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Aortic Valve Disease: State of the Art

Adam El Gamel

Abstract

Aortic valve replacement is the most commonly performed valve operation. It has been shown to be an effective therapy in all age groups, including the very elderly (age > 90 years). The most common etiologies for aortic stenosis are calcific degeneration, rheumatic disease, and congenital bicuspid valves. The most common causes of pure aortic regurgitation include annuloaortic ectasia and associated dilation of the aortic root, endocarditis, aortic dissection, and rheumatic disease. The indications for surgery depend on the pathophysiology and symptoms. The choice of the prosthesis can be difficult and depends on multiple clinical and lifestyle considerations. Early and late outcomes are generally quite good, even in high-risk patients.

Keywords: aortic valve, aortic stenosis, aortic incompetence, valve replacement, TAVI, aortic valve repair

1. Introduction

Valve disease still a significant health problem in the developed countries, In United states nearly 2.5% of the population has moderate or severe valve disease, with increased the prevalence for people older than 64 years and is 13% in those older than 75 years [1].

The commonest valve diseases in the elderly are calcific aortic valve disease and aortic dilation causing aortic regurgitation [2].

While rheumatic heart disease is the most prevalent pathology of valve disease globally, especially in the adolescent and young adults with a projected prevalence of 16–20 million, rheumatic fever is the most frequent trigger of valve disease in the young, particularly in Africa, India, the Middle East, South America, and parts of Australia and New Zealand, China, and Russia [3]. In western countries, the incidence of rheumatic disease declined in the latter half of the twentieth century, with the occurrence of transitory local episodes. In Africa, endomyocardial fibrosis is a common, poorly investigated pathology that leads to valve disease in all ages [4]. On the other hand, in the developed countries valve diseases of elderly predominate, particularly calcific aortic stenosis and functional mitral regurgitation, with a prevalence of 13% in those older than 75 years reported in North America [5–7].

Other pathological conditions like infective endocarditis and drug-induced valve disease (5-HT_{2B} receptor agonists) are on the rise [8–10].

Structural biological valves deterioration would be the future burden on health resources world-wide; this is due to its current popularity as a therapeutic option even in young patients, mainly to avoid the complications of anticoagulation [11, 12].

Lack of equitable access to health care takes place in all countries, as a consequence of many complex economic and social forces. Because of the escalating technological cost of health care around the world, the situation is the same, even those industrially developed countries.

The salient global errand is the prevention of rheumatic heart disease, which would necessitate cooperation among social, political, and medical programs that lead to creating enhancements in living conditions by better housing, nutrition and improved access to health care [13–16]. Penicillin for streptococcal throat infections and secondary prophylaxis would continue to be a cornerstone in the global fight against rheumatic heart disease [17–19]. It is also reported that there was a natural reduction in the virulence of streptococcal serotypes, but it happened after the incidence of rheumatic fever had declined.

Most of the serum biomarkers that have been shown related to VHD are detecting secondary effects on the ventricular myocardium. Biomarkers associated with myocardial stress include the natriuretic peptides and GDF-15. Troponin is linked to myocardial necrosis, and the micro RNAs, ST2, and galectin-3 are associated with myocardial hypertrophy and fibrosis. Of these, the natriuretic peptides are the most widely studied, but they are not specific to VHD, and there is considerable overlap in serum levels between different clinical groups [20–22].

2. Practical anatomy and physiology of the aortic valve

The aortic valve is the last gate the blood pumped from the heart to the rest of the organs. It is at the junction between the aorta and the outflow tract of the left ventricle. Its function is to maintain unidirectional blood flow during the diastole while allowing the blood forward flow with minimal resistance during systole. The aortic valve has typically three semilunar cusps (tricuspid) named by their relationship to the coronary Ostia: the left coronary and right coronary, and the third is the noncoronary cusp. Cusps are attached to the aortic annulus at the bottom of slight dilations of the aorta associated with each cusp (sinuses of Valsalva end at the sinotubular junction). The sinotubular junction is the narrowest part of the aortic

Figure 1.
Aortic valve anatomy.

root (**Figure 1**). The fibrous skeleton supports the aortic valve and is continuous with the anterior leaflet of the mitral valve [23, 24].

3. Managing a patient with suspected valvular heart disease

3.1 General principles

Detection of valvular heart disorder can be difficult. The state of the patient may range in gravity from asymptomatic to cardiogenic shock. Endocarditis may mimic systemic illness, vascular or neurologic condition, while acute aortic incompetence may be presented as a primary respiratory disorder (acute asthmatic episode). Making a timely, accurate diagnosis, while averting excessive laboratory studies, may try the acumen of a seasoned clinician.

Commonly, observing a murmur in a well individual or a patient with symptom referable to the cardiovascular system, arouse the suspicion of valvular abnormality. It is essential to reassure the patients; murmur is not synonymous with heart disease. It does represent turbulent blood flow which may result from several possible conditions. These include: (i) increased flow secondary to anaemia, pregnancy, or a hyperadrenergic state; accelerated flow through a restricted orifice (ii) regurgitant flow through a leaking valve; or (iii) abnormal shunting between two chambers. In an unselected population, most systolic murmurs are physiologic, caused by conditions of increased blood flow [25, 26]. The echocardiogram is the best way to evaluate the patients and reassure them [27, 28].

The practical approach to these patients relies upon an open-minded history and thorough physical examination.

3.2 History

As in nearly all of medicine, most cues to a diagnosis are from history.

The clinician assessment should not be compromised, trying to spare minutes at this stage drain hours in the wasted investigation later.

The patient may provide a history of rheumatic fever, previous episode of infective endocarditis, intravenous drug use, use of anorectic medications, carcinoid tumours, indwelling vascular devices, dental, genitourinary or gastrointestinal procedures; Marfan's syndrome, syphilis; congenital bicuspid aortic valve; treated or untreated coronary artery disease, radiation therapy.

Finally, a history of past surgery increases the risk of future valve problems by way of prosthetic valve endocarditis or structural failure.

Family genetics undoubtedly plays a role in so doing; the clinician may identify a family with a previously unrecognised genetic mutation and allowed early diagnosis of relatives. The social history may provide valuable information. For example, a childhood spent in a non industrialised region of the world dramatically increases the risk of rheumatic valve disease. History of unprotected sex or intravenous drug abuse raises the TE.

Course for valvular heart disease varies widely, ranging from minutes to decades dependent on primary pathology and age and risk factors related to patients as well as the geographical location in the world.

3.2.1 Dyspnea

Unfortunately, it is also very nonspecific, occurring in nearly any disturbance of cardiopulmonary function. Orthopnoea and paroxysmal nocturnal dyspnea are somewhat more specific for left ventricular failure.

3.2.2 Palpitations

The sensation of a rapid or unusually vigorous heartbeat may signal the development of atrial fibrillation.

3.2.3 Angina

Maybe the initial manifestation of valvular heart disease.

3.2.4 Weight gain, oedema, and abdominal discomfort

In hospitalised patients, excess extra cellular fluid is first presented as pitting oedema overlying the sacrum predominantly; the elevated systemic venous pressure is the cause of all the above.

3.3 Physical exam

3.3.1 General appearance

The toxic appearance of acute infection, wasting of cardiac cachexia, the distressed facial expression, wet cough, accessory muscle use, and diaphoresis of pulmonary oedema, and the cool skin characteristic of poor perfusion.

3.3.2 Vital signs

3.3.2.1 Tachycardia

Skin and mucosa cyanosis of the lips cold sweat (Osler nodes). (Janeway lesions), painless red macule lesions of the palms and soles (Janeway lesions), conjunctive petechial, and subungual hematomas (splinter haemorrhages).

Central venous pulsations jugular venous pulsation and mean central venous pressure (CVP) are often abnormal in valvular heart disease. In most cases, right heart failure is secondary left-sided valve disease-causing left heart failure. Less direct clues to the level of right atrial pressure; include the presence of pedal oedema, sacral oedema, anasarca, tender hepatomegaly, ecchymosis (hepatic synthetic dysfunction), hepatojugular pulsation and ascites.

