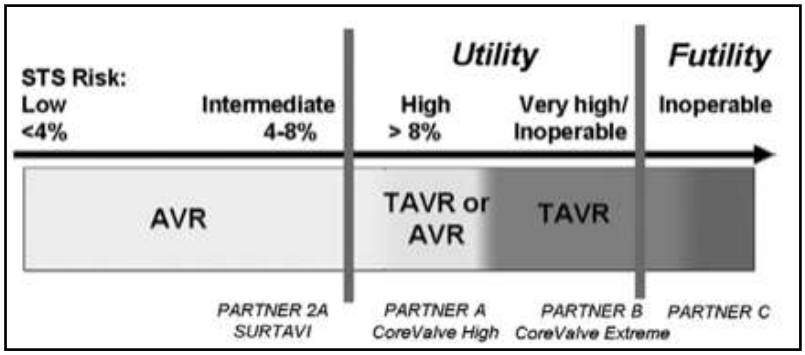


Figure 7. Application of the STS Score

2.3. TAVI Indications and Contraindications

When discussing about indications for TAVI, it must be considered that surgical AVR has been established in the 1960s, and has since been the standard of care for patients with AS, and has been shown to have good long-term results with improved survival, regardless of age. In the ideal candidate, surgical AVR has an estimated operative mortality of 4%. Over the decades, numerous studies and reviews were made, proving its benefits, and currently, the evidence-based bank of knowledge of SAVR is substantially more extensive compared to that for TAVI. Therefore, the choice of

candidates for TAVI has several crucial steps. Most importantly, patients must have severe aortic stenosis and a formal contraindication for surgical valve replacement. The procedure should be offered to patients who have a potential for functional improvement after valve replacement. It is not recommended for patients who simply refuse surgery on the basis of personal preference.

SAVR, on the other hand, despite its proved benefits in suitable patents, remains a highly invasive surgery and in combination with other comorbidities which are often present in patients with AS frequently does not present as a beneficial option. Therefore, TAVI has become an established therapy of choice in the treatment of symptomatic severe aortic stenosis in patients deemed too high risk for surgical aortic valve replacement and has pushed SAVR completely out of the picture in this group of patients.

The key element for establishing whether patients are at high risk for surgery is a multidisciplinary clinical judgment, which should be used in association with a more quantitative assessment, based on the combination of several scores (for example, expected mortality >20% with the EuroSCORE and >10% with STS score). This approach allows the team to take into account risk factors that are not covered in scores, but are often seen in practice, such as chest radiation, previous aortocoronary bypass with patent grafts, porcelain aorta, liver cirrhosis etc (16).

In the European Union, TAVI is commercially available, and the procedure is performed in patients with severe aortic stenosis who are high-risk surgical candidates with a logistic EuroScore of more than 20% and in patients who have a contraindication to surgical aortic valve replacement (16,17).

Once a patient is considered for transcatheter aortic valve implantation, the presence of contraindications is assessed. Contraindications for TAVI include the following (17):

- Surgical aortic valve replacement possible, but patient refused

- Mild to moderate aortic stenosis
- Asymptomatic patients
- Life expectancy <1 year
- Aortic annulus <18 or >25mm (balloon-expandable) and <20 or >27mm (self-expandable). This criterion is subject to change as the range of available device sizes changes
- Bicuspid aortic valve
- Asymmetric heavy valvular calcification
- Aortic root > 45mm at the aorto-tubular junction
- Presence of left ventricular apical thrombus

