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"Patient - Prosthesis Mismatch after Transcatheter or Surgical Aortic Valve Replacement: Hemodynamic and Clinical Impact"

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Content

1. ABBREVIATIONS

AR	- aortic regurgitation
AS	- aortic stenosis
AVR	- aortic valve replacement
BE	- balloon expandable
BMI	- body mass index
BSA	- body surface area
CAVD	- calcific aortic valve disease
CABG	- coronary artery bypass graft surgery
EOA	- effective orifice area
EF	- ejection fraction
HVD	- heart valve disease
iEOA	- index effective orifice area
LV	- left ventricular
LVEF	- left ventricular ejection fraction
NCS	- non cardiac surgery
NYHA	- New-York Heart Association
PPM	- patient-prosthesis mismatch
SE	- self expandable
SAVR	- surgical aortic valve replacement
THV	- transcatheter heart valve
TAVR	- transcatheter aortic valve replacement
TPG	- transvalvular pressure gradient
VIV TAVR	- valve-in-valve trancatheter aortic valve replacement
VHD	- valvular heart disease

2. SUMMARY

Patient-prosthesis mismatch (PPM) is a condition where the effective orifice area (EOA) of a prosthetic valve is smaller than expected in comparison to the patient's body surface area. It can be caused by baseline patient variations, ascertainment bias, and selection bias. Data have been published to classify and standardized definitions and evaluation procedures for PPM following surgical aortic valve replacement (SAVR) and transcatheter aortic valve replacement (TAVR). This literature review summarizes the epidemiology, etiology, and clinical impact of PPM after either surgical or transcatheter aortic valve replacement.

PPM has a significant impact after SAVR on clinical outcomes, including early mortality, renal failure, stroke, need for inotropes, or prolonged ventilation. It may impede left ventricular mass regression and predispose bioprosthetic valve degeneration and should therefore be avoided during surgery. PPM has been linked to higher surgical mortality and impairment of patients' quality of life postoperatively. Meanwhile, TAVR provides a wider orifice of bioprosthetic valve with better trans-prosthetic hemodynamics. TAVR using the Cribier-Edwards or Edwards Sapien valve was linked to lower trans-prosthetic gradients and greater EOAs early after the procedure, leading to a significant reduction in severe PPM at discharge and midterm (12 months) follow-up. TAVR has a lower prevalence of moderate, severe and overall PPM than SAVR due to its superior hemodynamic function.

Despite the available data, more evidence is needed on the impact of PPM on long-term survival after TAVR and SAVR. Therefore, there is a need to conduct high-quality clinical trials in this direction.

KEY WORDS

Aortic valve disease, aortic stenosis, patient-prosthesis mismatch, surgical aortic valve replacement, transcatheter aortic valve replacement, effective orifice area, echocardiography

3. INTRODUCTION

Rahimtoola first proposed the concept of proper prosthetic heart valve sizing in his 1978 Circulation article, "The problem of valve prosthesis-patient mismatch" (1). The purpose of this article was to describe the occurrence where a prosthetic heart valve's orifice area could be too small for a certain patient. There is still interest in the subject, even until this day. To classify and standardize definitions and evaluation procedures for prosthesis-patient mismatch (PPM) following SAVR, a sizable amount of data and studies have been published.

There is much debate surrounding the issue of PPM's clinical impact. Several new factors developed with the introduction of transcatheter aortic valves, including: does PPM also occur after TAVR? Is assessment distinct from that following SAVR? Compared to TAVR, are there any distinctions between SAVR? What effect does PPM following SAVR and TAVR have now and in the future for patient groups with growing TAVR indications (2)?

4. OBJECTIVE AND METHODS

With evolving medical techniques, the aim of this review is to investigate the epidemiology, etiology and clinical impact of PPM after aortic valve replacement. This review's objective is also to provide a concise summary of the most recent research on PPM following aortic valve replacement from the viewpoints of both surgeons and interventional cardiologists.

A two level search technique was used to find all studies that looked into PPM after TAVR and SAVR. MEDLINE and EMBASE databases were first searched using web-based search engines (Pubmed and Frontiers). Second, relevant studies were found by manually searching secondary sources, which included the references of the original publications that were found, as well as reviews and commentaries. All references were downloaded in order to consolidate, remove duplicates and conduct additional research.

5. REVIEW OF AORTIC VALVE DISEASES

Both regurgitations, which involve retrograde flow through the aortic valve, and stenosis, or narrowing of the orifice, which restricts anterograde flow through the valve, are diseases of aortic valve. Although the pathology may develop over a long period of time, symptoms may not become apparent until the condition is advanced; at this point, the morbidity and mortality of aortic valvular disease are very high. The early warning signs and symptoms of aortic valve disease must be recognised by medical practitioners. This activity emphasizes the results of the physical examination, the results of additional laboratory tests and imaging modalities to diagnose and stage aortic valve disease, and the importance of the multidisciplinary team in selecting the best therapy (3).

5.1. ETIOLOGY OF AORTIC VALVE DISEASE

Aortic stenosis (AS) is the most common primary valve lesion requiring surgery or transcatheter intervention in Europe and North America. Due to the predominance of

degenerative etiology, prevalence of AS dramatically rises with age. Given the prevalence of comorbidity and the elevated risk associated with intervention in this age group, the burden of cardiac valve disease in the elderly has a significant impact on patient treatment. The most frequent cause of endocarditis and a significant contributor to valve disease is Staphylococcus. The prevalence of rheumatic heart disease is still high in underdeveloped nations (4).

5.2. EPIDEMIOLOGY

The Heart Valve disease (HVD) epidemiology varies significantly between high-income and low-income countries as well as between various types of HVD. The most prevalent heart valve disease in low-income countries which is also responsible for the bulk of morbidity and mortality owing to HVD worldwide, is rheumatic heart disease. Calcific aortic valve disease (CAVD) is, however, the most common cause of HVD hospital referrals in high-income countries. Even though HVD has a lower prevalence than coronary heart disease, it yet has a disproportionately high impact on healthcare systems due to the need for long-term monitoring and high expenses associated with research and treatment. The term “next cardiac epidemic” has been given to HVD because of the strong relationship between HVD and advancing age, as well as the swift aging in population globally (5). Around a third of patients who are referred for the care of valvular disease have previously had surgery. Over the past ten years, the percentage of valve surgery has climbed, and they now make up more than 20% of all cardiac surgeries (4).

The most common cause for surgical valve replacement in the US and Europe is calcific aortic stenosis and affects 20% of those over the age of 65. Calcific aortic stenosis is becoming more common as the average age of the population rises. For a very long time, aortic valve disease was mostly brought on by rheumatic heart disease. However, due to improved access to healthcare in industrialized nations and the aging of the population in the US and Europe, over the past 50 years, rheumatic etiology has given way to a “degenerative” process. The passive calcium deposition on the surface of the aortic valve leaflet was for years thought to be the cause of “degenerative” aortic stenosis. The etiology of the aortic valve disease in the recent studies has however shown to have a similar pathophysiology as vascular atherosclerosis. As a result, the conditions’ management could therefore resemble that of chronic vascular atherosclerosis (5).

5.3. CLINICAL AORTIC VALVE DISEASE COURSE

Depending on the stage of the disease at when a patient is initially diagnosed, the prognosis for a patient with valvular heart disease treated medically varies. That is why, an evaluation of the pathophysiologic effects of the hemodynamic changes is required to assess a patient for surgery (6). Aortic stenosis diagnosis heavily depends on the patient's medical history and physical examination. For effective management, it is crucial to identify symptoms like exertional shortness of breath, angina, dizziness or syncope. Further diagnostic findings are guided by the distinctive systolic murmur. When compared to a late peaking murmur, an early peaking murmur typically indicates a valve that is less stenotic. Although not a sensitive indicator, the loss of the second aortic sound is unique to severe aortic stenosis. In many individuals, the murmur of aortic stenosis can be missed or misdiagnosed and it usually is more often seen in those who are obese, have underlying obstructive lung conditions (where the murmur is muffled), or have left ventricular failure (where the murmur is blunted) (7).

The survival rate is barely two to three years after the onset of symptoms. Mentioning the different symptoms and the typical time of death after their onset, the estimated survival rate according to the data collected during postmortem examination in patients who were not treated surgically, was for angina, three years; syncope, three years; dyspnea, two years; and congestive heart failure, one and a half to two years. Asymptomatic patients on the other hand who have significant aortic stenosis, have a good prognosis without an aortic valve replacement. However, the asymptomatic phase for each person lasts a different amount of time (7).

Unfortunately, sudden death is seen in 1-2% of asymptomatic patients as well as them progressing very rapidly to symptomatic stage and then to sudden death. The rate of progression to valve replacement happens in patients with congenital or degenerative disease first if they have a unicuspid valve, secondly if they have a bicuspid valve, and thirdly if they have a tricuspid valve (7). However, even when symptoms are modest, survival is poor in symptomatic individuals unless the outflow obstruction is resolved. After the onset of symptoms, the average survival without AVR is only about 1 to 3 years (8). 9.2% of symptomatic patients had cumulative 5 year incidences of sudden death, censored at aortic valve replacement, which accounted for the competing risk (9).

5.4. DIAGNOSTICS OF AORTIC VALVE DISEASES

The primary method of diagnosis is echocardiography. It determines the degree of valve damage, left ventricular (LV) function, and wall thickness, as well as the presence of other related valve disease or aortic pathology. It also validates the existence of aortic valve stenosis as depicted in Figure 1 (10, 11).