3.3.3 Pulse volume, contour

3.3.3.1 Auscultatory findings

However, auscultation technical skill like any other and improves with repetition [29]. Therefore, students' physicians-in-training reading this text should lose heart, but rather, should apply themselves diligently to acquire these valuable bedside skills. Listening to patients before and after echocardiographic findings are known is particularly helpful.

3.4 Electrocardiography

In majority of patients with aortic valve disease with have abnormal ECG which commonly non-specific such as left ventricle hypertrophy, with or without repolarization abnormalities is seen on electrocardiography (ECG). Left atrial enlargement, left axis deviation and conduction disorders are also common. Atrial fibrillation can be seen at late state and in older patients or those with hypertension.

3.5 Radiography

Pulmonary vascular congestion. Enlargement, valvular calcification, and type position of prosthetic valve may all be ascertained plain radiographs. Comparing changes over time particularly helpful; hence obtaining previous studies is very valuable (**Figure 2**).

3.6 Echocardiography

Echocardiography is the most valuable tool in valvular heart disease due to its portability, ease of use. Low cost, steadily improving resolution, and its ability to assess hemodynamics, additional ultrasound-based modalities can provide information about cardiac anatomy, function, and hemodynamics. These modalities include two dimensional (2D) or B-mode in which sound waves are in a fan-like distribution, yielding a real wedge-shaped tomographic image of the heart. There are three subtypes of Doppler ultrasound. Continuous-wave Doppler, all velocities along a continuous line through the heart are displayed as a spectrum over time. In pulse wave Doppler, the sample volume is placed on a 2D image, and the spectral splay of velocities represents the blood flow velocities in this region only.

Tissue Doppler is yet another form of Doppler echocardiography which measures the velocity of anatomic structures rather than red blood cells; it currently has very limited application in valvular heart disease [30, 31].

Hemodynamic assessment. Firstly, the pressure gradient a valve or between two chambers can be estimated by taking advantage of the relationship between pressure (P), and velocity (v) as described in is the conservation of flow and different diameter, the flow of fluid through one section match flow through the other end. Since flow equals the product of orifice area and flow velocity, this principle can be stated as $\text{Area 1} \times \text{Velocity 1} = \text{Area 2} \times \text{Velocity 2}$. This is used explicitly in the determination of aortic valve area (**Figure 3**) [30].

Another hemodynamic measure important valvular heart disease are the rate of pressure equilibration between two chambers (e.g. pressure half-time, deceleration).

Cardiac catheterisation and direct measure of intracardiac pressures, ventriculography, aortography, and assessment of coronary vessels before valve surgery all continue to be an essential tool in the evaluation of valvular heart disease.

Figure 2.
Cardiomegaly and pulmonary congestion.

Figure 3.
Echocardiogram assessment of aortic valve.

Occasionally, balloon valvotomy serves an important therapeutic and diagnostic role in mitral, and occasionally, aortic stenosis.

Positron emission tomography (PET) is an emerging imaging technique which allows improved resolution more flexibility than SPECT, including the possibility of imaging metabolic substrates and neural transmitters. In light of its expense and dependency mostly cyclotron-produced isotopes, its role in valvular heart disease remains to be determined.

3.7 Aortic stenosis

Aortic stenosis (AS) may be to congenital or acquired, and the congenital form could be above (supra), below (subvalvular) or at the valve level. A supra-ventricular is a rare form of long and tubular narrowing is associated with, (William's Syndrome) hypercalcemia, mental retardation, and peripheral pulmonic stenosis. Subvalvular stenosis may be caused by the septum extending into the outflow tract, a cylindrical constriction of the outflow tract or, in hypertrophic cardiomyopathy the obstruction caused by the anterior movement of the mitral valve leaflets. In some patients, this is present only at diminished ventricular (LV) volumes recreated in the echocardiography laboratory by Valsalva cause aortic regurgitation [32].

3.8 Epidemiology and aetiology

Isolated aortic stenosis (AS) is more frequent in men and is found in 2% of people 65 years of age and older. The most frequent causes of AS include age-related calcific degeneration, bicuspid aortic valve, and rheumatic aortic valve. The distribution of these causes diverges across age groups and geographic regions. Age-related degeneration is the commonest cause of AS in elderly patients. In comparison, bicuspid aortic valve calcification accounts for most surgical cases in younger patients (>65) [33].

3.9 Pathophysiology

There is 0 gradient exists across the standard aortic valve during the cardiac cycle. The cross-sectional area of a normal aortic valve is $>2 \text{ cm}^2$. While reductions in the valve area to 1.5–2.0 leads to minimal pressure gradient, further narrowing produces dramatic increases in the mean pressure gradient [34]. In AS, progressive obstruction of outflow tract increases afterload ventricular, and wall stress of the left ventricle leads to high left ventricular systolic and diastolic pressures, decreased aortic pressure, and prolonged left ventricular ejection time.

Obstruction to flow usually develops slowly allowing the LV to adapt by concentric thickening hypertrophy serves to reduce wall tension (the law of Laplace describes wall tension is proportional to pressure and radius and adversely proportional to thickness). As long as the process of muscular wall thickening keeps pace with narrowing of the aortic orifice, the 'wall tension' is maintained. Gradually, this results in compensatory concentric left ventricular hypertrophy (LVH) to maintain ejection fraction [35].

The stability comes at a price, now the hypertrophied walls are less compliant and LV less able to fill rapidly. Satisfactory end-diastolic volume becomes heavily reliant upon atrial contraction. Atrial fibrillation often precipitates dramatic acute congestive heart failure in patients with severe AS. The concentric hypertrophy increases myocardial oxygen requirement coupled with reduced coronary flow due to deviated diastole and low diastolic pressures, which aggravates subendocardial ischemia in the presence of normal coronary artery ventricular arrhythmias are common as well. The compensatory mechanism may become insufficient in patients with chronic severe AS, resulting in thinning and dilation of the left ventricle, leading to a decrease in ejection fraction and congestive heart failure [36].

Exertional syncope may develop resulting from peripheral vasodilation induced by exercise with the background of a fixed cardiac output. Blood pressure drop may reduce cerebral perfusion, below the minimum required for consciousness [37].

A negative balance between oxygen supply and demand is the norm in AS. LVH increased afterload, and the long systole increases myocardial oxygen demand. The high filling pressure and longer systolic time decrease myocardial oxygen supply by reducing myocardial perfusion time. Myocardial ischemia in patients with AS is due to the alteration in myocardial oxygen supply and demand even in the absence of coronary artery disease.

3.10 Clinical features

3.10.1 Clinical presentation

3.10.1.1 Symptoms

Patients with, mild or moderate AS are usually asymptomatic unless they have the coexisting cardiopulmonary disease or infective endocarditis. Patients often remain asymptomatic until the ventricle begins to fail. At this initially, they usually develop fatigue followed by cardinal symptoms of angina, syncope, and dyspnea expected survival following the onset of these symptoms is 2, 3, and 5 years, respectively [38].

In rare instances, sudden tragic death is the first manifestation of the disease. Patients may be sedentary; it unclear whether they are inactive by choice or have gradually restricted their activity to avoid symptoms. A treadmill stress test under close medical supervision may help in their assessment.

3.10.1.2 Physical findings

The classic finding in the assessment of peripheral pulses is a delayed and slowly rising wave contour pulsus parvus et tardus. However, it may be absent patients with associated aortic regurgitation or in patients with associated aortic regurgitation or calcified, inelastic arteries.

Precordial palpation may reveal a sustained and laterally displaced cardiac impulse. Because the hypertrophied LV is noncompliant, the critical contribution to filling provided by atrial contraction severe thrill is often palpable at the base of the heart.