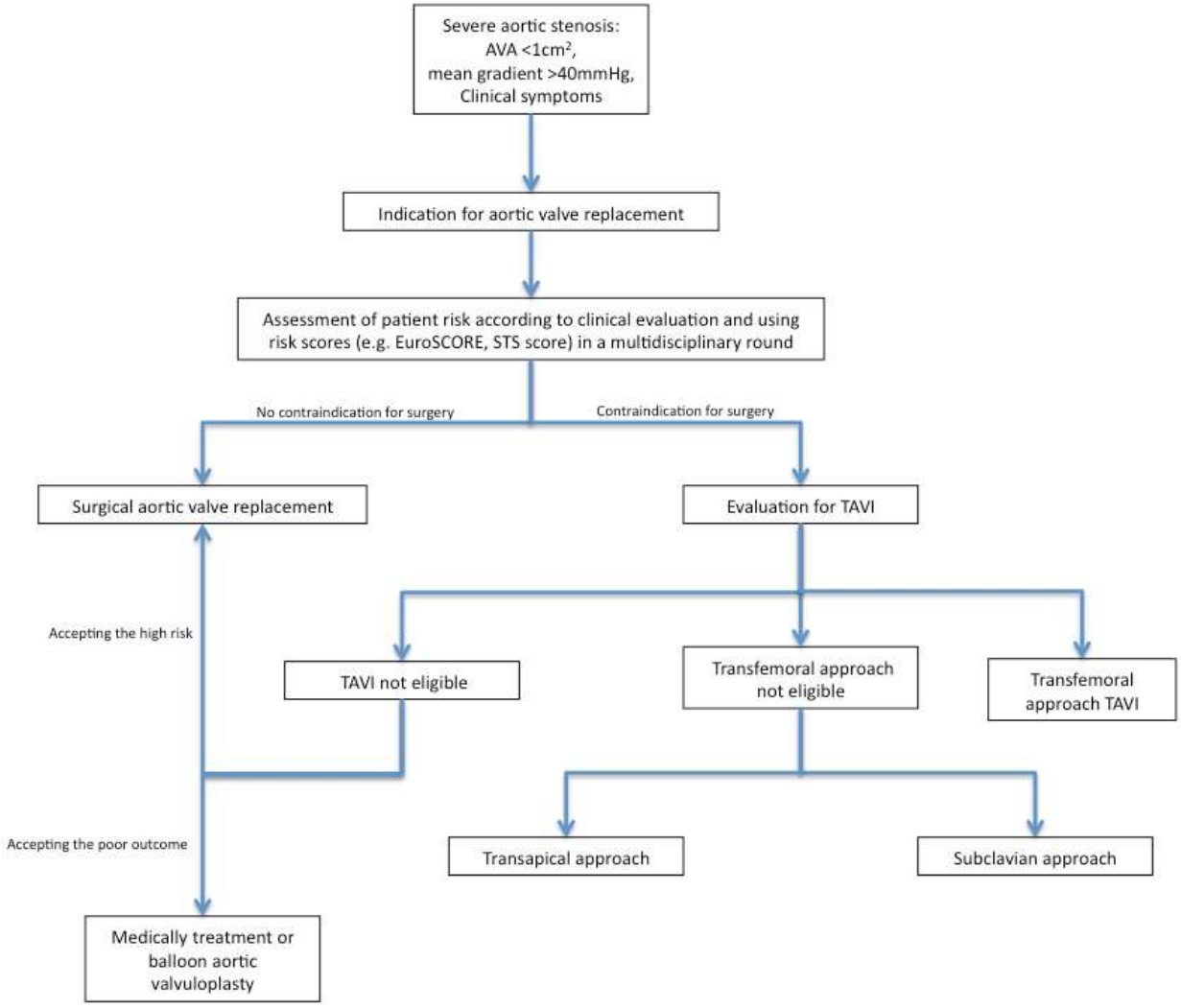


Figure 8. Algorithm to Determine the Treatment Options of Patients With Severe AS

Patients with low-flow, low-gradient severe aortic stenosis are a rare, but a challenging population to manage given the poor prognosis associated with conservative or surgical treatment. TAVI may be a viable alternative (18). Such patients have higher logistic Euro-Score and have more comorbidities such as CAD, peripheral vascular disease, pulmonary hypertension, and >2+ mitral regurgitation. Despite having improved New York Heart Association class symptoms and QoL, they have higher 30-day and 1-year mortality (12.8% and 36.9% respectively) and major adverse cardiac and cerebrovascular events.

Even though TAVI can be performed safely in this high-risk population, given the significant early and mid-term mortality, very careful selection among low-gradient aortic stenosis patients will be necessary to derive any potential long-term benefits (18).

2.4. Implantation approches

Several different approaches have been described and used for the access of the implantation site. Currently, the trans-femoral approach is the option of choice due to it being the least invasive method. However, this approach is not always feasible, and soon the need for other approaches appeared for patients that are suitable for TAVI but have contraindications for the trans-femoral approach. The explored pathways thus far can be divided into two main groups; anterograde and retrograde pathways, in respect to their introduction into the ascending aorta (19).

It is up to the heart team to choose the most appropriate approach in an individualised patient-oriented assessment with careful consideration of the various indications and contraindications to each approach separately.

TTE, TOE, CT scans and contrast-enhanced CT angiography are required to asses the vascular approaches and the choice of the most appropriate introduction site for each

patient. This emphasises the need for multidisciplinary consideration and the importance of the heart team.

2.4.1. TRANS-FEMORAL APPROACH

The trans-femoral approach is a retrograde approach where the catheter is introduced through the femoral artery. It is the most commonly used approach, and it has several important advantages. The procedure may be preformed purely trans-cutaneously in the catheterisation lab under local anaesthesia, or alternatively, the common femoral artery may be surgically prepared under local or general anaesthesia in the operating theatre. It can be used as long as the vessels are of appropriate diameter, i.e. >6mm and vascular closure devices are available.

Despite it's advantages, there are several different limitations to this approach, and the contraindications are as follows:

- Severe calcification of the femoral or iliac arteries
- Tortuosity of the peripheral or iliac arteries
- Small diameter of the iliac arteries
- Previous aorto-femoral bypass
- Severe angulation of the aorta
- Severe atheroma of the aorta
- Coarctation of the aorta
- Aneurysm of the aorta with protruding mural thrombus

Furthermore, the trans-femoral approach is sometimes associated with post-operative vascular complications that include vessel dissections, ruptures and avulsions. These complications must be timely and adequately attended in order to avoid catastrophic sequelae (20).

2.4.2. TRANS-APICAL APPROACH

Trans-apical approach is an anterograde approach where the catheter is introduced through the left ventricle. The cardiac apex is prepared through a small left anterolateral mini-thoracotomy. After the procedure, a chest tube is routinely inserted into the left pleura. This approach has several clear advantages. Primarily, peripheral vascular disease or previous aortic surgery do not represent contraindications. This approach has also been described as more straightforward and steady (21). Additionally, the potential risk for calcium dislodgement is diminished.

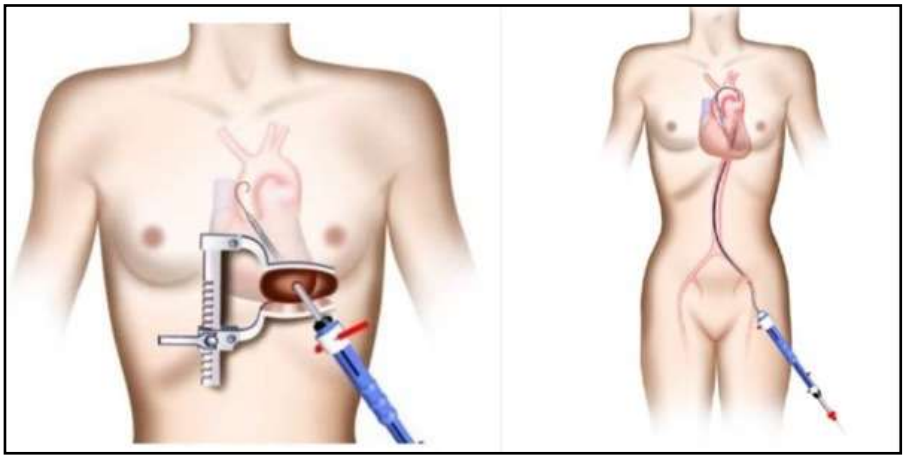


Figure 9. The Trans-apical (left) and the Trans-femoral approaches (right)

This procedure can be performed in the catheterisation lab, hybrid room or the operating theatre, under general anaesthesia. A high-quality fluoroscopic imaging is a prerequisite.