In both normal and low-flow severe aortic stenosis, natriuretic peptides predict symptoms-free survival and prognosis. They can be applied to decide which of a patient's symptoms have more than one possible cause and to find patients with high-risk asymptomatic aortic stenosis who might benefit from early intervention (11).

Exercise testing is advised for risk stratification of asymptomatic patients with severe aortic stenosis since it may reveal symptoms. By measuring the change in LV function and rise in mean pressure gradient, exercise echocardiography adds prognostic data (11).

The morphology of the aortic root and ascending aorta, the degree and distribution of valve and vascular calcification, and the feasibility of vascular access are all shown by cardiac computed tomography. When paired with geometric evaluation of valve area, quantification of valve calcification predicts disease progression and clinical events and may be helpful in determining the severity of aortic stenosis in patients with low valve gradient (11).

Cardiovascular magnetic resonance may identify and measure myocardial fibrosis, which is a key cause of LV decompensation in aortic stenosis (independent of the presence or absence of coronary artery disease). In older persons, amyloidosis and aortic stenosis co-occur often (9-15%). Based on symptoms (neuropathy and hematologic data) and clinical suspicion of cardiac amyloidosis, bone scintigraphy and/or cardiovascular magnetic resonance should be taken into consideration. Following valve intervention, both entities continue to exist and are linked to a poor long-term prognosis (11).

Prior to TAVI and SAVR, coronary angiography is necessary to assess the potential need for concurrent revascularisation. Unless there are symptoms and signs of significant aortic stenosis and non-invasive examinations are equivocal, retrograde LV catheterization is not advised (11).

Manufacturers of valves often provide predicted iEOA charts for surgical aortic valve bioprosthesis; more recently TAVR manufacturers provided comparable prediction data based on published data from Hahn, et al (12). In SAVR, the stent and sewing ring serve as a basis for a relatively stable prosthetic size. However, in TAVR, the size of the implant, and the use of post-deployment balloon dilation all affect the final size of prosthesis (12).

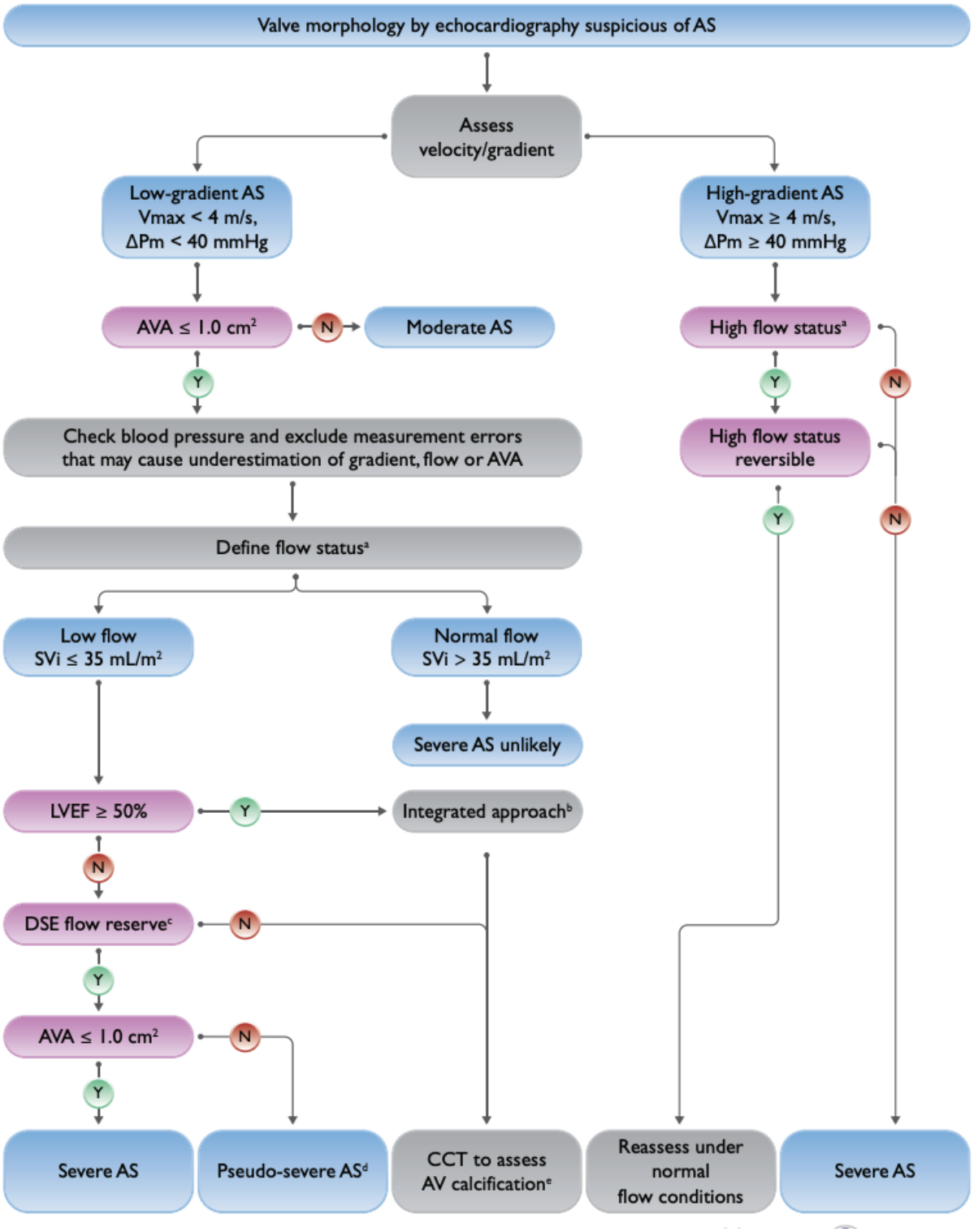

Figure 1. Integrated imaging assessment of aortic stenosis. AS = aortic stenosis; AV = aortic valve; AVA = aortic valve area; CT = computed tomography; △Pm = mean pressure gradient; DSE = dobutamine stress echocardiography; LV = left ventricle/left ventricular; LVEF = left ventricular ejection fraction; SVi = stroke volume index; Vmax= peak transvalvular velocity (11).

5.5. INDICATIONS FOR AORTIC VALVE REPLACEMENT

There are a few crucial questions that must be addressed and responded to while evaluating a patient with aortic valve disorders. What degree of aortic stenosis is present? Do they exhibit any symptoms? Are the signs and symptoms related to valve disease? What is the anticipated life expectancy and standard of living for the patient? Are the anticipated advantages of intervention greater than the risks? Are there adequate local resources for the proposed intervention? Which option does the patient prefer (10)?

Aortic valve replacement for acquired aortic stenosis is showing promising results these days in different age groups. For patients over the age of 65, age-corrected survival following aortic valve replacement is excellent and comparable to that of the general population at that age. Aortic valve replacement has a 2% to 3% operative mortality and an 85% age-corrected 10-year survival rate when there are no extracardiac comorbidities or coronary artery disease. This fantastic result can be due to a number of things, including the widespread use of intraoperative cardiac protection, the placement of reliable and excellent hemodynamic valve prosthesis and the timed replacement of the aortic valve (13).

Several factors, such as symptoms, valve anatomy, valve hemodynamics, and the impact of dysfunctional valves on ventricular and vascular function, are used to classify the severity of valve diseases (e.g. end-organ damage). While diagnosis, patient education, routine monitoring, and medical therapy are crucial components in the management of patients at risk of VHD and with the mild to moderate valve failure, surgical and transcatheter procedures are typically performed on patients with severe VHD (14).

It is important to ascertain whether a patient with severe AS has cardiac symptoms since symptomatic AS is a crucial indication for AVR. Dyspnea with exercise, presyncope or syncope, and exertional angina are common symptoms in patients being monitored for AS. Because they do not always always correlate with AS severity, cardiac symptoms are common in older adult patients with severe AS. Many AS patients have multiple potential cardiovascular symptom causes (e.g. coronary artery disease and severe AS). Furthermore, only 33% asymptomatic patients with severe AS who were longitudinally tracked continued to be free of cardiac symptoms without surgery after five years (15).

The hardest subgroup to decide on for intervention is those with low-flow, low-gradient aortic stenosis and preserved ejection fraction. There are few and disputed data on their natural history and outcome following surgical or catheter intervention. Intervention in these situations should only be carried out when symptoms are apparent and a thorough

evaluation indicates a severe valve obstruction. Symptoms continue to be the most compelling reason for intervention (either spontaneous or on exercise testing) (10). The current guidelines of European Society of Cardiology (ESC) on indications for intervention in symptomatic (A) and asymptomatic (B) AS and recommended mode of intervention are provided in Table 1 (11).