3.10.2 Ejection systolic crescendo murmur at the second aortic area

3.10.2.1 Electrocardiogram

Standard features on the electrocardiogram include ventricular hypertrophy (LVH) with a strain and a biphasic p wave in V1 corresponding to atrial (LA) hypertrophy. Atrioventricular and intra ventricular conduction abnormalities may be when calcification extends from the valve into the induction system.

3.10.2.2 Radiography

The chest X-ray rounding of the left heart border and apex, post stenotic dilation of the aorta calcification of the aortic valve, and pulmonary congestion may be apparent. Note, these findings are neither highly sensitive nor specific.

3.10.2.3 Echocardiography

Echocardiography serves as the principal modality for and quantitating AS. 2D imaging provides information on chamber size, degree of hypertrophy, LV systolic function, valve mobility, and calcification. Doppler measurement of transvalvular blood flow velocity can be used to estimate peak and mean pressure gradients using the.

The symptomatic triad of AS is angina, exertional syncope, and symptoms of congestive heart failure, such as shortness of breath. The mechanisms for angina and congestive heart failure are explained in the previous section. The mechanism for syncope is likely related to the blunting of exercise-induced augmentation in stroke volume as a result of outflow obstruction coupled with exercise-induced peripheral vasodilation. These changes cause a drop in systemic blood pressure leading to cerebral hypoperfusion and syncope.

The classic physical finding is a systolic ejection murmur heard loudest at the second right intercostal space, which commonly radiates to the carotid arteries. And maybe associated with severe cases of AS palpable thrill may be present. Palpation of the pulse may reveal a weak and delayed pulse known as *pulsus parvus et tardus*.

3.11 Diagnosis and grading

The most common method for the diagnosis and grading of AS is two-dimensional transthoracic echocardiography Doppler velocity measurement (**Table 1**). In most patients, this modality can reliably establish aortic jet velocity, aortic valve peak and mean gradients, and aortic valve area [39].

3.12 Natural history

Without valve replacement symptomatic AS has a bleak outcome. Numerous studies consistently reported survivals of 3 years for angina and syncope and 1.5–2 years for dyspnea and heart failure. These findings have determined the recommendations for timely surgical intervention in patients with symptomatic AS. Thirty percent of truly asymptomatic severe AS patients will become symptomatic in 2 years with mortality risks of less than 1–5% each year to 5% each year. Progression rate correlates with AS severity, which seems to progress faster with higher mean gradient. Moderate AS progress, with aortic valve area, decreases on average by 0.1 cm² per cent annually the pressure gradient across the valve rises on average by 7 mm Hg per year, and the jet velocity increases by 0.3 m/s per year [40, 41].

Parameter	Mild	Moderate	Severe
Aortic valve area (cm ²)	1.6–2.5	1.1–1.5	≤1.0
Mean pressure gradient (mm Hg)	<20	20–39	≥40
Aortic jet velocity (m/s)	2.0–2.9	3.0–3.9	≥4.0

Table 1.
The severity of aortic stenosis according to echocardiographic criteria.

The definitions of the conditions “low-gradient AS” and “high-gradient AS” are the most relevant new changes in the recommendations for the management of aortic valve stenosis (AS). Precise thresholds of biomarkers and pulmonary hypertension are considered, and the emphasis is focused on computed tomography, particularly for assessing the degree of calcification of the aortic valve and for planning therapy [42].

3.13 Aortic regurgitation

3.13.1 Epidemiology and aetiology

The reasons of aortic regurgitation (AR) are many and can be credited to a disruption of any components of the functional unit of the aortic root valve composite (e.g., cusps, sinuses of Valsalva, sinotubular junction, annulus). In general, the causes can be divided into those that involve the valve cusps (e.g., calcific degeneration, congenitally bicuspid valve, infective endocarditis, rheumatic disease, myxomatous degeneration) and those that encompass the aortic root (e.g., aortic dissection, aortitis of various etiologies such as syphilis, connective tissue disorders such as Marfan syndrome) [43].

3.13.2 Pathophysiology

The pathophysiology of AR is determined by the speed of onset and duration of the disease process. In acute AR, typically caused by aortic dissection, infective endocarditis, trauma, or valve prosthesis failure, there is an abrupt escalation in left ventricular end-diastolic volume because of the regurgitation. Since the left ventricle has restricted compliance and does not have enough time to gradually adapt to the extra volume, the left ventricular end-diastolic pressure (LVEDP) rises rapidly [44, 45].

In chronic AR, there is a gradual and stealthy evolution of left ventricular (LV) dilation and eccentric hypertrophy because of an increase in left ventricular end-diastolic volume, LVEDP, and wall stress. Dilation of the LV maintains normal systolic function and forward flow but requiring extra work to achieve normality. Sooner or later, the hypertrophic response is exhausted, and LVEF deteriorates as afterload increases, resulting in heart failure and its related clinical presentation [44].

3.13.3 Clinical features

Patients with acute AR present with unexpected or precipitously cardiovascular collapse, which is a life-threatening emergency. They often demonstrate ischemic symptoms because of the diminished coronary blood flow and heightened myocardial oxygen demand. In comparison, patients with chronic AR are often asymptomatic for an extended time because of the compensator remodelling of their LV mentioned earlier. Once the compensatory response is depleted, the patients

experience heart failure symptoms such as exertional dyspnea, orthopnea, and paroxysmal nocturnal dyspnea. Patients may also suffer palpitations and angina [46].

The classic murmur of AR is an early diastolic, blowing, a decrescendo murmur heard best at the level of the diaphragm at the left sternal border while the patient is sitting, leaning forward, and in deep exhalation.

Classic signs of widened pulse pressure may also be found, including Corrigan or water-hammer pulse, De Musset sign (bobbing of the head with heartbeats), Quincke pulse (pulsations of the lip and fingers), Traube sign (pistol shot sounds over the femoral artery), and Müller sign (pulsations of the uvula).

3.13.4 Diagnostic criteria

Transthoracic echocardiography with Doppler colour-flow is the most useful tool for the diagnosis of AR. The jet width and vena contracta width on Doppler colour-flow are used to qualitatively assess the severity of AR, whereas the regurgitant volume, regurgitant fraction, and regurgitant orifice area are used for the quantitative assessment.

3.13.5 Management of aortic valve disease

3.13.5.1 Medical management

Many adverse outcomes in adults with valvular heart disease are due to sequelae of the disease process, including atrial fibrillation, embolic events, left ventricular (LV) dysfunction, pulmonary hypertension, and endocarditis. Patients with valvular heart disease are best cared for in the context of a multidisciplinary heart valve clinic [47].

Medical therapy in adults with valvular heart disease focuses on prevention and treatment of complications because there are no specific therapies to prevent progression of the valve disease itself apart from primary and secondary prophylaxis of rheumatic fever. Rheumatic fever is a multiorgan inflammatory disease that occurs 10 days to 3 weeks after group A streptococcal pharyngitis. The clinical diagnosis is based on the conjunction of an antecedent streptococcal throat infection and classic manifestations of the disease, including carditis, polyarthritides, chorea, erythema marginatum, and subcutaneous nodules [48]. Reducing the frequency of streptococcal pharyngitis with benzylpenicillin monthly intramuscular injection helps to reduce the progression of Rheumatic heart disease. The risk of recurrent disease is related to the number of previous episodes, time interval since the last episode, the risk of exposure to streptococcal infections (contact with children or crowded situations), and patient age. A longer duration of secondary prevention is recommended in patients with evidence of carditis or persistent valvular disease than in those with no evidence of valvular damage [49].

Endocarditis prophylaxis guidelines recommend antibiotics therapy before dental procedures, or other procedures associated with bacteraemia, in adults with prosthetic valves but not in patients with native valve disease unless the patient had an episode of endocarditis, dental hygiene and gum health are the primary preventive measure to reduce endocarditis [50].

Prevention of embolic events in patients with valvular heart disease, particularly those with prosthetic valves, MS, or AF, is a key component of optimal medical therapy.