Contraindications for the trans-apical approach include the following:

- Previous surgery of the left ventricle using a patch
- Calcified pericardium
- Severe respiratory insufficiency
- Non-reachable left ventricular apex

A possible complication of this approach is apical bleeding through the introduction site. Main factors affecting the occurrence of apical bleeding are those endogenous to the patient (i.e. tissue fragility) or those attributable to the experience of the team performing the surgery.

2.4.3. TRANS-AORTIC APPROACH

This is another novel retrograde approach proposed for the small group of patients that have a concomitant contraindication to both the trans-femoral and trans-apical approach. The delivery system is introduced into the ascending aorta through a small J-shaped hemi-sternotomy and secured with a double-string suture, with the procedure thereafter carried on as in the trans-femoral approach (22). Alternatively, a right anterior mini-thoracotomy may be performed in order to access the aorta.

It is, however, contraindicated in the presence of porcelain aorta. The main setback for this approach is the risk of massive postoperative bleeding.

2.4.4. TRANS-SUBCLAVIAN APPROACH

Trans-subclavian approach is another retrograde approach for TAVI through a surgically exposed left subclavian artery. It is also known as the trans-axillary approach.This is a novel, recently introduced approach, but several clear advantages have been described. Compared to the trans-femoral approach, the distance from the site of introduction to the site of implantation is significantly shorter, with a consequent steadier pathway of delivery. Equally important, it can be used regardless of the presence of peripheral artery disease or a diseased abdominal aorta, and unlike the trans-apical approach, does not require thoracotomy (23).

Limitations of this approach include the size of the subclavian artery if it cannot withstand a 18F catheter and the presence of a patent internal mammary artery, such as a

diseased subclavian artery, in redo coronary surgery which contraindicates this approach (23).

Currently, however, this approach is still not recommended due to scarcity of clinical and evidence-based data favouring this approach over formerly mentioned ones.

2.5. Bioprosthetic Valves used in TAVI

Currently, there is an increasing number of transcatheter heart valves (THV) that can be found on the market. Depending on the manufacturer, the bioprosthetic valve can be self-expandable or balloon-expandable. Balloon- expandable bioprosthetic heart valves need to be mounted on a deflated balloon catheter which is then inflated once the valve is in the desired position, hence securing the valve to its place. Some of the bioprosthetic heart valves have been well studied, such as the Edwards Sapien valve in the PARTNER trial, while investigation for others are still ongoing (15). Some of the valves are currently recommended for only one mode of approach, while others can be used for multiple approaches.

The bioprosthetic valve consists of 3 main subunits:

- a bearing solid structure made of stainless steel, cobalt chromium or nitinol which serves as mechanical support to valve placement and in its nature it is a stent
- the valves themselves, which are usually made of processed porcine or bovine pericardium
- the covering for the entire structure that offers functional properties such as haemodynamics, and resistance to thrombosis that are made similar to those of native valves.

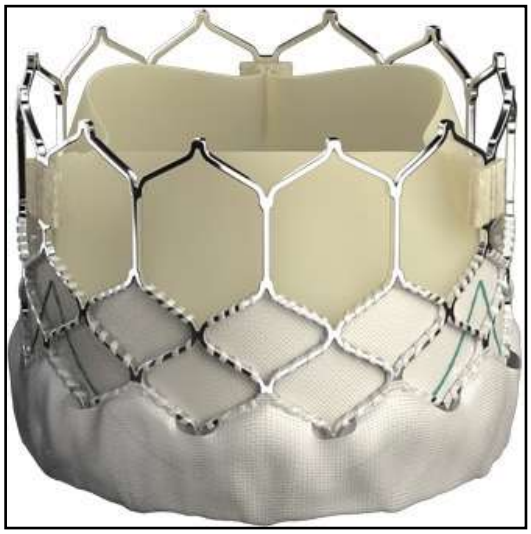


Figure 10. The 3rd generation Edward Sapien Bioprosthetic Aortic Heart Valve

The most prominent bioprosthetic heart valves currently encountered on the market are the Medtronic CoreValve system, Edwards Sapien XT system, Direct Flow system, Sadra Lotus by Boston Scientific, St Jude Medical Portico, but many others. A summary of the ongoing trials for new-generation valves is as follows:

Company	Valve Name, Sizes, and Delivery Route	Status
Boston Scientific	Lotus Valve System, 23, 27 mm, TF	REPRISE II CE Mark trial of 120 patients underway
Direct Flow Medical Inc	23, 26 mm, TF	DISCOVER trial with planned enrollment of 100 patients
Edwards Lifesciences	Sapien XT, 20, 23, 26, 29 mm, TF/TA	SOURCE XT registry
Edwards Lifesciences	Sapien 3, 20, 23, 26, 29 mm, TF	CE Mark trial has begun
Edwards Lifesciences	Centera, 23, 26, 29 mm, TF/TS	First-in-man study in 10 patients. CE Mark trial expected late 2012
JenaValve	23, 25, 27 mm, TA	CE Mark 9/2011
JenaValve	23, 25, 27 mm, TF	Animal studies ongoing
Medtronic	Engager valve, 23, 26 mm, TA	First-in-man and feasibility trials completed. Data on 60/150 patients (mid-term analysis) from CE Mark study will be presented at the 2012 European Association for Cardiothoracic Surgery meeting
Medtronic	CoreValve Evolut, 23 mm, TF	Enrolled in the Evolut registry
St. Jude Medical	Portico, 23, 25, 27, 29 mm, TF	CE Mark study ongoing with 45/50 patients enrolled. US pivotal trial expected 2013
Symetis	Acurate (S, M, L), TA	CE Mark approved in 9/2011 based on 2 trials. Postmarket registry ongoing
Symetis	Acurate (S, M, L), TF	First 20-patient study completed. Further trial in 150 patients planned. CE Mark submission expected in 2013