A) Symptomatic aortic stenosis	Class[b]	Level[c]
Intervention is recommended in symptomatic patients with severe, high-gradient aortic stenosis [mean gradient ≥40 mmHg, peak velocity ≥4.0 m/s, and valve area ≤1.0 cm^2 (or ≤0.6 cm^2/m^2)].[235,236]	I	B
Intervention is recommended in symptomatic patients with severe low-flow (SVi ≤35 mL/m^2), low-gradient (<40 mmHg) aortic stenosis with reduced ejection fraction (<50%), and evidence of flow (contractile) reserve.[32,237]	I	B
Intervention should be considered in symptomatic patients with low-flow, low-gradient (<40 mmHg) aortic stenosis with normal ejection fraction after careful confirmation that the aortic stenosis is severe[d] (*Figure 3*).	IIa	C
Intervention should be considered in symptomatic patients with low-flow, low-gradient severe aortic stenosis and reduced ejection fraction without flow (contractile) reserve, particularly when CCT calcium scoring confirms severe aortic stenosis.	IIa	C
Intervention is not recommended in patients with severe comorbidities when the intervention is unlikely to improve quality of life or prolong survival >1 year.	III	C
B) Asymptomatic patients with severe aortic stenosis		
Intervention is recommended in asymptomatic patients with severe aortic stenosis and systolic LV dysfunction (LVEF <50%) without another cause.[9,238,239]	I	B
Intervention is recommended in asymptomatic patients with severe aortic stenosis and demonstrable symptoms on exercise testing.	I	C
Intervention should be considered in asymptomatic patients with severe aortic stenosis and systolic LV dysfunction (LVEF <55%) without another cause.[9,240,241]	IIa	B
Intervention should be considered in asymptomatic patients with severe aortic stenosis and a sustained fall in BP (>20 mmHg) during exercise testing.	IIa	C
Intervention should be considered in asymptomatic patients with LVEF >55% and a normal exercise test if the procedural risk is low and one of the following parameters is present: • Very severe aortic stenosis (mean gradient ≥60 mmHg or V_{max} >5 m/s).[9,242] • Severe valve calcification (ideally assessed by CCT) and V_{max} progression ≥0.3 m/s/year.[164,189,243] • Markedly elevated BNP levels (>3× age- and sex-corrected normal range) confirmed by repeated measurements and without other explanation.[163,171]	IIa	B

C) Mode of intervention		
Aortic valve interventions must be performed in Heart Valve Centres that declare their local expertise and outcomes data, have active interventional cardiology and cardiac surgical programmes on site, and a structured collaborative Heart Team approach.	I	C
The choice between surgical and transcatheter intervention must be based upon careful evaluation of clinical, anatomical, and procedural factors by the Heart Team, weighing the risks and benefits of each approach for an individual patient. The Heart Team recommendation should be discussed with the patient who can then make an informed treatment choice.	I	C
SAVR is recommended in younger patients who are low risk for surgery (<75 years[e] and STS-PROM/EuroSCORE II <4%)[e,f], or in patients who are operable and unsuitable for transfemoral TAVI.[244]	I	B
TAVI is recommended in older patients (≥75 years), or in those who are high risk (STS-PROM/EuroSCORE II[f] >8%) or unsuitable for surgery.[197–206,245]	I	A
SAVR or TAVI are recommended for remaining patients according to individual clinical, anatomical, and procedural characteristics.[202–205,207,209,210,212 f,g]	I	B
Non-transfemoral TAVI may be considered in patients who are inoperable and unsuitable for transfemoral TAVI.	IIb	C
Balloon aortic valvotomy may be considered as a bridge to SAVR or TAVI in haemodynamically unstable patients and (if feasible) in those with severe aortic stenosis who require urgent high-risk NCS (*Figure 11*).	IIb	C
D) Concomitant aortic valve surgery at the time of other cardiac/ascending aorta surgery		
SAVR is recommended in patients with severe aortic stenosis undergoing CABG or surgical intervention on the ascending aorta or another valve.	I	C

Table 1. Recommendations on indications for intervention in symptomatic (A) and asymptomatic (B) aortic stenosis and recommended mode of intervention (11).

5.6. MODE OF AORTIC VALVE REPLACEMENT

All patients should have their individual age and expected life expectancy, comorbidities (including frailty and overall quality of life), anatomical and procedural characteristics, the relative risk of SAVR/TAVR and their long-term outcomes, the durability of prosthetic heart valves, the feasibility of transfemoral TAVR, and other factors into careful consideration by the Heart Team before choosing the most appropriate mode of intervention (Table 1). Aortic valve interventions must be carried out in Heart Valve Centers with active interventional cardiology and cardiac surgical programs on site, a structured collaborative Heart Team approach, and a declaration of their competency and results data (11).

Younger patients who are at low risk for surgery (<75 years and STS-PROM/EuroSCORE II <4%) or those who are operable but unsuitable for transfemoral TAVR are advised to undergo SAVR. Patients with severe aortic stenosis who are having CABG or other surgical procedures involving the ascending aorta or another valve are also advised to get SAVR (11).

Patients who are over 75 years old, at high risk (STS-PROM/EuroSCORE IIF >8%), or who are not candidates for surgery should consider TAVR. Patients who are both inoperable and unfit for transfemoral TAVR may be evaluated for non-transfemoral TAVR. Individual clinical, anatomical, and procedural variables determine whether SAVR or TAVR is advised for the remaining patients. In patients with hemodynamically instability and (if possible) those who need urgent high-risk NCS (non-cardiac surgery) because of severe aortic stenosis, balloon aortic valvotomy may be explored as a bridge to SAVR or TAVR (11).

5.7. SELECTION OF PROSTHESIS

The choice of a suitable prosthesis is frequently a difficult choice influenced by the preferences of both patients and doctors. Mechanical prosthetic valves (often bileaflet) and biological prosthetic valves (porcine or bovine pericardial) are the two primary options for surgical AVR . Although mechanical valves have remarkable structural durability, patients with mechanical prosthesis need systemic anticoagulation for the rest of their lives. In contrast, individuals who have bioprosthesis may no longer need to take oral anticoagulants in relation to prosthesis, although structural valve failure frequently requires reoperation 10 to 15 years after implantation. Additionally, compared to patients who are older, younger patients experience deterioration of biological prosthesis more quickly. Due to the technical difficulty of implantation and inconsistent durability, other valve substitutes, such as aortic

valve homograft and pulmonary autografts (Ross procedure), are typically saved for special circumstances, such as aortic root reconstruction following infection (homografts) or young patients who have not yet reached full somatic growth (pulmonary autografts) (16).

Bioprosthetic valves should be used in patients older than 65 years according to the most recent recommendations for the selection of valve prosthesis based on clinical data, including two randomized trials. This is because 1) elderly patients have a lower risk of structural valve degeneration, 2) shorter expected life duration and 3) there are benefits to avoiding systemic anticoagulation in frail patients with additional comorbidities. Although many of these data were collected from clinical practice two to three decades ago, there has been a significant evolution in surgical methods, valve design, and anticoagulation tactics. Several doctors continue to use outdated studies supporting the use of biological valves in younger patients (65 years) despite the interim changes in clinical practice and recent clinical outcome trials data. According to the ACC/AHA recommendations, the purpose of employing bioprosthesis in persons younger than 65 years is to reduce the risk of hemorrhagic events associated with anticoagulants and relieve patients from lifestyle constraints associated with the use of warfarin. However, there are two assumptions that are implicit in this strategy; the first is that patient survival after AVR is comparable with mechanical valves and bioprosthesis, and the second is that the current third-generation bioprosthesis will be more durable than the short lifespan associated with earlier designs (16).

The poor lifetime of bioprosthetic valves necessitates repeated valve replacement surgeries over time. This is especially important for young, low-risk patients who are expected to live a long time because the implanted valve's structural valve degeneration is most likely to manifest itself 10 to 15 years following surgery. As a result, it is anticipated that more and more patients may soon arrive with failing surgical heart valves. When compared to standard redo surgical aortic valve replacement (redo SAVR), valve-in-valve (VIV) transcatheter aortic valve replacement (VIV-TAVR) has become a less invasive option for treating patients with degenerated surgical bioprosthesis. Over the past ten years, the use of VIV-TAVR has increased significantly, and each year, numerous procedures are carried out across the globe (17).

All of the information that is currently available for treating deteriorated aortic structural valve degeneration refers to observational studies because there are no randomized studies that compare VIV-TAVR versus redo SAVR. VIV-TAVR patients had improved short-term results in terms of mortality and significant complications, according to a recent French Statewide propensity-matched investigation that compared VIV-TAVR vs redo SAVR in more

than 1400 patients (717 for each group). After a median follow-up of 516 days, the longest trial to date comparing long-term data found no difference between groups for the primary endpoints (mortality, stroke), although the VIV-TAVR group had a greater rate of heart failure hospitalization (18).

6. PATIENT-PROSTHESIS MISMATCH

There are situations with prosthetic valves where the gradients are significant but the valve has a normal look and a calculated EOA that is typical for the kind and size of the valve. PPM must be taken into account in this situation (18).

Rahimtoola was the first to describe patient-prosthesis mismatch in his 1978 original stating “Mismatch can be considered to be present when the effective prosthetic valve area, after insertion into the patient, is less than that of a normal human valve”. This notion assumes that larger transvalvular gradients will occur if the effective orifice area (EOA) is smaller than anticipated in comparison to the patient’s body surface area (BSA). According to observational clinical studies, the most typical definition of severe PPM is an indexed effective orifice area (iEOA) less than 0.65 cm^2/m^2 after aortic valve replacement, while the moderate PPM is defined by an iEOA between 0.65 and 0.85 cm^2/m^2. However, a recent definition from the Valve Academic Research Consortium 3 (VARC-3) recommends taking body mass index (BMI) into account. The VARC-3 definition identifies PPM in patients with BMI $\geq$30 kg/m^2as an iEOA $\leq$0.70 cm^2 and severe PPM as iEOA $\leq$0.55 cm^2. PPM in patients with BMI<30 kg/m^2 is still defined according to the previous definition (19).

With prevalence ranging from about 9% to almost 80% in different studies and an estimated overall frequency of 44% based on meta-analysis of 34 observational studies (20) with a total of 27 186 individuals, the occurrence of PPM following AVR is uncertain. According to studies that rated PPM severity, moderate PPM prevalence ranged from 11% to 90%, whereas severe PPM prevalence ranged from 0.5% to 62%. Although the causes of the broad range in PPM prevalence are unknown, they may include baseline patient variations, ascertainment bias, and selection bias (variability in diagnosis) (20).