Therapy for the prevention of embolic events in patients with valvular heart disease typically includes antiplatelet agents or long-term warfarin anticoagulation [51, 52]. There is data on the use of newer anticoagulants, such as direct thrombin

inhibitors and anti-Xa agents, for prevention of embolic events in patients with valve disease [53]. At the initiation of therapy, a target INR and acceptable range are defined by the referring physician for each patient on the basis of published guidelines and clinical factors unique to that patient. In addition, patient education about anticoagulation, possible dietary and drug interactions, recognition of complications of therapy, and the need for careful monitoring of the INR is provided verbally and through the use of a variety of media (such as pamphlets, recorded presentations, and computer-based material).

Periodic evaluation of disease severity by echocardiography and clinical evaluation of the LV response to chronic volume and/or pressure overload allows optimal timing of surgical and percutaneous interventions. General health maintenance is important, including evaluation and treatment of coronary disease risk factors, regular exercise, standard immunisations. Both pneumococcal and annual influenza vaccinations are recommended for all adults older than 65 years and are especially important in patients with valvular disease, in whom the increased hemodynamic demands of acute infection may lead to cardiac decompensation. In younger patients with valve disease, routine immunisation is only indicated in conditions associated with immunocompromise are also present and optimal dental care. Management of concurrent cardiovascular disease follows standard approaches with modification, as needed, based on the potential confounding effects of valve haemodynamics. Evaluation of coronary anatomy usually is needed before valve surgery because of the high prevalence of coronary disease and improved surgical outcomes with concurrent coronary revascularisation.

Periodic noninvasive monitoring is essential for the optimal timing of interventions in patients with valve dysfunction. Disease progression may be evident as changes in valve anatomy or motion; an increase in the severity of valve stenosis or regurgitation; LV dilation, hypertrophy, or dysfunction in response to pressure and/or volume overload; or secondary effects of the valvular lesion, such as pulmonary hypertension or AF.

Although the goal in the management of patients with valvular disease is to avoid symptoms and the need for medical therapy by optimising the timing of surgical intervention, some patients have persistent symptoms after surgery, have symptoms only in response to superimposed hemodynamic stress (such as pregnancy), or are not candidates for surgical intervention. In these situations, medical therapy is based primarily on adjustment of loading conditions and control of heart rate and rhythm.

Most adverse outcomes of noncardiac surgery in adults with valve disease are due to failure to recognise the presence of valve disease preoperatively. When valve disease is suspected from history or physical examination findings, echocardiography is appropriate to identify and define the severity of any valve lesions. In patients with valvular disease undergoing noncardiac surgery, management focuses on an accurate assessment of disease severity and symptom status, with appropriate hemodynamic monitoring and optimisation of loading conditions in the perioperative period [54].

3.13.5.2 Patient education

Patient education is the key to compliance with periodic noninvasive monitoring, prevention of complications, and the early recognition of symptoms in patients with valvular heart disease. Each patient should understand the expected long-term prognosis, potential complications, typical symptoms, the rationale for sequential monitoring, and the indications for surgical intervention. Appropriate education avoids needless concern and prompts early reporting of symptoms, allowing

optimal timing of surgical intervention. Increasingly, patients are actively involved in decisions about the timing of surgery and choice of intervention.

Patients also should be knowledgeable about the risk of infective endocarditis and the importance of maintaining optimal oral hygiene, including regular dental care.

Patients undergoing long-term anticoagulation need both education and a reliable and available source for consultation regarding warfarin dose, interactions with other medications, and prompt evaluation of any complications.

3.13.5.3 Aortic valve replacement

The decision for intervention for a faulty aortic valve needs to incorporate the natural history of the medically managed disease, the risks associated with the intervention, and longer-term problems that might build up as a result of prosthetic valve implantation.

Currently, the heart team plays a decisive role in decision making. In addition, it is prudent to cultivate and set up heart valve centres with specialist services in order to generate an ideal environment for the treatment of patients with valvular heart disease.

3.13.5.4 Management of Aortic valve stenosis

Criteria for decision-making are clear for surgical valve and transcatheter aortic valve implantation (TAVI) from the current European guidelines. Recently TAVI is also recommended for patients with intermediate surgical risk. Currently, published literature also supports TAVI implantation in low risk patients as non-inferior to surgical therapy [55, 56].

For symptomatic, AS recommendations are made with regard to the choice of procedure. For high risk (STS score or EuroSCORE II $<4\%$ or a log EuroSCORE $<10\%$) TAVI is the default choice. Surgical replacement is indicated for patients with a low perioperative risk (STS score $>4\%$). Patients with an intermediate surgical risk, the heart team, should consider other criteria for decision making such as anatomical and functional parameters [57, 58], and frailty to reach the best option for the patients considering the current knowledge.

Current data from two large prospective randomised studies, have confirmed that TAVI was noninferior to surgical treatment with regard to mortality, stroke and additional endpoints in both in patients with a low perioperative risk (the mean STS score in both trials was 1.9%), expansion of the indication for TAVI which would also include younger patients, can be expected [59].

3.13.6 Choice of a valve in surgically treated patients

3.13.6.1 Choice of prosthesis

Choice of prosthesis is a complex decision in a patient undergoing AVR with profound long-term consequences for the patient. Currently available prostheses are different with regard to key features, such as the requirement of anticoagulation, incidence of thromboembolism, durability, ease of implantation, haemodynamic performance, and susceptibility for infection. Currently age-based guidelines do exist, but the final choice must be tailored to the individual patient including consideration of general lifestyle and physical activity, surgeon expertise, diseases, especially those affecting life expectancy, and, ultimately, overall patient preference.

The patient age is a primary factor in prosthesis selection. Elderly patients have lower life expectancy and physical activity than Younger patients. Which place

a greater demand on the prosthesis with regard to durability and hemodynamic performance. Age has long been recognised as a major determinant of bioprosthesis durability. Traditionally target age between 65 and 70 years has been the indications for bioprosthesis and like hood of a second operation for structural valve dysfunction in a life time 65-year-old person is less than 10%. As a result, it is not common to choose a mechanical valve in an old patient. Even if the patient is already treated with warfarin for another condition, for example AF, which should not necessarily favour the choice of a mechanical valve because it converts a relative indication for low-level anticoagulation to an absolute indication for higher levels. It also removes the option to stop warfarin in a case of a significant bleeding event. Moreover even if the patient had previously received mechanical valve, the choice does not mandate a second mechanical valve, because risk of complications thromboembolic and bleeding is higher with two mechanical valves than it is with one.

It is more complex and controversial to choose of prosthesis in patients younger than 65 years. Although traditionally, these patients would receive a mechanical valve; the current, improved durability in bioprosthesis and lower operative risk of a redo operation for a failed prosthesis have increased the number of patients younger than 65 years who receive bioprosthesis, including patients in their 50s and even younger.

A particular dilemma women of child-bearing age often it is safer avoid warfarin so they choose a bioprosthesis, with the knowledge that they will face at least one reoperation in their lifetime.

Stentless valves may provide a larger effective orifice area such as the Toronto SPV, Freestyle, and Prima Plus valves although the hemodynamic profiles of stentless valves are superior to those of stented valves, especially at the smaller sizes [42] durability and survival benefits still is unproven [47, 48]. Some reports suggest fewer thromboembolic complications [49]. Currently no specific indication form stentless valve. Maybe these hemodynamic benefits justify implanting stentless valves in younger active patients.

The use of homografts has declined in recent years as a primary aortic valve substitute because without a durability advantage, it is cumbersome to recommend their routine while they have limited availability and the cumbersome storage requirements. However, their ability to resist infection renders them an excellent solution for patients with endocarditis.