Table 2. Most Commonly Encountered Bioprosthetic Heart Valves

2.6. TAVI Complications

Despite advances in TAVI technology and experience, a number of important issues impacting outcomes remains unresolved. Additional, it seems that the choice of a particular THV plays a role in the incidence of some of these complications.

2.6.1. STROKE

Stroke represents one of the most significant adverse outcomes of TAVI. There are several intertwining factors that play a role in the occurrence of stroke, most prominently old age, aortic atherosclerotic burden and the severity of calcification of the aortic valve. Factors increasing the risk for stroke that are related to the procedure itself include crossing a stiff guidewire across the aortic arch, balloon aortic valvuloplasty and valve deployment. According to the results presented by the PARTNER trial, cohort B patients (TAVI vs. medical therapy) who underwent TAVI presented with higher stroke rates than those treated medically. This difference was significant and persistent: 13.8% for TAVI vs. 5.5% for medical therapy at 2 years, P=0.009. Strokes occurring within 30-days of TAVI were predominantly ischemic while those occurring afterwards were predominantly hemorrhagic. Cohort A of the PARTNER study (TAVI vs. SAVR), on the other hand, did not show meaningful difference in the post-procedural incidence of stroke up to 2 years, but did show a difference in stroke rate within 30 days: 4.6% for TAVI vs. 2.4% for SAVR (24).

2 hazard phases for neurological events have been identified: early phase events that occurred more frequently in TAVI than SAVR, and late phase events that are mainly influenced by factors endogenous to the patient and disease related factors (24).

Recent large multi-centre series and national registries reported stroke risk ranging from 0.6% to 5.0% (25). A meta-analysis of >10,000 patients in 53 studies further confirmed that TAVI results in a reasonable procedural stroke rate of 1.5% and a 30-day stroke/TIA rate of 3.3% (26).However, the 30-day mortality in stroke patients was 25.5%, 3.5 times higher than the overall rate of 8.1%.

In order to intervene in the rates of stroke occurrence, several different devices for deflection or capture of emboli have been developed and are currently under trial. The results are thus far encouraging, but not yet adequately conclusive.

Such devices include the Embol-X (Edwards Lifesciences Inc, CA) filter, TriGuard^{TM} embolic deflection device (Keystone Heart Ltd, Israel) and the Claret CE Pro (Claret Medical Inc, CA) cerebral protection device (27,28,29). Further refinement of such devices represent a huge opportunity for improving survival and diminishing morbidity in patients undergoing TAVI.

Figure 11. Embol-X Filter

2.6.2. PARAVALVULAR LEAK AND AORTIC REGURGITATION

Paravalvular leak (PVL) is proved to be a very important issue and complication of TAVI. It might be the single most important aspect of AVR where SAVR shows to be significantly more advantageous than TAVI, and there is still much space for progress to be made in this area.

The main factor influencing the higher rates of PVL in TAVI is attributable to the nature and mechanical characteristics of valve mode of implantation. SAVR allows for the total excision of the stenotic valve, leaving behind a smooth, non-aberrant aortic annulus with no irregular surfaces allowing for placement of the prosthesis with a tight seal resulting in no PVL. TAVI, on the other hand, requires the stenotic valve as an anchor for placement of the implant, not allowing for furbishing and smoothening the surface which therefore results in a significant rate of PVL.

SAVR rarely has the problem of paravalvular leak or significant aortic regurgitation (AR), and in cases where it is present, immediate surgical correction is mandated. The cohort A of the PARTNER trial clearly shows a significantly higher PVL and AR rates compared to SAVR, with more than 50% of TAVI patients showing at least mild PVL and/or AR in 2-year follow-up (30).

The more concerning aspect of these complications is that even mild PVL and AR after TAVI are associated with 10-15% higher mortality rates at 2-years than patients with no evidence of PVL or AR. Additionally, another study showed that moderate or severe aortic regurgitation is the strongest independent risk factor for all-cause as well as cardiovascular mortality (31). Although a majority of patients with mild regurgitation of the native aortic valve can remain asymptomatic and tolerate the condition for a long time, for unknown reasons TAVI patients do not appear to tolerate even mild PVL or AR.

In order to address these concerns, various investigations attempted to determine risk factors associated with increased risk for PVL and AR. Currently, the suggested factors include several anatomic characteristics, such as asymmetrically calcified cusps, large annular size, elliptical annular shape, and calcified LV outflow tract may be associated with a higher risk of PVL. An improved implantation technique, particular in TA-TAVI, may reduce the incidence of PVL (32).

Given the significant mortality risk associated with mild or greater PVL or AR after TAVI, improvement in deployment strategy and advance in TAVI technology will be necessary to address this issue. For now, identifying certain avoidable risk factors and pitfalls, as suggested by the above studies, or determining the appropriate THV size by MDCT, may be all that can be done to minimise these important side effects of TAVI.