The hydraulic equation $TPG = Q^2/[k \times EOA^2]$, which demonstrates that the transvalvular pressure gradient (TPG) is directly proportional to the square of transvalvular flow (Q) and inversely related to the square of the valve EOA while k is a constant, serves as the greatest example of this. For gradients to remain low, the EOA must be appropriate to the amount of flow needed (21).

Transvalvular flow is mostly influenced by cardiac output, which is governed by BSA, when the body is at rest. Thus, PPM happens when the EOA of the prosthetic valve is too tiny in comparison to the patient's body size. The immediate effect is the continued occurrence of excessively high TPGs (21).

6.1. PPM after SAVR

6.1.1. EPIDEMIOLOGY

The greatest studies examining the prevalence of PPM following SAVR were published by Fallon et al. (22) and Sá et al. (23), both of which demonstrated that PPM is a prevalent issue. Fallon et al. recently found that among 59,779 patients undergoing SAVR, the incidence of PPM was 46.8% for moderate PPM and 6.2% for severe PPM using the STS Adult Cardiac Surgery Database. Similar to this, Sá et al. recently reported a systematic review with meta-analysis that included 70 publications (22) and 108,182 patients. They found that the incidence of moderate/severe PPM following AVR ranged from 6.1% to 93.8% and that it was 53.7% in some publications (24).

6.1.2. ETIOLOGY

The most significant factor contributing to the disparity between the reported frequencies and clinical impact of PPM in TAVR versus SAVR series is probably the method employed to determine EOA and, consequently, to classify PPM. In fact, all TAVR series up until this point have utilized the measured iEOA, but the vast majority of SAVR series have used the predicted iEOA to diagnose PPM. The primary drawback of the measured iEOA is that it is susceptible to measurement mistakes, variables, and affected by the patient’s hemodynamic situation, particularly the flow state. The EOA and iEOA, as well as the left ventricular outflow tract diameter, may be overestimated by two-dimensional echocardiography, leading to an overestimation of PPM. Low transvalvular flow may prevent the EOA from being fully opened, which could result in the incorrect diagnosis of a severe PPM. This “pseudo-severe” PPM phenomenon is comparable to “pseudo-severe” stenosis in individuals with native AS that have low flow and low gradient. Therefore, a significant portion of patients were in a low-flow state at the 30-day echocardiogram, and as a result, had pseudo-severe rather than true severe PPM on the basis of the measured iEOA. This may be one of the main reasons for the significantly higher incidence of severe PPM with the measured versus predicted iEOA.

The predicted iEOA enables, at least in part, resolving these measurement variability and pseudo-severe PPM difficulties, perhaps enhancing the identification of patients with true-severe PPM (25).

6.1.3. RISK FACTORS FOR PPM

The main risk factors for PPM include female sex, advanced age, hypertension, diabetes, and renal failure. Women frequently have smaller annuli, which could make PPM riskier. The additional risk factors may limit the surgeon's ability to install a bigger valve since females are linked to an increased risk of aortic annulus and aorta calcification. Moreover, bioprosthetic valves are more frequently used on older patients than mechanical valves. Elderly people have a bigger risk for heart failure with preserved ejection fraction. Heart failure with a preserved ejection fraction is frequently accompanied by paradoxical low-flow, which is a lower stroke volume index despite a preserved LVEF. This condition has been demonstrated to increase the risk of death after AVR. Hence, it is challenging to pinpoint exactly how PPM, heart failure with intact ejection fraction/paradoxical low-flow, and related comorbidities (such as coronary artery disease, diabetes, hypertension, and renal failure) contribute to the increased risk of adverse outcomes (26). However, a study done by Dania and colleagues (27), paradoxical low-flow aortic stenosis and PPM both increase the risk of mortality after AVR, and having both of these conditions together was linked to the worst outcome (27).

6.1.4. CLINICAL IMPACT OF PPM AFTER SAVR

Many researchers have looked into the relationship between PPM and clinical outcomes. Among them, there were variations in the evaluation of PPM and the setting of cut-off levels. There is inconsistent evidence about the impact of PPM on early outcomes following SAVR, including early mortality, renal failure, stroke, the need for inotropes, or prolonged ventilation. It is yet unknown whether increased likelihood of surgical complications is attributable to PPM specifically or merely a proxy indicator of comorbidity and a more complex patient. The persistently greater gradient in PPM patients may impede left ventricular mass regression following SAVR. Higher PPM levels have been associated with less complete left ventricular mass regression in some studies, compared to others (2). Following aortic valve replacement, the same mechanism may predispose to quicker bioprosthetic valve deterioration. (2,28).

Patients may continue to experience symptoms because they may be identified as having a residual stenosis after SAVR due to PPM. Cardiopulmonary exercise testing in patients with PPM showed lower percentages of anticipated VO_2max reached during exercise and considerably higher mean aortic gradients during exercise. Long term survival may be impacted by the negative consequences of a residual stenosis, such as incomplete left ventricular mass regression or quicker bioprosthetic degradation. In a major meta-analysis (29) involving more than 27,000 patients, it was discovered that moderate and severe PPM had a substantial effect on overall and cardiac-related survival after five years (2). Another meta-analysis (26) involving more than 40,000 patients discovered that PPM in patients under age of 70 or with a body mass index (BMI) of less than 28 kg/m^2 have a greater impact on mortality (2). Several groups also discovered an age-dependent effect of PPM on longer-term survival (2).

6.1.5. PREVENTION/TREATMENT

There is general agreement that PPM should be avoided during surgery given the substantial body of data demonstrating a significant influence of PPM on clinical outcomes. Older age, female sex, higher BSA and BMI, diabetes, hypertension, renal failure, and implantation of a bioprosthesis rather than a mechanical valve are clinical indicators linked to an increased risk for PPM (2). Reoperations for symptomatic PPM are extremely uncommon because the projected risks and benefits of a reintervention must be weighed.

Before a specific prosthesis is implanted for a given patient, the iEOA must be predicted in order to select an appropriately sized prosthesis that will fit the patient, not just those in the risk population mentioned above. The observed EOA of a specific prosthetic valve type and size in this situation varies from patient to patient as well as between serial measurements taken from the same patient, which is crucial to understand. While the flow status is responsible for intra-individual variations, the inter-individual variation is mostly caused by different aortic root anatomies. As a result, the observed EOAs for a certain kind and size of regularly used surgical prostheses may exhibit a wide range of values. Before surgery, it can be helpful to estimate and anticipate the individual patient's iEOA by using the mean EOA values obtained from a large number of echocardiographically assessed patients. It is recommended to use reference charts derived from echocardiographic measures (2).

If the needed prosthesis size cannot be placed in an individual anatomy, annular enlargement with patch augmentation can be done. Younger patients and those with left ventricular failure, in whom the relationship of PPM with unfavorable clinical outcomes is

most obvious, should be considered preferably for additional surgical maneuvers. When adjusting for concurrent procedures with annular expansion, the risk of surgery is not noticeably higher. The Manougian method should be chosen over the Nicks treatment since it is more successful at increasing the EOA (2).

An incision is made using the Manougian technique, and it is extended posteriorly into the commissure between the left coronary cusp and noncoronary cusp. After that, the anterior mitral valve leaflet can be reached through the incision. A vertical commissure incision is made using the Nicks-Nunes technique. The aortic outflow tract is then lengthened by extending the incision between the left coronary cusp and noncoronary cusp all the way to the inner leaflet triangle. The Nicks-Nunez approach often permits the installation of at least one larger valve size (30).

Interventional therapy may be chosen over surgical aortic valve replacement and aortic root expansion in some patients with limited aortic anatomy. Even though they only demonstrate a modest surgical risk, elderly patients with appropriate anatomy for TAVR may make good candidates for interventional treatment. Thorough discussion among the Heart Valve team given that under these circumstances, joint decision-making is vitally essential (2).

6.2. PPM AFTER TAVR

6.2.1. EPIDEMIOLOGY

In a meta-analysis conducted in Shizuoka at al (31), researchers found 21 studies that qualified and contained information on 4.000 patients who had had TAVR. The initial meta-analysis (32,33,34) discovered a prevalence of moderate PPM of 26.7%, severe PPM of 8.0%, and overall PPM of 35.1% (28). With TAVR compared to SAVR, there were statistically significant decreases in the prevalence of moderate ($p = 0.03$), severe ($p = 0.0003$), and overall PPM ($p = 0.02$), according to the second meta-analysis (34,35,36,37,38,39) of six studies involving 745 patients. There were no statistically significant differences in late mortality between patients with severe PPM and patients without PPM ($p = 0.44$) or between patients with overall PPM and patients without PPM ($p = 0.97$), according to the third meta-analysis (39,40,41,42,43) of five studies that included 2,654 patients (28).

The prevalence of moderate and severe PPM was, overall, 35%, 27%, and 8% following TAVR, respectively, which may be lower than that after SAVR. PPM following TAVR may not negatively impact late survival, in contrast to PPM after SAVR (28).
The incidence of PPM ranges from 24-48% for moderate and 8-18% for severe PPM in the most recent literature (28). Only 19.7% of patients in the randomized PARTNER A cohort experienced severe PPM, compared to 48% of individuals with moderate PPM (39).