The Ross procedure involves replacing the aortic valve with the patient's own pulmonic valve, which have to be is replaced with a homograft or a stentless xenograft. The benefits are near-normal haemodynamic and excellent durability; the disadvantages are the technical complexity and need for reoperation for the homograft or Late AR. The procedure peaked in popularity in the mid to late 1990s, but procedure volume has declined since then. On the basis of the data from the Ross Procedure International Registry, several centres continue to report excellent results [50, 51] although it is now primarily a procedure for paediatric patients, in whom the potential for growth is important, and for young adults in their 20s and 30s when no other good alternatives exist.

3.13.7 Special situations

3.13.7.1 Low-flow, low-gradient aortic valve

The precise assessment within the heart team of the pathology and anatomy, as well as the evaluation of the patient, are emphasised in the new graduated recommendations regarding low-flow, low-gradient aortic valve stenosis in symptomatic patients [60].

It is also highly recommended to take into account the morphology of the device landing zone and the resulting individual risks for TAVI procedures.

For asymptomatic patients with an indication for aortic valve replacement, surgical replacement is still the gold standard, because no data are available for this patient cohort concerning TAVI treatment.

3.13.7.2 Management of aortic regurgitation

Surgical aortic valve replacement remains the standard gold treatment of aortic valve regurgitation (AR). Transcatheter aortic valve implantation (TAVI) plays only a minor role. Currently, the Jena Valve (Jena Valve Technology GmbH, Munich, Germany) is the only prosthesis available for pure AR as an investigational device [61]. All other prostheses are used off label [61]. Concerning the choice of the type of prosthesis, criteria used in aortic stenosis are not merely interchangeable. The percentage of oversizing has to be calculated in a different way because of the absence annular calcification. Although outcomes have improved with newer-generation TAVI devices outcomes are still inferior to surgery. In a few circumstances, TAVI might be an option for patients with severe AR and high surgical risk.

The class I recommendations for aortic valve intervention, in patients with AR according to the 2014 American College of Cardiology and the American Heart Association are the following: symptomatic patients with chronic severe AR, asymptomatic patients with chronic severe AR and LV dysfunction (ejection fraction < 50%) at rest, and patients with chronic severe AR who are undergoing concomitant coronary artery bypass grafting, aortic surgery, or other heart valve surgery.

The class IIa recommendation is for patients with asymptomatic AR and normal LV systolic function (ejection fraction > 50%) but with severe LV dilation (end-systolic diameter > 50 mm). The class IIb recommendation is for patients with moderate AR who are undergoing coronary artery bypass grafting, aortic surgery, or other heart valve surgery. Aortic valve intervention may also be reasonable in asymptomatic patients with chronic severe AR, normal LV systolic function, and severe LV dilation (end-diastolic diameter > 65 mm) if the operative risk is low. Other considerations can include evidence of progressive LV dilation, declining exercise tolerance, or abnormal hemodynamic response to exercise [62, 63].

However, aortic valve repair carries a similar, if not lower, risk of perioperative complication with a low risk of valve-related events over time. Similar to mitral valve repair for mitral regurgitation,^{six} there is some suggestion that aortic valve intervention should be considered earlier in patients in whom aortic valve repair is likely [64].

Another broad category of patients who undergo aortic valve preservation and repair are those with primary aortic pathology involving the aortic root or the ascending aorta and varying degrees of associated aortic valvular disease. In these patients, the primary indication for intervention is driven by aortic size, discussed in the American, European, and Canadian Guidelines.

From a technical perspective, all patients with primary aortic insufficiency are potential candidates for repair. However, the success of aortic valve repair is determined largely by the quality of cusp tissue available. Thus, patients with significant leaflet calcification, destruction owing to active endocarditis, or rheumatic involvement are least likely to undergo successful and durable aortic valve repair. In contrast, repair has been shown to have good results in patients with bicuspid (and in smaller series, unicuspid, and quadricuspid aortic valves), despite the abnormalities in cusp anatomy. An important limitation to the universal application of aortic valve repair techniques is the lack of surgical expertise and experience in this field; however, this is changing rapidly with increasing interest in aortic valve repair. Patients who are candidates for repair should be referred to centres with appropriate expertise.

3.13.7.3 Procedures

Surgery of the aortic valve can now be accomplished with greater safety and efficacy in the majority of patients. In patients with higher operative risks, TAVI is already a proven acceptable alternative to AVR. The choice of valve prosthesis is guided by patient preference, life expectancy, and comorbidities relevant to SVD and anticoagulation. Aortic valve repair in the young patient with AR avoids the risks associated with valve prostheses, but long-term durability is unknown. Aortic root surgery similarly can be performed with the replacement of both the aortic valve and aortic wall, but valve-sparing techniques may offer the advantage of durability equivalent to that of normal native aortic valves with avoidance of prosthetic valve-related complications. Reoperative aortic valve and aortic root surgery, like isolated AVR, can be performed safely with best outcomes at high-volume centres.

Aortic valve replacement (AVR) is becoming safe despite the elderly population of patients is now being treated, with the best outcomes achieved at high-volume centres. The standard approach is a median sternotomy aortic valve and aortic root replacement. However, minimally invasive approaches, including the upper hemisternotomy and right anterior thoracotomy (**Figure 4**), can be performed with equivalent safety and better outcomes. The use of stented bioprosthetic valves surpassed the use of mechanical valves, homografts, and pulmonary autografts combined, reflecting advances in valve technology. The Novel Sutureless valves combine the advantages of a surgical AVR procedure (control of aortic atheroemboli, resection of the diseased native valve) with transcatheter technique (decreased procedure time, improved valve hemodynamic function). Bentall procedure: root replacement with a composite valve-graft is the gold standard for aortic root aneurysm (**Figure 5**). However, for patients who want to avoid the long-term oral anticoagulation required for mechanical valves and structural valve deterioration of the bioprosthetic valves, valve-sparing aortic root replacement (David or Yacoub procedures) is a good option (**Figure 6**).

Indications for aortic root replacement include aneurysms of the ascending aorta, aortic valve endocarditis with annular abscess, and acute type A aortic dissection. The most common indication is an aneurysm of the aortic root or ascending aorta. The size threshold for aneurysm repair depends on whether the aneurysm is the primary indication for surgery or whether it coexists in a patient already requiring cardiac surgery.

Figure 4.
Aortic valve replacement.

Figure 5.
Bio Bentall procedures.

Figure 6.
Valve sparing repair.

Primary aneurysms of the aortic root are secondary to either genetically mediated disorders or acquired disorders. The acquired disorders include degenerative thoracic aortic aneurysm, chronic aortic dissection, intramural hematoma, penetrating atherosclerotic ulcer, mycotic aneurysm, and pseudoaneurysm. The size threshold for surgical repair in this group of patients is 5.5 cm for both the aortic root and ascending aorta according to class I recommendations by the 2010 ACC/AHA Guidelines for the Diagnosis and management of Patients with Thoracic Aortic Disease developed by a multigroup-sponsored task force [65]. The genetically mediated disorders include Marfan syndrome, vascular Ehlers-Danlos syndrome, Turner syndrome, BAV, familial thoracic aortic aneurysm and dissection, and Loeys-Dietz syndrome. These disorders are associated with a greater risk of rupture, dissection, and death, in particular Loeys-Dietz syndrome. The size threshold for operative intervention in this group of patients is 5.0 cm, according to the same guidelines [51]. This recommendation is consistent with a size threshold of 5.0 cm in patients with BAV in the 2006 ACC/AHA Guidelines for the Management of Patients with Valvular Heart Disease [9]. Surgical repair may be considered

in patients with Loeys-Dietz syndrome and aortic diameters as small as 4.2 cm, depending on imaging modality [66].

Reoperative aortic valve and aortic root surgery can also be performed safely, utilisation CT/MRI imaging, meticulous myocardial protection, and safe management of existing bypass grafts.

Two devices of aortic valves for percutaneous transcatheter aortic valve implantation (TAVI) have been used in a large number of patients: balloon-expandable and self-expanding. Many new valve technologies are in development [67] (**Figure 7**).