2.6.3. HEART BLOCK

Several risk factors predispose TAVI patients to new-onset left bundle branch block (LBBB) and a subsequent heart block requiring a pacemaker. They include the compression of the Bundle of His by the device itself or by a post-procedural localised haematoma, procedural factors such as balloon aortic valvuloplasty injuring the conducting system, as well as device-related factors such as the continuous radial force exerted by the CoreValve and the depth of device implant in the left ventricular outflow tract. Equally important, patient related risk factors such as the pre-existing right bundle branch block (RBBB) may be a predisposing factor for the development of heart block, especially if new onset LBBB occurs (33). Studies have showed that the occurrence of these complications may be significantly influenced by the choice of the THV device (33).

The incidence of pacemaker implant after SAVR has been 3–8%, and in a recent comparison study from among 411 TAVI patients using the Edwards THV and 411 electrocardiography-matched patients who underwent SAVR, the new pacemaker implant rate was higher in the TAVI group (7.3% vs 3.4% in SAVR, $P = 0.014$) (34). Despite the higher incidence of new onset LBBB, heart block and pacemaker implant among TAVI patients, there has been no proven adverse impact on survival.

The incidence of heart block requiring a new pacemaker was 3–6% for the Sapien valve in the PARTNER trial, and ranged from 4.8% to 18% among institutions, multi-centre studies and national databases. However, the incidence was much more variable for CoreValve, ranging from 12.1% to 49% (35).

2.6.4. VASCULAR COMPLICATIONS

The occurrence of vascular complications in TAVI is attributed to the nature of the procedure and it’s transcatheter approach. As mentioned earlier, most important catheter-related vascular complications include vascular dissection, vascular perforation, and

access site haematoma. Rare but more significant potential complications include aortic dissection and left ventricle perforation. The most concerning implications of the occurrence of vascular complications are the associated higher 30-day and 1-year mortality rates (36). Minimal arterial diameter smaller than the external sheath diameter, moderate or severe vessel calcification, and peripheral vascular disease are the most significant risk factors associated with the occurrence of vascular complications.

The PARTNER trial demonstrated that vascular access complications during TAVI were associated with decreased survival and were risk factors of late mortality (OR 2.78, CI 1.58–4.82, $P < 0.001$) (30,36). The rate of vascular complications among contemporary registries range from 2.0% to 13% and decrease with increasing procedural experience (37). Contralateral balloon occlusion technique during delivery sheath removal and percutaneous arterial closure have been effective in reducing vascular complications following TAVI, with technique failure attributing only to obesity, vessel calcification, small vessel diameter, and “high” arterial access (38). A recent review of 986 TAVI patients performed with the trans-femoral approach in 5 European centres, with an overall major vascular complication rate of 14.2%, showed a majority of complications were due to closure device failure in those who had percutaneous access (39).

2.6.5. ATRIAL FIBRILLATION

The incidence of new-onset atrial fibrillation following cardiac surgery ranges from 10% to 60%, with a higher frequency following valve surgery. Postoperative AF is known to be associated with increased hospital stay, stroke, and mortality rate (40). The incidence of post-procedural AF was significantly lower in the TAVI compared to the SAVR group (6.0% vs 33.7%, $P < 0.05$). Interestingly, patients in the TAVI group most likely developed post-procedural AF within the first 24 hours, compared to SAVR patients who most likely developed AF on postoperative day 3 (41).

The adverse impact of AF after TAVI has only recently been identified by a study finding chronic AF as an independent predictor of late mortality (>30 days) in a study analysing 1262 TAVI patients (42). Prior investigations yielded diverse conclusions, but increased left atrial size (≥27 mm/m^2) and the trans-apical approach were identified as predictive factors, and at 30 days of follow-up, the new-onset AF was associated with increased stroke/systemic embolism (13.6% vs 3.2%, *P* = 0.047) but no increase in mortality at 30 days and 12 months (15.9% vs 21.3%, *P* = 0.58) (43).

When discussing atrial fibrillation in the context of TAVI, it needs to be stressed out that there have been some conflicting results in studies, namely the ones conducted in Canada and Germany. (40,41,42,43). This mandates a greater scale studies on larger populations of patients undergoing TAVI to appropriately evaluate the mechanisms of new-onset AF or conversion from preexisting AF to sinus rhythm after TAVI (12).

2.7. TAVI Procedure

2.7.1 PRE-PROCEDURE PLANNING

Main aspects of the pre-procedure planning were already described in the text earlier, in regards to the selection of patients that are candidates for TAVI, and more elaborately in regards to the choice of the most appropriate approach for TAVI.

In summary, echocardiography is used to confirm the severity of aortic stenosis, aortic valve anatomy, and extent of calcification and to evaluate the diameter of the aortic annulus, ascending aorta, sinus of Valsalva, the distance of the aortic valve leaflets to sinotubular junction, the presence of concomitant severe other valvular disease, and the LVEF.

CT angiography of the aortic root is used to determine the optimal image orientation for valve positioning. Left and right cardiac catheterisation is used to evaluate for concomitant coronary artery disease or pulmonary hypertension that may require

treatment prior to TAVI. CT angiography of the thoraco-abdominal and ilio-femoral arteries is used to evaluate the diameter, tortuosity of the vessels, and calcifications and to plan for the access site.

Figure 12. 3D reconstruction of contrast-enhanced CT angiography to assess morphology of femoral arteries

Patients are pretreated with *aspirin* (80-325 mg) daily and *clopidogrel* 300 mg loading dose at least one hour prior to the procedure and continued at 75 mg oral daily dose. After the procedure, *aspirin* (at least 80 mg daily) is continued indefinitely, and *clopidogrel* 75 mg daily is continued for 1-6 months.