6.2.2.RISK FACTORS AND ETIOLOGY

An entirely new method of treating aortic valve diseases was made possible by using TAVR. The possible area for trans-prosthetic valve flow may be constrained since the native valve calcium is not removed but rather pushed aside. However, TAVR prosthesis differ from SAVR prostheses because they do not have a thicker sewing ring, which may result in a bigger area for trans-prosthetic valve flow with better hemodynamics in TAVR patients (2).
The factors significantly linked to PPM after TAVI are following: 1) larger weight, height, body surface area (BSA), body mass index (BMI), LV mass, and prosthesis/annulus ratio; 2) younger age; 3) smaller aortic valve area, aortic valve area index, and LV ejection fraction; 4) obesity, hypertension, diabetes, chronic obstructive pulmonary disease, oxygen dependence, peripheral vascular disease, moderate mitral regurgitation, major arrhythmia, acute myocardial infarction, and prior coronary artery bypass grafting (CABG) (31).
The incidence of PPM in various self-expanding TAVR valves (Evolut R, Evolut Pro, Accurate, and Portico) in 859 patients was examined by the TAVI-SMALL registry in a retrospective analysis because it is well known from data on surgical prosthesis that the risk for PPM is higher in a small aortic annulus anatomy (44). The baseline features were evenly distributed throughout the groups despite the retrospective methodology. The Portico group (30) had a considerably greater rate of moderate PPM (38%) than the other TAVR valves, which may be related to its intra-annular design as opposed to the other self-expanding valves' with supra-annular design. Total rate of severe PPM was 9.4% in this registry. The incidence of severe PPM was marginally greater (13.7%) in a sample of individuals with a very tiny annulus, with no significant difference of severe PPM between analyzed prosthetic valves (30).

It is abundantly obvious that because of their intra-annular design, balloon-expandable valves are more susceptible to PPM than self-expanding valves. In patients with both big and small annuli (59.2 vs 33.3%), the CHOICE-Extended registry

revealed a significantly greater rate of PPM for SAPIEN 3 (43.2%) compared to Evolut R (21.7%) valves (45).

According to a multinational propensity-matched comparison (46), the balloon-expandable SAPIEN 3 group experienced a considerably greater rate of severe PPM than the self-expanding ACURATE neo group (822 vs 3%) in 246 patients having an aortic annulus smaller than 400 mm2. In addition to small LVOT, tiny aortic annulus, and TAVR valve selection, PPM has been seen more frequently in patients with higher BMI (2,39,44).

6.2.3. CLINICAL IMPACT OF PPM AFTER TAVR

While long-term findings are lacking and initial TAVR patients had numerous comorbidities, it is currently unclear whether PPM affects prognosis after TAVR. In the PARTNER A TAVI cohort, PPM was predictive when paravalvular leakage was absent as previously noted (44).

In a single-center registry (46) with a lower frequency in self-expanding TAVR valves, severe PPM was seen in 12.9% of the patients. Severe PPM was an independent predictor of all-cause death after 3 years in patients with a reduced ejection fraction (LVEF ≤40%), but this was not the case in the entire group. Those with LVEF levels above 40% did not experience any significant relationship between presence of severe PPM and worse prognosis (47).

Another single-center analysis (47) showed that 25% of the study cohort's participants had severe PPM (34). For event-free 3-year survival, severe PPM had an independent prognostic effect (52 vs 84%, p = 0.04). The rates of stroke and heart failure rehospitalization were not significantly affected. PPM rates of 32.8% were reported by the multicenter WIN-TAVI registry (48), which only included female patients. As noted in the earlier research, the only independent predictors of PPM in this cohort of female patients were higher BMI and smaller TAVR prosthesis. The fact that PPM had no effect on 1-year mortality or major cardiovascular events is noteworthy (48).

In the OCEAN - TAVI registry (49), which included 1,546 Japanese patients, moderate and severe PPM were found in 8.9 and 0.7% of individuals, respectively. Younger age, a smaller aortic annulus and the installation of a balloon-expandable valve were all identified by multivariate analysis as independent predictors of PPM. Patients with or without PPM experienced the same level of all-cause mortality (49).

There is an indication, according to the most recent literature, that PPM affects outcomes of the patient having low LVEF. In this patient population, PPM should be avoided

by choosing a self-expanding TAVR valve with a supra-annular design. The choice of valve should take into account that patients with small aortic annulus are more likely to develop PPM. It is currently unclear how TAVR will affect overall survival, thus more research with a longer follow-up is required. PPM may affect premature TAVR valve degeneration, just as it does in surgical patients, however this issue hasn't been looked into yet (47).

6.2.4. PREVENTION/TREATMENT

Although there is presently little reference data for the EOA of some transcatheter heart valves (Figure 2), they should be used to forecast the iEOA (12). As previously mentioned, it has been demonstrated that self-expanding TAVR valves with supra-annular design (Acurate Neo and Evolut R/Pro) exhibit lower transvalvular gradients and thus higher measured iEOA (50). The relative size of the stent and skirt in patients with tiny aortic areas may even lower the potential opening area, and the hemodynamic needs should also be considered in individuals with bigger body sizes (50).

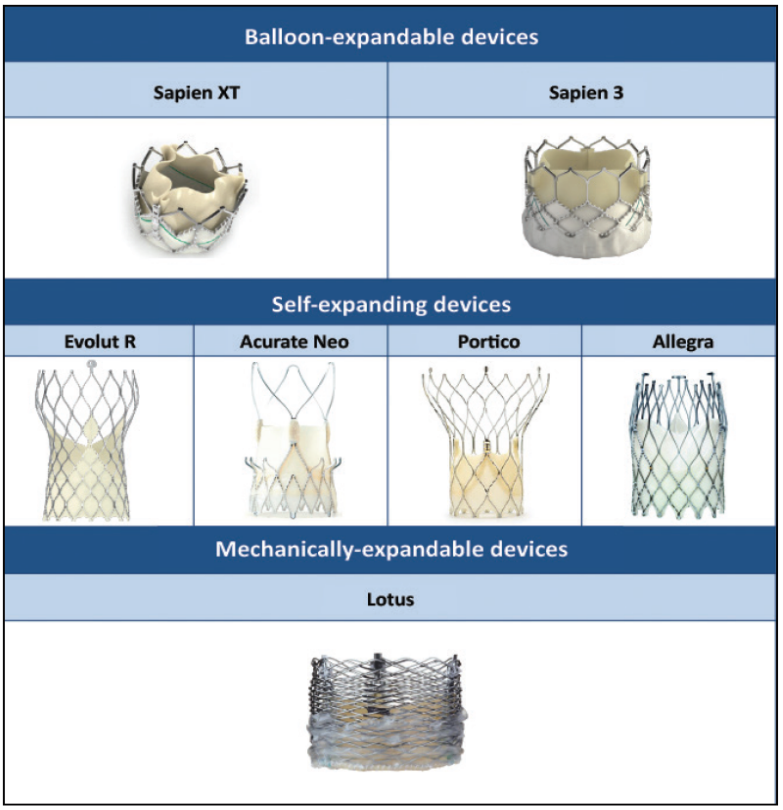

Figure 2. Overview of the current FDA- and CE Mark-approved TAVR devices (51).

It is advised for patients at risk for PPM to utilize a TAVR valve with a supra-annular design based on the available data. Further preventive measures should be regularly used, such as post-dilatation in the event of a higher gradient or valve oversizing (28).

PPM can be identified in advance of intervention or predicted at that time (44,45). The incidence of severe PPM has decreased by 55% from 13.8% in 2004 to 6.2% in 2014 as a result of increased awareness of the issue and the application of strategies to reduce its occurrence (52). The TAVR community should follow this lead by identifying patients at risk for severe PPM and considering techniques to reduce the risk. Jilaihawi et.al. (53) showed that the appropriate location of a self-expanding prosthesis (lower LV depth) was connected to a drop in moderate and severe PPM from 48% to 16% (39). Many studies have shown lower gradients and fewer PPM with the use of self-expanding as opposed to balloon-expandable prosthesis in a nonrandomized comparison of devices used for valve-in-valve TAVR (39).

Self expanding prosthesis had a higher EOA for the same labeled-size device, according to a recent hemodynamic research (12). Last but not least, the installation of bigger TAVR prosthesis for valve-in-valve implants can be made possible by the fracture of a prior surgical prosthesis before TAVR (50). To aid in the decision-making process for this population, a future study comparing devices and strategies to restrict PPM in patients at risk for severe PPM would be interesting (54).

7. DISCUSSION

There is much debate surrounding the issue of PPM's clinical impact. Several new factors develop with the introduction of TAVR's, including: does PPM also happen after TAVR? Is assessment distinct from that following SAVR? Compared to TAVR, are there any distinctions between SAVR?

Although some research has indicated that PPM is linked to higher surgical mortality and impairment of quality of life postoperatively, other studies have proved that these findings are false. As a result, there is a great deal of disagreement on how PPM affects postoperative cardiac function and survival, as well as postoperative physical activity levels.

For the treatment of aortic valve disease, TAVR presented a new option and entirely distinct methodology. The possible area for trans-prosthetic valve flow may be constrained since the native valve calcium is not eliminated but rather pushed aside. The smaller stent frame used in TAVR prostheses, as compared to the bigger sewing ring used in SAVR

prostheses, may result in a wider region for trans-prosthetic valve flow with better hemodynamics (2).