Current data from randomised trials confirmed that TAVI is superior to medical therapy in patients with prohibitive risks for surgery, and it is equivalent to surgical aortic valve replacement in high-risk and medium-risk patients with aortic stenosis [68].

TAVI is technically possible in most patients with aortic stenosis. The larger question is when should TAVI be offered? Evaluation should identify patients in whom a significant improvement in quality and duration of life is likely and avoid unnecessary intervention in patients in whom the procedure can be performed, but the benefit is unlikely. For this reason evaluation of neurocognitive functioning, frailty, functional status, mobility, and social support is important in patient selection [68].

Transthoracic and transesophageal echocardiography, cardiac computed tomography, and invasive angiography are all used to perform anatomic evaluations specific to TAVI.

Evaluation of appropriate candidates for TAVI requires a non-competitive team approach involving interventional cardiologists with expertise in structural heart disease, cardiac and vascular surgeons, anesthesiologists, imaging specialists, and specialised nurses. The proper equipment and a minimum volume of TAVI procedures performed per operator are required.

Randomised trials and large registries of TAVI indicate procedural success rates of more than 95%, 30-day survival of more than 90%, meaningful improvement in the quality of life, and acceptable complication rates (procedure-related stroke < 2%, vascular access site complications < 5%, permanent pacemaker rates < 5%) [69].

Experience with TAVI within failed bioprostheses (valve-in-valve procedures) has been reported. Critical issues in achieving a successful valve-in-valve procedure include an understanding of the manufacturer sizing and labelling of surgical bioprostheses and correct positioning of the valve in the valve. Early experience suggests that TAVI will be an important option for the treatment of patients with failed bioprostheses [70].

More than 100,000 TAVI procedures have been performed to date. Alternatives to TAVI include surgical aortic valve replacement, aortic balloon valvuloplasty (with or without external beam radiation), and apical-to-aortic conduits.

Figure 7.
Current commonly implanted TAVI valves.

3.13.7.4 Outcomes

Data from the STS indicates that the operative mortality for patients 70 years of age or older who underwent isolated AVR or AVR with coronary artery bypass grafting surgery (CABG) between 1994 and 2003 fell from 10% to less than 6% [71]. In the most recent analysis using the STS database on 108,687 patients from 1997 to 2006 with a mean age of 68 years undergoing isolated AVR, the in-hospital mortality was 2.6% with an observed stroke rate of 1.3% and length of stay of 7.8 days for the year 2006. Among patients 80–85 years of age, 30-day mortality was 4.9% with an observed stroke rate of 2.0%.

Experience at centres of excellence within the last 5 years has demonstrated significantly improved operative mortality, less than 1%, after isolated AVR. The incidence of perioperative stroke in these contemporary series ranged from 0% to 1.9%, and the length of stay was as short as 5 days [72].

In the prospective, randomised, multicenter Placement of Aortic Transcatheter Valves (PARTNER) trial comparing high-risk patients (mean STS score 11.8%) receiving TAVI or AVR for severe, symptomatic AS, outcomes for both procedures were excellent [73]. Patients undergoing AVR ($n = 351$, mean age 85 years) had a 30-day mortality of 6.5%, setting a new benchmark for operative outcomes in a high-risk cohort of patients treated at centres of excellence [74]. Moreover, comparative results showed that early and late strokes and transient ischemic attacks were significantly lower in the AVR group than the TAVI group (30 days, 2.4% vs. 5.5%, respectively, $P = 0.04$; 1 year, 4.3% vs. 8.3%, respectively, $P = 0.04$) [75].

Freedom from reoperation depends on both the prosthesis and patient age. Although they do not degenerate, modern mechanical valves do have a finite reoperation rate of 0.5–1% per year from endocarditis, pannus overgrowth, and thrombosis. Actual freedom from reoperation of modern bioprostheses at 15 years approaches 100% in elderly patients older than 70 years, but it can be as low as 50% in patients younger than 50 years.

3.13.7.5 Complications

The most common complications following aortic valve surgery are similar to those of other cardiac surgeries and include stroke (1–4%), deep sternal wound infection (1–2%), reoperation for bleeding (1–3%), and myocardial infarction (MI; 1–5%). Transient heart block is not uncommon, presumably as a result of traction or oedema of the bundle of His in the vicinity of the right noncoronary commissure. It usually resolves within 5–6 days of surgery. The risk of complete heart block requiring pacemaker insertion is 3–5% [76].

4. Summary

Aortic valve replacement is the most commonly performed valve operation. It has been shown to be an effective therapy in all age groups, including the very elderly (age > 90 years). The most common etiologies for AS are calcific degeneration, rheumatic disease, and congenital bicuspid valves. The most common causes of pure aortic regurgitation include annuloaortic ectasia and associated dilation of the aortic root, endocarditis, aortic dissection, and rheumatic disease. The indications for surgery depend on the pathophysiology and symptoms. The choice of the prosthesis can be difficult and depends on multiple clinical and lifestyle considerations. Early and late outcomes are generally quite good, even in high-risk patients.

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References

- [1] Filip G, Litwinowicz R, Kapelak B, Sadowski J, Tobota Z, Maruszewski B, et al. Trends in isolated aortic valve replacement in middle-aged patients over the last 10 years: Epidemiology, risk factors, valve pathology, valve types, and outcomes. *Kardiologia Polska*. 2019;**77**:688-695
- [2] O'Brien KD. Epidemiology and genetics of calcific aortic valve disease. *Journal of Investigative Medicine*. 2007;**55**:284-291
- [3] Noubiap JJ, Agbor VN, Bigna JJ, Kaze AD, Nyaga UF, Mayosi BM. Prevalence and progression of rheumatic heart disease: A global systematic review and meta-analysis of population-based echocardiographic studies. *Scientific Reports*. 2019;**9**:17022
- [4] Moloi AH, Watkins D, Engel ME, Mall S, Zuhlke L. Epidemiology, health systems and stakeholders in rheumatic heart disease in Africa: A systematic review protocol. *BMJ Open*. 2016;**6**:e011266
- [5] Coffey S, Cox B, Williams MJ. The prevalence, incidence, progression, and risks of aortic valve sclerosis: A systematic review and meta-analysis. *Journal of the American College of Cardiology*. 2014;**63**:2852-2861
- [6] Gaibazzi N, Reverberi C, Ghillani M, Brunazzi B, Faggiano P. Prevalence of undiagnosed asymptomatic aortic valve stenosis in the general population older than 65 years. A screening strategy using cardiac auscultation followed by Doppler-echocardiography. *International Journal of Cardiology*. 2013;**168**:4905-4906
- [7] Osnabrugge RL, Mylotte D, Head SJ, Van Mieghem NM, Nkomo VT, LeReun CM, et al. Aortic stenosis in the elderly: Disease prevalence and number of candidates for transcatheter aortic valve replacement: A meta-analysis and modeling study. *Journal of the American College of Cardiology*. 2013;**62**:1002-1012
- [8] Shah ASV, McAllister DA, Gallacher P, Astengo F, Perez JAR, Hall J, et al. Incidence, microbiology and outcomes in patient hospitalized with infective endocarditis. *Circulation*. 2020;**141**:2067-2077
- [9] Thornhill MH, Dayer MJ, Nicholl J, Prendergast BD, Lockhart PB, Baddour LM. An alarming rise in incidence of infective endocarditis in England since 2009: Why? *Lancet*. 2020;**395**:1325-1327
- [10] Thornhill MH, Gibson TB, Cutler E, Dayer MJ, Chu VH, Lockhart PB, et al. Antibiotic prophylaxis and incidence of endocarditis before and after the 2007 AHA recommendations. *Journal of the American College of Cardiology*. 2018;**72**:2443-2454
- [11] Takkenberg JJ. Biological valves: Is durability really the bottle neck? *Heart*. 2010;**96**:1691-1692
- [12] al-Khaja N, Belboul A, Rashid M, el-Gatit A, Roberts D, Larsson S, et al. The influence of age on the durability of Carpentier-Edwards biological valves. Thirteen years follow-up. *European Journal of Cardio-Thoracic Surgery*. 1991;**5**:635-640
- [13] Terzuolo D. Epidemiology and prophylaxis of the rheumatic fever. Medico-social considerations. *Archivio per le Scienze Mediche (Torino)*. 1968;**125**:391-398
- [14] Nagayama T. Social-economic problems of rheumatic fever. *Japanese Circulation Journal*. 1966;**30**:1339-1340
- [15] Cannon JW, Abouzeid M, de Klerk N, Dibben C, Carapetis JR,