Routing laboratory tests prior to the procedure include complete blood cell (CBC) count, international normalised ratio (INR), partial thromboplastin time (PTT), albumin and transaminase levels, renal function testing, and 12-lead electrocardiography (ECG). Cardiac biomarker levels (ie, CK and CK-MB) are also tested within 48 hours of the procedure.

To minimise the risk of prosthetic valve infection, prophylactic intravenous antibiotic therapy at least 1 hour before the procedure is also recommended. *Cefuroxime* 750 mg IV 1 hour pre-procedure is usually administered, and the dose is repeated 6 and 12 hours after the procedure. In patients who are allergic to penicillin (or cephalosporins), vancomycin may be considered.

2.7.2. VALVE IMPLANTATION

TAVI is performed in the catheterisation lab, hybrid room or the operating theatre by a cardiac surgeon or an interventional cardiologist. At this point, all pre-procedural examinations must have been completed, with the assessment of the introduction sight, the choice of the appropriate approach technique and the visualisation of the diseased valve. The procedure is usually performed in general anaesthesia, but in certain cases deep sedation with local anaesthesia to the introduction site can be administered. The patient remains in the supine position during the procedure. Cardiopulmonary bypass equipment should be easily available in case of complications. The room should also be equipped with supplies required to treat vascular and coronary complications.

At this point, the heart team has already chosen the approach, the appropriate prosthetic heart valve, as well as the catheter size in concordance with the selected approach.

Depending on the selected approach, the introduction site must be exposed, with the exception of the purely percutaneous trans-femoral approach where the catheter is introduced directly into the femoral artery through the skin.

After surgical exposure of the introduction site, an introducer sheath is inserted into the blood vessel. Through the introducer sheath, the guidewire is inserted into the blood vessel in a retrograde fashion and guided to the aorta until the stenotic valve is reached, and then through the aortic valve into the left ventricle.

The imaging methods used to navigate the guidewire (as well as the catheters and the prosthetic valve) are fluoroscopy and angiography - as the primary imaging modality during device implantation. Echocardiography is frequently used as an adjunct imaging tool.

Computed tomography (CT), which is critical in preparing for the procedure, is increasingly integrated with intra-procedural imaging. The fusion of images from various

modalities is rapidly evolving with 3-dimensional (3D) visualisation of anatomy and devices. Fluoroscopy has a large field of view and depicts 3D information on a 2-dimensional (2D) monitor, whereas echocardiography can show 2D or 3D information that limits field of view on mostly 2D monitors. Details of the devices are much better seen on radiographic imaging, whereas non-calcified tissues are better visualised by ultrasound.

Once the guidewire is fully in place, a catheter with a deflated expandable balloon is mounted on the guidewire and delivered all the way to the aortic valve. The balloon is positioned to be exactly in the level of the valves.

Once properly placed, the balloon is inflated and expanded to widen the opening of the valves to allow room for the prosthetic valve. The balloon is then deflated and removed. Now another ballon catheter is prepared for the valve delivery. The valve is compressed and mounted on the tip of the catheter over the expandable balloon and introduced over the guidewire to the position of the aortic valve in the already described fashion.

Once the compressed valve is visualised to be in the necessary position, the balloon is inflated to expand the prosthetic valve and now the new prosthetic aortic valve is finally in place. The native heart valve is used as an anchor to the prosthesis, and the stent, which is part of the prosthetic valve, will support and secure the artificial valve in place. The second catheter and the guidewire are then removed.

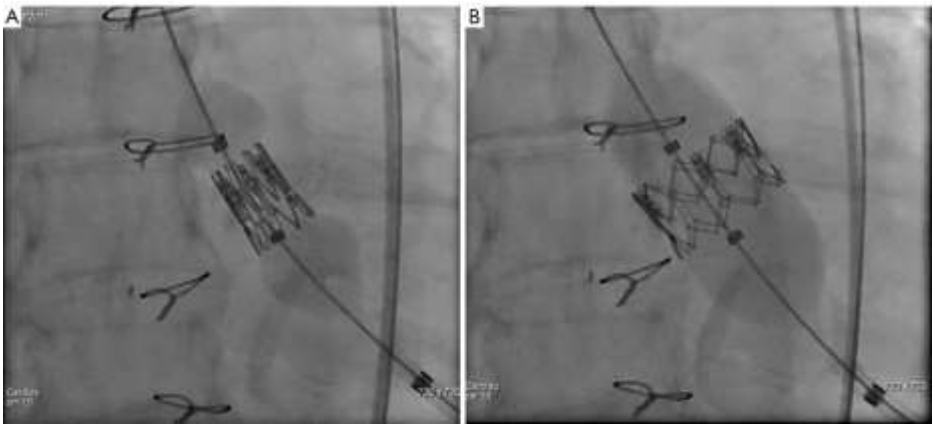


Figure 13. Fluoroscopy Showing the THV Before (A) and After (B) balloon expansion

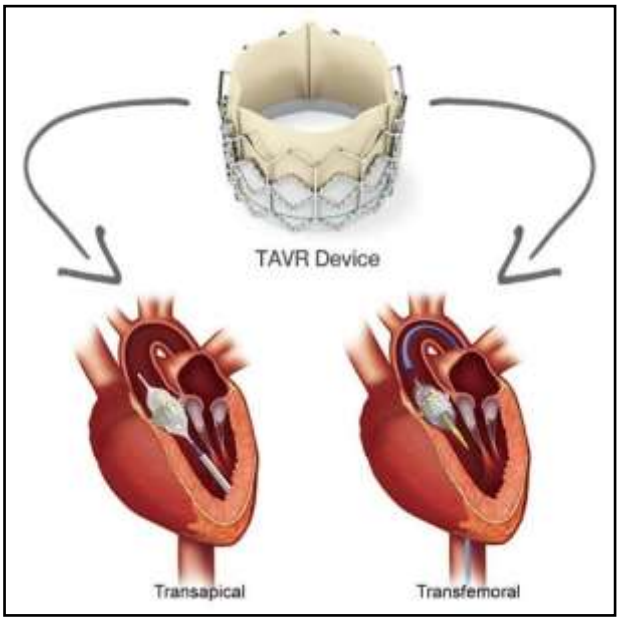


Figure 14. Anterograde and Retrograde Delivery of the Bioprosthetic Heart Valve

The function of the newly placed valve must be assessed and visualised by echocardiography. Proper position, mechanical function of the valve, AVA, paravalvular leakage, regurgitation, pressures and velocities are assessed.