One of the studies (35) to discuss would be the one done in Quebec City, where authors did a comparison of the hemodynamic performance of transcatheter and surgical bioprosthesis for the treatment of severe AS. For the study, 50 patients were included with symptomatic severe AS who received successful TAVR using the Cribier-Edwards or Edwards SAPIEN valves. All patients were included in a prospective registry database with full clinical and echocardiographic follow-up at 6-12 months. These individuals were drawn from a group of 89 patients who received TAVR in row and the ones who had unsuccessful TAVR were excluded (failure to implant the valve or procedural death). From a prospective registry database that included all patients who had undergone SAVR, the 50 TAVR patients were case-matched with 50 patients who had successfully undergone SAVR with a stented Carpentier-Edwards Perimount Magna bioprosthesis and with 50 patients who had successfully undergone SAVR with a stentless Freestyle bioprosthesis (41).

With regard to sex (exact match), aortic annulus diameter (within 0.05 mm), lLVEF (withthin 5%), body surface area (within 0.3 m^2), and body mass index (within 5 kg/m^2), each TAVI patient was matched 1:1 with both a SAVR with stented valve and a SAVR with stentless valve patient. The individuals with bicuspid aortic valves were disqualified from the research because they had a contraindication for TAVR (41).

The findings of this study demonstrated that when compared to SAVR using the Magna (stented) and Freestyle (stentless) valves, TAVR using the Cribier-Edwards or Edwards SAPIEN valve was linked with lower trans-prosthetic gradients and greater EOAs early after the treatment. The hemodynamic parameters of the percutaneously implanted valves did not alter at the halfway point of the study, and they continued to perform more hemodynamically effectively than surgically implanted stented valves. When compared to stented (severe PPM at discharge: 26%; severe PPM at follow-up: 28%) and stentless (severe PPM at discharge: 28%; severe PPM at follow-up: 20%) surgical valves, the superior hemodynamic results obtained with TAVR resulted in a significant reduction in the incidence of severe PPM at discharge (11%) and at follow-up (6%). TAVR was linked to a significant decrease in severe PPM in patients with a narrow (20 mm) aortic annulus, however there were no appreciable differences between the SAVR and TAVR groups in patients with a bigger annulus and a considerably lower overall incidence of PPM (41).

Furthermore, although there were no changes in LVEF values between TAVR and SAVR patients at follow-up, only TAVR patients showed a substantial early increase in LVEF

(between baseline and hospital discharge), and this result was more prominent in patients with low LVEF at baseline. In the early postoperative period, TAVR (88%) had a higher rate of aortic regurgitation (AR) incidence than SAVR (46%) did. However, there were no cases of severe AR and the majority (91%) of TAVR patients had trivial or mild residual AR that was stable at the follow-up (41).

In an article investigated by the Cardiovascular department in Shizuoka, Japan, authors presented their study stating that overall, moderate and severe PPM prevalence after TAVR was 35.1%, 26,7%, and 8.0% respectively, according to the current pooled data, which is somewhat lower than that after SAVR (31).

The EOAi criterion of 0.85 cm^2/m^2 was utilized in 27 trials with 21.802 patients included in a meta-analysis by Head and colleagues (29), and it was discovered that 44.2% of patients receiving SAVR had PPM (28). Seven investigations also revealed that 9.8% of patients had severe PPM and 34.2% had moderate PPM. According to their pooled analysis of six studies with direct comparison of after TAVR compared to after SAVR, there were statistically significant decreases in the prevalence of moderate, severe, and overall PPM. Only one of these randomized controlled trials, the PARTNER(39), found a statistically nonsignificant decrease in the incidence of moderate PPM but a significant decrease in the prevalence of severe and overall PPM after TAVR compared to after SAVR. This variation could be attributed to surgical valves' inferior hemodynamic function compared to transcatheter valves. The transcatheter valves are stented valves, but because the stent is thinner and there isn't a sewing ring in the annular area, blood flow is obstructed less. This distinction would be more significant if the transcatheter valves were implanted in a small aortic annulus (28).

Only BSA was found to be an independent predictor for severe PPM in the current analysis (41), despite bigger weight, height, BSA and BMI (all of which are directly related to iEOA defining PPM) being associated with higher PPM prevalence. It is unknown why the comorbidity that was previously discussed and found in the study is negatively correlated with PPM. Comorbidity related to PPM is inevitable and cannot be altered. Aortic root augmentation to make room for a larger prosthesis is a drastic treatment for PPM following SAVR for tiny annulus. In the meantime, the only position that can avoid PPM following TAVR is the ideal position, which is described as 5 to 10 mm below the natural aortic annulus (28).

In contrast, paravalvular regurgitation is uncommon in SAVR regardless of PPM status, although patients with PPM have less post-procedural AR than patients without PPM.

Presence of paravalvular regurgitation may hinder LV mass regression and negatively impact survival. Patients without PPM after SAVR have the best valve hemodynamic performance (i.e., no residual AS and no paravalvular regurgitation) (28).

Only one of the studies analyzed in the research (28) suggests that PPM following TAVR may influence 6-month improvements in NYHA functional class status. However, no differences in NYHA functional status or self-assessed health status were detected between the PPM and no-PPM groups in a study by Bleiziffer and colleagues (20), and the improvement in self-assessed health condition was less noticeable among patients with severe PPM. At six months, Tzikas and associates (33) also found no distinction in functional status between individuals with severe PPM and those without it. Also, there was no difference in the percentage of patients in NYHA classes I or II after 1-year follow- up in a research by Van Linden and colleagues (43). Moreover, there was no noticeable difference between patients with and without PPM in terms of major adverse valve-related and cardiovascular events during the 17.6 +- 7.0 month follow-up period. PPM following TAVR may not have an overall impact on late clinical state (28).

Given the definitions of PPM, it is clear that factors related to small aortic annular dimensions, which would dictate the size of the prosthesis, inherent valve design elements, which dictate the EOA for any given annular size, and a higher body mass index (BMI) could all be linked to a higher incidence of PPM. Older age, female sex, hypertension, diabetes, renal failure, greater body surface, higher BMI, and the presence of a bioprosthesis (vs. mechanical valve) were predictors of PPM in one meta-analysis that included both SAVR and TAVR patients (26). Patients under the age of 70 and/or those receiving concurrent CABG appear to have a bigger impact of PPM on mortality, and patients with greater BMIs (>28 kg/m^2) compared to those with lower BMIs appear to have lesser impact. The latter result lends support to using various iEOA criteria according to body mass. Younger age, non-white/Hispanic ethnicity and small prosthesis (<23 mm diameter) have all been linked to PPM in TAVR studies (52,55).

According to earlier research, PPM is more common in SAVR than TAVR (56). Given that a stented transcatheter heart valve will enlarge to the size of the native annulus and has a thinner stent frame than a surgical sewing ring, this makes anatomic sense. However, compared to prior studies, the most recent PARTNER 3 trial (58) used larger SAVR valves and underwent more aortic root enlargements, which most likely caused the smaller TAVR EOAs (1.7 ± 0.02 cm^2 vs 1.8 ± 0.02 cm^2) compared to SAVR EOAs (57). PPM was still more severe after SAVR compared with TAVR (6.3% vs. 4.3%), despite greater LV ejection

fraction after TAVR (84.2% ± 0.71% vs. 76.6% ± 0.81%) and bigger LV stroke volume index (41.9 ± 0.35 mL/m^2 vs 38.0 ± 0.40 mL/m^2) as compared with SAVR (58).

The SAVR population with severe PPM has higher perioperative and total mortality rate, according to numerous studies and meta-analyses (26, 29, 39). PPM is also linked to more cardiac events, a slower and less complete recovery from pulmonary hypertension and regression of left ventricular hypertrophy, a worse functional class, a decreased physical activity, and a lower quality of life. Patients who have PPM may also be more vulnerable to structural valve degeneration (59).

There aren't many direct comparisons of transcatheter aortic valve (THV) designs that assess potential variation in the incidence of PPM with various valve types. PPM is more prevalent with balloon-expandable (BE) TAVR than self-expandable (SE) TAVR when comparing reported incidences of PPM by valve type (56). However, outcomes related to PPM with BE TAVR are less important than SE TAVR (HR, 0.58-1,2 vs. about 1.7, respectively). Some of these variations might be attributed to variations in valve design and pressure recovery phenomenon (44).

The computation of the pressure gradient across the valve and, consequently, the aortic valve area, is significantly influenced by pressure recovery downstream of the aortic valve (60). The greatest pressure difference across a stenotic orifice is represented by the pressure gradient measured at the vena contracta (i.e., the pressure gradient measured by echo Doppler); however, downstream from the vena contracta, the blood's kinetic energy is changed back into potential energy (pressure) with the pressure recovery in the ascending aorta. The recovered pressure represents the net pressure experienced by the left ventricle and may be the most relevant hemodynamic parameter, even if both the vena contracta gradient and pressure recovered gradients occur in vivo (61). Numerous variables, including turbulence, the velocity of blood at the orifice, and the geometry of the aorta, influence how much pressure is recovered (62).

Hatoum et al. (63) recently conducted an in vitro comparison of the two commercially available THVs and found that while gradient at the vena contracta are higher with the BE THV, in part because of a slight gradient increase within the stent frame, the net gradient after pressure recovery was significantly lower with the BE THV than with the SE THV (63). Due to stent interference with recovering blood flow, efficiency of pressure recovery thus differs greatly depending on the type of valve, and the computed EOA using vena contracta gradients underestimates the downstream valve area and overestimates the severity of PPM for the BE valve (64).

Because of the low flow state (also known as pseudo-PPM), pressure recovery, and obesity, the occurrence and impact of PPM may have been overstated after TAVR (56). As said, PPM happens when the EOA of a prosthetic valve that is regularly functional is too tiny according to the patient's body size; however, the flow requirements for muscle are different from those for fat. The Valve Academic Research Consortium-2 consensus paper has therefore recommended using several indexed cutoffs to grade PPM severity, as noted previously (19). Numerous studies have exaggerated the prevalence of PPM and maybe understand its effects in patients with normal body weight because they failed to utilize varied cutoffs for PPM severity.