- Katzenellenbogen JM. Environmental and social determinants of acute rheumatic fever: A longitudinal cohort study. *Epidemiology and Infection* 2019;**147**:e79
- [16] Hashkes PJ. 50 years ago in the journal of pediatrics: Social factors in relation to participation in follow-up care of rheumatic fever. *The Journal of Pediatrics*. 2013;**162**:535
- [17] Kaplan EL, Duckett Jones T. Memorial lecture. Global assessment of rheumatic fever and rheumatic heart disease at the close of the century. Influences and dynamics of populations and pathogens: A failure to realize prevention? *Circulation*. 1993;**88**:1964-1972
- [18] Stollerman GH. Streptococcal vaccines and global strategies for prevention of rheumatic fever. *The American Journal of Medicine*. 1980;**68**:636-638
- [19] Remond MG, Coyle ME, Mills JE, Maguire GP. Approaches to improving adherence to secondary prophylaxis for rheumatic fever and rheumatic heart disease: A literature review with a global perspective. *Cardiology in Review*. 2016;**24**:94-98
- [20] Duchnowski P, Hryniewiecki T, Kusmierczyk M, Szymanski P. The usefulness of selected biomarkers in patients with valve disease. *Biomarkers in Medicine*. 2018;**12**:1341-1346
- [21] Small A, Kiss D, Giri J, Anwaruddin S, Siddiqi H, Guerraty M, et al. Biomarkers of calcific aortic valve disease. *Arteriosclerosis, Thrombosis, and Vascular Biology*. 2017;**37**:623-632
- [22] Moesgaard SG, Falk T, Teerlink T, Guethmundsdottir HH, Sigurethardottir S, Rasmussen CE, et al. Brain-natriuretic peptide and cyclic guanosine monophosphate as biomarkers of myxomatous mitral valve disease in dogs. *Veterinary Journal*. 2011;**189**:349-352
- [23] Christie GW. Anatomy of aortic heart valve leaflets: the influence of glutaraldehyde fixation on function. *European Journal of Cardio-Thoracic Surgery*. 1992;**6**(Suppl 1):S25-S32
- [24] de Kerchove L, Jashari R, Boodhwani M, Duy KT, Lengele B, Gianello P, et al. Surgical anatomy of the aortic root: Implication for valve-sparing reimplantation and aortic valve annuloplasty. *The Journal of Thoracic and Cardiovascular Surgery*. 2015;**149**:425-433
- [25] Rein AJ, Omokhodion SI, Nir A. Significance of a cardiac murmur as the sole clinical sign in the newborn. *Clinical Pediatrics (Phila)*. 2000;**39**:511-520
- [26] Shaver JA. Cardiac auscultation: A cost-effective diagnostic skill. *Current Problems in Cardiology*. 1995;**20**:441-530
- [27] Carreras F, Pons-Llado G, Borrás X, Padro JM, Caralps JM, Aris A, et al. Non-invasive preoperative assessment of chronic valvular heart disease by Doppler ultrasound. *European Heart Journal*. 1988;**9**:874-878
- [28] Kenny J, Griffin B, McCarthy C, Counihan T. Non-invasive assessment of valvular heart disease using Doppler echocardiography. *Irish Medical Journal*. 1986;**79**:311-314
- [29] Barrett MJ, Lacey CS, Sekara AE, Linden EA, Gracely EJ. Mastering cardiac murmurs: The power of repetition. *Chest*. 2004;**126**:470-475
- [30] Assi ER, Tak T. Assessment of valvular heart disease. Why echocardiography is an essential component. *Postgraduate Medical Journal*. 1998;**104**:99-102
- [31] Chan KL, Stinson WA, Veinot JP. Reliability of transthoracic echocardiography in the assessment of aortic valve morphology: Pathological correlation in

178 patients. *The Canadian Journal of Cardiology*. 1999;15:48-52

[32] Kimura K, Morimoto S. Symptoms and electrocardiographic findings in cardiomyopathies. *Nihon Rinsho*. 2000;58:23-28

[33] Kontogeorgos S, Thunstrom E, Basic C, Hansson PO, Zhong Y, Ergatoudes C, et al. Prevalence and risk factors of aortic stenosis and aortic sclerosis: A 21-year follow-up of middle-aged men. *Scandinavian Cardiovascular Journal*. 2020;54:115-123

[34] Carabello BA. Selection of patients with aortic stenosis for operation: The asymptomatic patient and the patient with poor LV function. *Advances in Cardiology*. 2002;39:49-60

[35] Carabello B. Pathophysiology of valvular heart disease: Implications for nuclear imaging. *Journal of Nuclear Cardiology*. 2002;9:104-113

[36] Zheng KH, Tzolos E, Dweck MR. Pathophysiology of aortic stenosis and future perspectives for medical therapy. *Cardiology Clinics*. 2020;38:1-12

[37] Thrasher JR, Talley JD. Syncope and aortic valve stenosis: Clues to diagnosis and pathophysiology. *The Journal of the Arkansas Medical Society*. 1996;93:191-193

[38] Ross J Jr, Braunwald E. Aortic stenosis. *Circulation*. 1968;38:61-67

[39] Bhattacharyya S, Mittal T, Abayalingam M, Kabir T, Dalby M, Cleland JG, et al. Classification of aortic stenosis by flow and gradient patterns provides insights into the pathophysiology of disease. *Angiology*. 2016;67:664-669

[40] Braunwald E. On the natural history of severe aortic stenosis. *Journal of the American College of Cardiology*. 1990;15:1018-1020

[41] Lee HJ, Kim HK. Natural history data in symptomatic severe aortic stenosis alerts cardiologists to the dangers of no action. *Korean Circulation Journal*. 2019;49:170-172

[42] Herrmann S, Fries B, Liu D, Hu K, Stoerk S, Voelker W, et al. Differences in natural history of low- and high-gradient aortic stenosis from nonsevere to severe stage of the disease. *Journal of the American Society of Echocardiography*. 2015;28:1270-1282

[43] Ishii K, Hirota Y, Suwa M, Kita Y, Onaka H, Kawamura K. Natural history and left ventricular response in chronic aortic regurgitation. *The American Journal of Cardiology*. 1996;78:357-361

[44] Dervan J, Goldberg S. Acute aortic regurgitation: Pathophysiology and management. *Cardiovascular Clinics*. 1986;16:281-288

[45] Pisacane C, Pacileo G, Santoro G, Sarubbi B, Iacono C, Russo MG, et al. New insights in the pathophysiology of mitral and aortic regurgitation in pediatric age: Role of angiotensin-converting enzyme inhibitor therapy. *Italian Heart Journal*. 2001;2:100-106

[46] Shigenobu M, Sano S. The clinical and pathological features of isolated aortic regurgitation in relation to its etiology. *Surgery Today*. 1994;24:393-398

[47] Lancellotti P, Rosenhek R, Pibarot P, Iung B, Otto CM, Tornos P, et al. ESC working group on valvular heart disease position paper—Heart valve clinics: Organization, structure, and experiences. *European Heart Journal*. 2013;34:1597-1606

[48] Markowitz M, Gerber MA. The Jones criteria for guidance in the diagnosis of rheumatic fever. Another perspective. *Archives of Pediatrics & Adolescent Medicine*. 1995;149:725-726