If TAVI is deemed successful, the introduction site may be closed by a closure device, and the patient is then transferred into an intensive care unit.

The above described procedure, however, may vary significantly from one TAVI to another. As mentioned earlier in this text, various different manufacturers produce different types of valves that may require different steps in TAVI. Some of the bioprosthetic valves currently encountered are self-expandable and therefore do not require to be mounted on a balloon catheter.

Furthermore, also described earlier in this text, sever different approaches in TAVI exist, and depending on the particular approach as well as depending on factors endogenous to the patient, different sized catheters are used for native valve expansion and THV valve delivery. In the trans-apical approach, the valve is not reached through a blood vessel but directly through the heart instead. All these variations further emphasise the need for a multidisciplinary patient-oriented Heart Team approach and experience.

2.8. TAVI in Croatia

The TAVI program is relatively new in Croatia, with the first procedure performed in 2011. Currently, the program is present in 2 institutions in Croatia, namely the University Hospital Dubrava and the University Hospital Centre Zagreb.

By 2014, 87 TAVI procedures were performed, out of which >55% were performed in the University Hospital Dubrava, where the program is supervised by a Heart Team consisting of a cardiologist, cardiac surgeon and an anaesthesiologist. The team evaluates each patient in an individualised approach to asses the eligibility for the procedure, as well as the appropriate approach, valve and equipment that should be used (13).

All patients had previous TTE, TEE, aortography and CT made, and the procedures were performed by a Heart Team. All but one patient underwent general anaesthesia, with the one patient that was deeply sedated. 89% of the patients had TAVI performed by the trans-femoral approach, 39% out of which the artery was surgically prepared.

The average echocardiography findings prior to and after TAVI are represented by the following table:

	Before TAVI	After TAVI
AVA	0,60	
Vmax AO	4,76	2,27
Aortic regurgitation	1-2	0-1
Pulmonary pressure	36,8mmHg	31,75mmHg
Mitral regurgitation	2-3	1-2
Tricuspid regurgitation	1-2	1

Table 3. Comparison of Echocardiographic Findings Before and After TAVI

The outcomes of the procedures are summarised in the following table:

30 d mortal	1y mortal	2y mortal	3y mortal	CVI	PV leak	AMI	PCI before	PCI + TAVI	Pci after

Table 4. Outcomes

In conclusion, TAVI is available for patients in Croatia with very high success rates, but with certain limitations, most notably the procedural price. The Heart Team has a pivotal role in the development of the program with the responsibility of careful patient selection and evaluation.

3. FOLLOW-UP

TAVI is less invasive than traditional AVR – no sternotomy is performed, cardiopulmonary bypass (CPB) is not necessary, and patients may be extubated in the operating room (OR). Despite its less invasive nature, over the past few years as the number of TAVIs have increased, a unique set of postoperative events and complications have been identified. While some ICU management issues are shared with patients undergoing traditional AVR, TAVI patients are predisposed to ICU concerns that the attending specialist needs to recognise and manage appropriately.

3.1. Pre-discharge Follow-Up

After the procedure, the patients that underwent TAVI are extubated and transferred to the ICU. The patient should be observed with a temporary pacemaker for up to 48 hours to monitor for any conduction system abnormalities. If no conduction system disturbances are detected, the patient is monitored for an additional 72 hours and then discharged.

The patient should continue taking *aspirin* 80-325 mg daily and *clopidogrel* 75 mg daily for at least 3 months following the procedure. Repeated doses of *cefuroxime* 750 mg IV should be administered at 6 and12h post-procedure.

Both trans-thoracic echocardiography (TTE) and trans-oesophageal echocardiography (TOE) may be used to evaluate for complications, as needed. The complications have been described earlier in the text in the context of complications of TAVI.

Apart from the earlier mentioned cardiovascular, prosthesis and procedure related complications, some of the other potential sequelae of the procedure include postoperative delirium, postoperative pain and renal failure. The occurrence of such events should be early recognised and treated appropriately.

3.2. Post-discharge Follow-Up

Once the patient has shown not to have any complications requiring the prolongation of pre-discharge care, and the physician is satisfied with the function of the prosthetic valve, the patient may be discharged.

The patient should continue aspirin therapy indefinitely, but clopidogrel treatment may be ceased after 3 months.

The physician must schedule follow-up visits at 30 days, 3 months, 6 months and 1 year after the procedure. Beyond that, the visits may be on annual basis, providing that no reasons for concern have been identified by the patient or the physician.

In this rapidly expanding era of TAVI where constantly increasing evidence of benefit encourage the wide-spread use of TAVI, numerous studies are constantly being published in many countries presenting the statistical analysis and meta-analysis of their patients at 30 day, 1 year, 2 year and 5 year post-procedure. The results of the relatively young program in Croatia have already been summarised earlier in this text.