8. CONCLUSION

Transcatheter aortic valve replacement (TAVR) has a wider effective orifice area with better hemodynamics. TAVR using the Cribier-Edwards or Edwards Sapien valve was linked to lower trans-prosthetic gradients and greater EOAs early after the treatment, leading to a significant reduction in severe PPM at discharge and midterm follow-up. TAVR has a lower prevalence of moderate, severe and overall PPM than SAVR due to its superior hemodynamic function. Following SAVR, higher PPM levels have been associated with less complete left ventricular mass regression and quicker bioprosthetic valve deterioration.

9. PRACTICAL RECOMMENDATIONS

- The EOAi of the prosthesis must be anticipated before the procedure (either SAVR or TAVR) in order to avoid PPM. To forecast the individual patient's EOAi, reference tables of mean effective orifice area values obtained from a large number of echocardiographic measurements should be employed.
- PPM can be avoided in the setting of SAVR by additional surgical procedures, such as annular expansion, or other techniques, including TAVR, if the anticipated size and type of surgical prosthesis cannot be placed.
- PPM prevention for TAVR patients is a recent area focused on prediction of the EOAi, choosing the most suitable from hemodynamic point of view prosthesis f and procedural precautions. It is recommended to use self-expanding TAVR valves with a supra-annular design in patients having risk of PPM. Regular use of additional preventive measures, such as post-dilatation in the setting of a higher gradient during procedure or valve oversizing, is advised.

- Despite the available data, more evidence is needed on the impact of PPM on long-term survival after TAVR and SAVR. Therefore, there is a need to conduct high-quality clinical trials in this direction.

10. REFERENCES

1. Rahimtoola SH. The problem of valve prosthesis-patient mismatch. Circulation. 1978 Jul;58(1):20–4.
2. Bleiziffer S, Rudolph TK. Patient Prosthesis Mismatch After SAVR and TAVR. Front Cardiovasc Med. 2022 Mar 30;9:761917.
3. Wenn P, Zeltser R. Aortic Valve Disease. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 [cited 2023 May 3]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK542205/
4. Iung B, Vahanian A. Epidemiology of valvular heart disease in the adult. Nat Rev Cardiol. 2011 Mar;8(3):162–72.
5. The modern epidemiology of heart valve disease | Heart [Internet]. [cited 2023 May 3]. Available from: https://heart.bmj.com/content/102/1/75
6. Rapaport E. Natural history of aortic and mitral valve disease. Am J Cardiol. 1975 Feb 1;35(2):221–7.
7. Degenerative aortic stenosis | The BMJ [Internet]. [cited 2023 May 3]. Available from: https://www.bmj.com/content/336/7643/550
8. Pujari SH, Agasthi P. Aortic Stenosis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 [cited 2023 May 3]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK557628/
9. Sudden Death in Patients With Severe Aortic Stenosis: Observations From the CURRENT AS Registry | Journal of the American Heart Association [Internet]. [cited 2023 May 5]. Available from: https://www.ahajournals.org/doi/10.1161/JAHA.117.008397
10. Comprehensive update on the new indications for transcatheter aortic valve replacement in the latest 2017 European guidelines for the management of valvular heart disease | Open Heart [Internet]. [cited 2023 May 5]. Available from: https://openheart.bmj.com/content/5/1/e000753
11. 2021 ESC/EACTS Guidelines for the management of valvular heart disease | European Heart Journal | Oxford Academic [Internet]. [cited 2023 May 5]. Available from: https://academic.oup.com/eurheartj/article/43/7/561/6358470
12. Hahn RT, Leipsic J, Douglas PS, Jaber WA, Weissman NJ, Pibarot P, et al. Comprehensive Echocardiographic Assessment of Normal Transcatheter Valve Function. JACC Cardiovasc Imaging. 2019 Jan;12(1):25–34.
13. Timing of Valve Replacement in Aortic Stenosis | Circulation [Internet]. [cited 2023 May 5]. Available from: https://www.ahajournals.org/doi/10.1161/01.CIR.95.9.2241
14. 2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines | Circulation [Internet]. [cited 2023 May 5]. Available from: https://www.ahajournals.org/doi/10.1161/CIR.0000000000000923
15. Indications for valve replacement for high gradient aortic stenosis in adults - UpToDate [Internet]. [cited 2023 May 5]. Available from: https://www.uptodate.com/contents/indications-for-valve-replacement-for-high-gradient-aortic-stenosis-in-adults
16. Selection of Aortic Valve Prostheses: Contemporary Reappraisal of Mechanical Versus Biologic Valve Substitutes | Circulation [Internet]. [cited 2023 May 5]. Available from: https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.113.001681

17. Transcatheter valve-in-valve implantation in degenerated surgical aortic and mitral bioprosthesis: Current state and future perspectives - ScienceDirect [Internet]. [cited 2023 May 5]. Available from: https://www.sciencedirect.com/science/article/pii/S0033062021001080
18. Gillam LD, Koulogiannis KP, Marcoff L. Bioprosthetic Aortic Valve Deterioration. Circulation. 2018 Sep 4;138(10):986–8.
19. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document (VARC-2) - PubMed [Internet]. [cited 2023 May 5]. Available from: https://pubmed.ncbi.nlm.nih.gov/23026738/
20. Chen J, Lin Y, Kang B, Wang Z. Indexed effective orifice area is a significant predictor of higher mid- and long-term mortality rates following aortic valve replacement in patients with prosthesis-patient mismatch. Eur J Cardio-Thorac Surg Off J Eur Assoc Cardio-Thorac Surg. 2014 Feb;45(2):234–40.
21. Prosthesis-patient mismatch: definition, clinical impact, and prevention | Heart [Internet]. [cited 2023 May 5]. Available from: https://heart.bmj.com/content/92/8/1022
22. Fallon JM, DeSimone JP, Brennan JM, O'Brien S, Thibault DP, DiScipio AW, et al. The Incidence and Consequence of Prosthesis-Patient Mismatch After Surgical Aortic Valve Replacement. Ann Thorac Surg. 2018 Jul;106(1):14–22.
23. Surgical aortic valve replacement and patient-prosthesis mismatch: a meta-analysis of 108 182 patients - PubMed [Internet]. [cited 2023 May 17]. Available from: https://pubmed.ncbi.nlm.nih.gov/30657945/
24. Rayol SDC, Sá MPBO, Cavalcanti LRP, Saragiotto FAS, Diniz RGS, Sá FBCDAE, et al. Prosthesis-Patient Mismatch after Surgical Aortic Valve Replacement: Neither Uncommon nor Harmless. Braz J Cardiovasc Surg [Internet]. 2019 [cited 2023 May 5];34(3). Available from: https://bjcvs.org/pdf/3146/v34n3a16.pdf
25. Ternacle J, Pibarot P, Herrmann HC, Kodali S, Leipsic J, Blanke P, et al. Prosthesis-Patient Mismatch After Aortic Valve Replacement in the PARTNER 2 Trial and Registry. JACC Cardiovasc Interv. 2021 Jul 12;14(13):1466–77.
26. Dayan V, Vignolo G, Soca G, Paganini JJ, Brusich D, Pibarot P. Predictors and Outcomes of Prosthesis-Patient Mismatch After Aortic Valve Replacement. JACC Cardiovasc Imaging. 2016 Aug;9(8):924–33.
27. Mohty D, Boulogne C, Magne J, Pibarot P, Echahidi N, Cornu E, et al. Prevalence and Long-Term Outcome of Aortic Prosthesis–Patient Mismatch in Patients With Paradoxical Low-Flow Severe Aortic Stenosis. Circulation. 2014 Sep 9;130(11_suppl_1):S25–31.
28. Predictors and Clinical Impact of Prosthesis-Patient Mismatch After Self-Expandable TAVR in Small Annuli - ScienceDirect [Internet]. [cited 2023 May 5]. Available from: https://www.sciencedirect.com/science/article/pii/S1936879821005926
29. The impact of prosthesis-patient mismatch on long-term survival after aortic valve replacement: a systematic review and meta-analysis of 34 observational studies comprising 27 186 patients with 133 141 patient-years - PubMed [Internet]. [cited 2023 May 5]. Available from: https://pubmed.ncbi.nlm.nih.gov/22408037/
30. Bishop MA, Borsody K. Manougian. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 [cited 2023 May 5]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK564328/
31. Prosthesis–Patient Mismatch After Transcatheter Aortic Valve Implantation - The Annals of Thoracic Surgery [Internet]. [cited 2023 May 5]. Available from: https://www.annalsthoracicsurgery.org/article/S0003-4975(15)01956-6/fulltext