- [49] Shulman ST, Amren DP, Bisno AL, Dajani AS, Durack DT, Gerber MA, et al. Prevention of rheumatic fever. A statement for health professionals by the committee on rheumatic fever and infective endocarditis of the council on cardiovascular disease in the young. *Circulation*. 1984;**70**:1118A-1122A
- [50] Wilson W, Taubert KA, Gewitz M, Lockhart PB, Baddour LM, Levison M, et al. Prevention of infective endocarditis: Guidelines from the American Heart Association: A guideline from the American Heart Association Rheumatic Fever, Endocarditis and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. *Journal of the American Dental Association*. 2008;**139**(Suppl):3S-24S
- [51] Whitlock RP, Sun JC, Fries SE, Rubens FD, Teoh KH. Antithrombotic and thrombolytic therapy for valvular disease: Antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012;**141**:e576S-e600S
- [52] Whitlock RP, Eikelboom JW. Prevention of thromboembolic events after bioprosthetic aortic valve replacement: What is the optimal antithrombotic strategy? *Journal of the American College of Cardiology*. 2012;**60**:978-980
- [53] Fuster V, Ryden LE, Cannom DS, Crijns HJ, Curtis AB, Ellenbogen KA, et al. ACCF/AHA/HRS focused updates incorporated into the ACC/AHA/ESC 2006 Guidelines for the management of patients with atrial fibrillation: A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines developed in partnership with the European Society of Cardiology and in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. *Journal of the American College of Cardiology*. 2011;**57**:e101-e198
- [54] Fleisher LA, Beckman JA, Brown KA, Calkins H, Chaikof E, Fleischmann KE, et al. ACC/AHA 2006 guideline update on perioperative cardiovascular evaluation for noncardiac surgery: Focused update on perioperative beta-blocker therapy: A report of the American College of Cardiology/American Heart Association task force on practice guidelines (writing committee to update the 2002 guidelines on perioperative cardiovascular evaluation for noncardiac surgery): Developed in collaboration with the American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, and Society for Vascular Medicine and Biology. *Circulation*. 2006;**113**:2662-2674
- [55] Michalski B, Dweck MR, Marsan NA, Cameli M, D'Andrea A, Carvalho RF, et al. The evaluation of aortic stenosis, how the new guidelines are implemented across Europe: A survey by EACVI. *European Heart Journal Cardiovascular Imaging*. 2020;**21**:357-362
- [56] Kolkailah AA, Doukky R, Pelletier MP, Volgman AS, Kaneko T, Nabhan AF. Cochrane corner: Trans-catheter aortic valve implantation versus surgical aortic valve replacement for severe aortic stenosis in people with low surgical risk. *Heart. Cochrane Database of Systematic Reviews*. John Wiley & Sons, Ltd; 2019. Issue No. 12. SN: 1465-1858
- [57] Kanwar A, Thaden JJ, Nkomo VT. Management of patients with aortic

- valve stenosis. Mayo Clinic Proceedings. 2018;**93**:488-508
- [58] Harris AW, Pibarot P, Otto CM. Aortic stenosis: Guidelines and evidence gaps. *Cardiology Clinics*. 2020;**38**:55-63
- [59] Malik AH, Zaid S, Ahmad H, Goldberg J, Dutta T, Undemir C, et al. A meta-analysis of 1-year outcomes of transcatheter versus surgical aortic valve replacement in low-risk patients with severe aortic stenosis. *Journal of Geriatric Cardiology*. 2020;**17**:43-50
- [60] Monin JL, Quere JP, Monchi M, Petit H, Baleynaud S, Chauvel C, et al. Low-gradient aortic stenosis: Operative risk stratification and predictors for long-term outcome: A multicenter study using dobutamine stress hemodynamics. *Circulation*. 2003;**108**:319-324
- [61] Yoon SH, Schmidt T, Bleiziffer S, Schofer N, Fiorina C, Munoz-Garcia AJ, et al. Transcatheter aortic valve replacement in pure native aortic valve regurgitation. *Journal of the American College of Cardiology*. 2017;**70**:2752-2763
- [62] Bando K. Filling the gap between guidelines and current surgical practice: Is early surgery justified in patients with asymptomatic severe aortic regurgitation with normal left ventricular function? *Seminars in Thoracic and Cardiovascular Surgery*. 2019;**31**:771-772
- [63] Yang LT, Michelena HI, Scott CG, Enriquez-Sarano M, Pislaru SV, Schaff HV, et al. Outcomes in chronic hemodynamically significant aortic regurgitation and limitations of current guidelines. *Journal of the American College of Cardiology*. 2019;**73**:1741-1752
- [64] David TE, Feindel CM. An aortic valve-sparing operation for patients with aortic incompetence and aneurysm of the ascending aorta. *The Journal of Thoracic and Cardiovascular Surgery*. 1992;**103**:617-621
- [65] Milewicz DM, Regalado ES, Guo DC. Treatment guidelines for thoracic aortic aneurysms and dissections based on the underlying causative gene. *The Journal of Thoracic and Cardiovascular Surgery*. 2010;**140**:S2-S4
- [66] Cooper MA, Upchurch GR Jr. The society of vascular surgery practice guidelines on the care of patients with abdominal aortic aneurysms. *JAMA Surgery*. 2019;**154**:553-554
- [67] Scherman J, Weich H. SASCI/ SCTSSA joint consensus statement and guidelines on transcatheter aortic valve implantation (TAVI) in South Africa. *Cardiovascular Journal of Africa*. 2016;**27**:399-400
- [68] Lung B. Aortic stenosis in the elderly: Surgery or TAVI. New European guidelines. *Presse Médicale*. 2013;**42**:986-994
- [69] Pighi M, Serdoz R, Kilic ID, Sherif SA, Lindsay A, Di Mario C. TAVI: New trials and registries offer further welcome evidence—U.S. CoreValve, CHOICE, and GARY. *Global Cardiology Science and Practice*. 2014;**2014**:78-87
- [70] Giordana F, Bruno F, Conrotto F, Saglietto A, D'Ascenzo F, Marra WG, et al. Incidence, predictors and outcomes of valve-in-valve TAVI: A systematic review and meta-analysis. *International Journal of Cardiology*. 2020;**316**(2020):64-69
- [71] Ram E, Amunts S, Zuroff E, Peled Y, Kogan A, Raanani E, et al. Outcomes of isolated surgical aortic valve replacement in the era of transcatheter aortic valve implantation. *Journal of Cardiac Surgery*. 20 July 2020;**35**(7):1395-1748

[72] Mazine A, El-Hamamsy I.
Procedures and outcomes of surgical
aortic valve replacement in adults.
Cardiology Clinics. 2020;**38**:89-102

[73] Mack MJ, Leon MB, Smith CR,
Miller DC, Moses JW, Tuzcu EM, et al.
5-Year outcomes of transcatheter
aortic valve replacement or
surgical aortic valve replacement
for high surgical risk patients with
aortic stenosis (PARTNER 1): A
randomised controlled trial. *Lancet*.
2015;**385**:2477-2484

[74] Tang GH, Lansman SL, Panza JA.
Beyond PARTNER: Appraising the
evolving trends and outcomes in
transcatheter aortic valve replacement.
Cardiology in Review. 2015;**23**:1-10

[75] Thourani VH, Jensen HA,
Babaliaros V, Kodali SK, Rajeswaran J,
Ehrlinger J, et al. Outcomes
in nonagenarians undergoing
transcatheter aortic valve replacement
in the PARTNER-I trial. *Annals of
Thoracic Surgery*. 2015;**100**:785-792

[76] Tamburino C, Barbanti M,
Capodanno D, Mignosa C,
Gentile M, Aruta P, et al. Comparison
of complications and outcomes to
one year of transcatheter aortic valve
implantation versus surgical aortic valve
replacement in patients with severe
aortic stenosis. *The American Journal of
Cardiology*. 2012;**109**:1487-1493