In 2013, a large scale study obtained results from all eligible USA TAVI cases (n=7710) from 224 participating registry hospitals following the Edwards Sapien XT device commercialisation (November 2011-May 2013). The results of the study show that the 7710 patients who underwent TAVI included 1559 (20%) cases that were inoperable and 6151 (80%) cases that were high-risk but operable. The median age was 84 years (interquartile range [IQR], 78-88 years); 3783 patients (49%) were women and the median STS predicted risk of mortality was 7% (IQR, 5%-11%). At baseline, 2176 patients (75%) were either not at all satisfied (1297 patients [45%]) or mostly dissatisfied (879 patients [30%]) with their symptom status; 2198 (72%) had a 5-m walk time longer than 6 seconds (slow gait speed). The most common vascular access approach was trans-femoral (4972 patients [64%]), followed by trans-apical (2197 patients [29%]) and other alternative approaches (536 patients [7%]); successful device implantation occurred in 7069 patients

(92%; 95% CI, 91%-92%). The observed incidence of in-hospital mortality was 5.5% (95% CI, 5.0%-6.1%). Other major complications included stroke (2.0%; 95% CI, 1.7%-2.4%), dialysis-dependent renal failure (1.9%; 95% CI, 1.6%-2.2%), and major vascular injury (6.4%; 95% CI, 5.8%-6.9%). Median hospital stay was 6 days (IQR, 4-10 days), with 4613 (63%) discharged home. Among patients with available follow-up at 30 days (n=3133), the incidence of mortality was 7.6% (95% CI, 6.7%-8.6%) (non-cardiovascular cause, 52%); a stroke had occurred in 2.8% (95% CI, 2.3%-3.5%), new dialysis in 2.5% (95% CI, 2.0%-3.1%), and re-intervention in 0.5% (95% CI, 0.3%-0.8%) (44).

A similar study but on a significantly smaller scale was performed in the UK. In this study, however, the follow-up was up to 6 years, thus giving insight to a longer term survival rate. The study assessed trends in the performance of transcatheter aortic valve implantation in the United Kingdom from the first case in 2007 to the end of 2012. A total of 3980 transcatheter aortic valve implantation procedures were performed. In successive years, there was an increase in frequency of impaired left ventricular function, but there was no change in Logistic EuroSCORE. Overall 30-day mortality was 6.3%; it was highest in the first cohort (2007-2008), after which there were no further significant changes. One-year survival was 81.7%, falling to 37.3% at 6 years. Discharge by day 5 rose from 16.7% in 2007 and 2008 to 28% in 2012.

The only multivariate pre-procedural predictor of 30-day mortality was Logistic EuroSCORE ≥40. During long-term follow-up, multivariate predictors of mortality were pre-procedural atrial fibrillation, chronic obstructive pulmonary disease, creatinine >200 μmol/L, diabetes mellitus, and coronary artery disease. The strongest independent procedural predictor of long-term mortality was peri-procedural stroke (hazard ratio=3.00; P<0.0001). Non-femoral access and post-procedural aortic regurgitation were also significant predictors of adverse outcome (45).

4. CONCLUSION

SAVR, as the treatment of choice for aortic stenosis has existed since the 1960s. The outcome of patients undergoing AVR has been increasing through the decades as numerous advances in medicine allowed for increasing quality in surgical techniques, medication and peri-procedural events that keep positively influencing the short-term and long-term outcomes of these patients.

Since, however, up to 30% of patients with severe symptomatic aortic stenosis are not considered eligible for surgery, the need for an alternative method for these patients culminated with an introduction of a new approach to the replacement of the aortic valve. In 2002, the first transcatheter aortic valve implantation procedure was performed, opening a new era in interventional cardiology and cardiac surgery. Since 2002, over 50.000 TAVI procedures were made in over 40 countries worldwide, offering a new life to a substantial number of patients that could not undergo SAVR.

TAVI is procedure where a bioprosthetic aortic valve is introduced into the native heart valve through the means of a flexible catheter through a blood vessel or the left ventricle. The prosthetic valve is set into place and expanded and is immediately thereafter functional.

All clinical decisions, including patient selection and procedural approach are made by a multidisciplinary heart team which plays a pivotal role in TAVI. Once a patient is selected and the procedure is made, the patient is followed-up for several days and may be discharged as soon as within 6 days after the procedure.

TAVI has many advantages over SAVR, but at the same time, there are still many disadvantages and concerning issues that need to be refined to maximise the benefits of this approach to valve replacement. It is, nonetheless, impressive that a procedure that is not older than 13 years is showing to have almost equal results in terms of outcome as a procedure that has been used for about 50 years, even more so when stressed that the

patients undergoing TAVI are all either at high surgical risk or inoperable - in other words in bad conditions and with multiple comorbidities.

TAVI is a procedure in an ever expending period of development, and various factors influencing the procedure outcome (both those endogenous to the patient and those related to the procedure and the equipment) are being identified on daily basis.

The advances made in TAVI has been more than impressive thus far, yet still much space for further improvements are present which can significantly alter the long-term outcomes and complications of the procedure.

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7. BIOGRAPHY

Jamal Ahel was born on September 8th 1989 in Zagreb, Croatia. Originally he is Palestinian as both his parents, M. Zaky Ahel, MD, MSc and Wafa Sonallah are from Palestine. He attended ‘’Žuti Brijeg’’ elementary school in Zagreb, and finished his high school education at ‘’XV Gymnasium’’, also in Zagreb. He was enrolled in the University of Zagreb School of Medicine, Medical Studies in English in the academic year 2009/2010 where he is currently in his final year of study.

During his studies, Jamal was involved in many extracurricular activities including being a student demonstrator and participating in congresses and workshops. He was a member and a spokesperson of the MSE student council for the academic year 2010/2011. Since 2014, he has been working for the Croatian Ministry of Health as a National Transplant Coordinator. During his final year of study, Jamal completed an elective course in internal medicine in the Republic of Botswana in the duration of 4 weeks.

Jamal is fluent in Croatian, Arabic and English.