32. Unbehaun A, Pasic M, Drews T, Buz S, Dreysse S, Kukucka M, et al. New 29-mm balloon-expandable prosthesis for transcatheter aortic valve implantation in large annuli. Ann Thorac Surg. 2013 Jun;95(6):1982–90.
33. Bleiziffer S, Hettich I, Hutter A, Wagner A, Deutsch MA, Piazza N, et al. Incidence and impact of prosthesis-patient mismatch after transcatheter aortic valve implantation. J Heart Valve Dis. 2013 May;22(3):309–16.
34. Sherif MA, Abdel-Wahab M, Awad O, Geist V, El-Shahed G, Semmler R, et al. Early hemodynamic and neurohormonal response after transcatheter aortic valve implantation. Am Heart J. 2010 Nov;160(5):862–9.
35. Comparison of the Hemodynamic Performance of Percutaneous and Surgical Bioprostheses for the Treatment of Severe Aortic Stenosis - ScienceDirect [Internet]. [cited 2023 May 5]. Available from: https://www.sciencedirect.com/science/article/pii/S073510970900624X
36. Finkelstein A, Schwartz AL, Uretzky G, Banai S, Keren G, Kramer A, et al. Hemodynamic performance and outcome of percutaneous versus surgical stentless bioprostheses for aortic stenosis with anticipated patient-prosthesis mismatch. J Thorac Cardiovasc Surg. 2014 Jun;147(6):1892–9.
37. Giannini C, Petronio AS, Nardi C, De Carlo M, Guarracino F, Delle Donne MG, et al. Left ventricular reverse remodeling in percutaneous and surgical aortic bioprostheses: an echocardiographic study. J Am Soc Echocardiogr Off Publ Am Soc Echocardiogr. 2011 Jan;24(1):28–36.
38. Kamperidis V, van Rosendael PJ, de Weger A, Katsanos S, Regeer M, van der Kley F, et al. Surgical sutureless and transcatheter aortic valves: hemodynamic performance and clinical outcomes in propensity score-matched high-risk populations with severe aortic stenosis. JACC Cardiovasc Interv. 2015 Apr 27;8(5):670–7.
39. Pibarot P, Weissman NJ, Stewart WJ, Hahn RT, Lindman BR, McAndrew T, et al. Incidence and sequelae of prosthesis-patient mismatch in transcatheter versus surgical valve replacement in high-risk patients with severe aortic stenosis: a PARTNER trial cohort--a analysis. J Am Coll Cardiol. 2014 Sep 30;64(13):1323–34.
40. Ewe SH, Muratori M, Delgado V, Pepi M, Tamborini G, Fusini L, et al. Hemodynamic and clinical impact of prosthesis-patient mismatch after transcatheter aortic valve implantation. J Am Coll Cardiol. 2011 Oct 25;58(18):1910–8.
41. Kukucka M, Pasic M, Dreysse S, Mladenow A, Habazettl H, Hetzer R, et al. Patient-prosthesis mismatch after transapical aortic valve implantation: incidence and impact on survival. J Thorac Cardiovasc Surg. 2013 Feb;145(2):391–7.
42. Muñoz-García AJ, Muñoz-García M, Carrasco-Chinchilla F, Molina-Mora MJ, Rodríguez-Bailón I, Domínguez-Franco AJ, et al. Incidence and clinical outcome of prosthesis-patient mismatch after transcatheter aortic valve implantation with the CoreValve prosthesis. Int J Cardiol. 2013 Aug 10;167(3):1074–6.
43. Van Linden A, Kempfert J, Blumenstein J, Rastan A, Holzhey D, Lehmann S, et al. Prosthesis-patient mismatch after transcatheter aortic valve implantation using the Edwards SAPIEN™ prosthesis. Thorac Cardiovasc Surg. 2013 Aug;61(5):414–20.
44. Regazzoli D, Chiarito M, Cannata F, Pagnesi M, Miura M, Ziviello F, et al. Transcatheter Self-Expandable Valve Implantation for Aortic Stenosis in Small Aortic Annuli: The TAVI-SMALL Registry. JACC Cardiovasc Interv. 2020 Jan 27;13(2):196–206.
45. Abdelghani M, Mankerious N, Allali A, Landt M, Kaur J, Sulimov DS, et al. Bioprosthetic Valve Performance After Transcatheter Aortic Valve Replacement With Self-Expanding Versus Balloon-Expandable Valves in Large Versus Small Aortic Valve Annuli: Insights From the CHOICE Trial and the CHOICE-Extend Registry. JACC Cardiovasc Interv. 2018 Dec 24;11(24):2507–18.

46. Mauri V, Kim WK, Abumayyaleh M, Walther T, Moellmann H, Schaefer U, et al. Short-Term Outcome and Hemodynamic Performance of Next-Generation Self-Expanding Versus Balloon-Expandable Transcatheter Aortic Valves in Patients With Small Aortic Annulus: A Multicenter Propensity-Matched Comparison. Circ Cardiovasc Interv. 2017 Oct;10(10):e005013.
47. Schofer N, Deuschl F, Rübsamen N, Skibowski J, Seiffert M, Voigtländer L, et al. Prosthesis-patient mismatch after transcatheter aortic valve implantation: prevalence and prognostic impact with respect to baseline left ventricular function. EuroIntervention J Eur Collab Work Group Interv Cardiol Eur Soc Cardiol. 2019 Mar 20;14(16):1648–55.
48. Panoulas VF, Chandrasekhar J, Busi G, Ruparelia N, Zhang Z, Mehilli J, et al. Prevalence, predictors, and outcomes of patient prosthesis mismatch in women undergoing TAVI for severe aortic stenosis: Insights from the WIN-TAVI registry. Catheter Cardiovasc Interv Off J Soc Card Angiogr Interv. 2021 Feb 15;97(3):516–26.
49. Miyasaka M, Tada N, Taguri M, Kato S, Enta Y, Otomo T, et al. Incidence, Predictors, and Clinical Impact of Prosthesis-Patient Mismatch Following Transcatheter Aortic Valve Replacement in Asian Patients: The OCEAN-TAVI Registry. JACC Cardiovasc Interv. 2018 Apr 23;11(8):771–80.
50. Okuno T, Khan F, Asami M, Praz F, Heg D, Winkel MG, et al. Prosthesis-Patient Mismatch Following Transcatheter Aortic Valve Replacement With Supra-Annular and Intra-Annular Prostheses. JACC Cardiovasc Interv. 2019 Nov 11;12(21):2173–82.
51. https://fyra.io. Current TAVR Devices [Internet]. Cardiac Interventions Today. Bryn Mawr Communications; [cited 2023 May 5]. Available from: https://citoday.com/articles/2017-mar-apr/current-tavr-devices
52. Prosthesis–Patient Mismatch in Patients Undergoing Transcatheter Aortic Valve Replacement: From the STS/ACC TVT Registry - ScienceDirect [Internet]. [cited 2023 May 5]. Available from: https://www.sciencedirect.com/science/article/pii/S0735109718382871
53. Jilaihawi H, Chin D, Spyt T, Jeilan M, Vasa-Nicotera M, Bence J, et al. Prosthesis-patient mismatch after transcatheter aortic valve implantation with the Medtronic-Corevalve bioprosthesis. Eur Heart J. 2010 Apr 1;31(7):857–64.
54. Bioprosthetic Valve Fracture Improves the Hemodynamic Results of Valve-in-Valve Transcatheter Aortic Valve Replacement | Circulation: Cardiovascular Interventions [Internet]. [cited 2023 May 5]. Available from: https://www.ahajournals.org/doi/10.1161/CIRCINTERVENTIONS.117.005216
55. Stamou SC, Chen K, James TM, Rothenberg M, Kapila A, Faber C, et al. Predictors and outcomes of patient-prosthesis mismatch after transcatheter aortic valve replacement. J Card Surg. 2020 Feb;35(2):360–6.
56. Pibarot P, Clavel MA. Prosthesis-Patient Mismatch After Transcatheter Aortic Valve Replacement: It Is Neither Rare Nor Benign. J Am Coll Cardiol. 2018 Dec 4;72(22):2712–6.
57. Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patients - PubMed [Internet]. [cited 2023 May 5]. Available from: https://pubmed.ncbi.nlm.nih.gov/30883058/
58. Popma JJ, Deeb GM, Yakubov SJ, Mumtaz M, Gada H, O'Hair D, et al. Transcatheter Aortic-Valve Replacement with a Self-Expanding Valve in Low-Risk Patients. N Engl J Med. 2019 May 2;380(18):1706–15.
59. Patient-prosthesis mismatch in patients undergoing bioprosthetic aortic valve implantation increases risk of reoperation for structural valve deterioration - PubMed [Internet]. [cited 2023 May 5]. Available from: https://pubmed.ncbi.nlm.nih.gov/24773571/
60. Bahlmann E, Cramariuc D, Gerdts E, Gohlke-Baerwolf C, Nienaber CA, Eriksen E, et al. Impact of pressure recovery on echocardiographic assessment of asymptomatic aortic stenosis: a SEAS substudy. JACC Cardiovasc Imaging. 2010 Jun;3(6):555–62.
61. Lancellotti P, Pibarot P, Chambers J, Edvardsen T, Delgado V, Dulgheru R, et al. Recommendations for the imaging assessment of prosthetic heart valves: a report from the European

Association of Cardiovascular Imaging endorsed by the Chinese Society of Echocardiography, the Inter-American Society of Echocardiography, and the Brazilian Department of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging. 2016 Jun;17(6):589–90.
62. Is pressure recovery an important cause of "Doppler aortic stenosis" with no gradient at cardiac catheterisation? | Heart [Internet]. [cited 2023 May 5]. Available from: https://heart.bmj.com/content/76/5/381
63. Hatoum H, Hahn RT, Lilly S, Dasi LP. Differences in Pressure Recovery Between Balloon Expandable and Self-expandable Transcatheter Aortic Valves. Ann Biomed Eng. 2020 Feb;48(2):860–7.
64. Prosthesis–patient mismatch in high-risk patients with severe aortic stenosis: A randomized trial of a self-expanding prosthesis - ScienceDirect [Internet]. [cited 2023 May 5]. Available from: https://www.sciencedirect.com/science/article/pii/S0022522315021339