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# Current Management of Severe Aortic Stenosis in Intermediate Risk Patients

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and Juan Bustamante-Munguira*

## Abstract

The management of aortic stenosis has improved and evolved to a reduction in surgical aggression. Nowadays, patients with intermediate risk are in the frontier of transcatheter aortic valve implantation (TAVI) and aortic valve replacement (AVR). Our goal is to update the treatment of severe aortic stenosis in those patients through a research of the recent literature, in order to analyze the current treatment options and their results. This cohort of patients has two therapeutic options, surgical AVR or TAVI, and the decision pathway goes through the accurate interpretation of all data by the Heart Team. It is clear that both strategies will be the cornerstones in the modern AVR era, but the situations in which to apply each strategy have not yet been clearly delineated. More studies are needed to compare TAVI and miniAVR in low- and intermediate-risk patients. However, the current practice guidelines give a good pathway to choose the adequate therapeutic option in each individual case.

**Keywords:** aortic stenosis, aortic stenosis surgery, aortic stenosis management, aortic stenosis open heart surgery, aortic stenosis treatment, aortic stenosis valve replacement, TAVR procedure, TAVR approaches, TAVR access sites, TAVR, TAVI

## 1. Introduction

Aortic stenosis is the most frequent valve disease leading to intervention in developed countries, either surgery or catheter, and its incidence increases due to the aging population [1].

The management of aortic stenosis has improved and evolved to a reduction in surgical aggression. Nowadays, the patients with intermediate risk are in the frontier of transcatheter aortic valve implantation (TAVI) and aortic valve replacement (AVR) and more than ever, the heart team has to be more accurate to choose between the different treatment options available, making the decision pathway more complex than a few year before. Our goal is to update the treatment of severe aortic stenosis in those patients where risk assessment scales indicate an intermediate risk. Here, we analyze the current treatment options and their results.

## 2. Etiology and natural history

Nowadays, degenerative calcific AS is the most common cause of AS in adults at older ages and represents the leading cause for aortic valve intervention [2–4]. In the other hand, bicuspid aortic valve affects 2% of the population and represents the most common indication for intervention at younger patients [5].

The development of symptoms identifies a paramount point in the natural history of AS, and the interval from the onset of symptoms to the time of death is approximately 2 years in patients with heart failure, 3 years in those with syncope, and 5 years in those with angina, with a high risk of sudden death [6].

## 3. Evaluation and severity classification of aortic stenosis

Careful exploration for the presence of symptoms (shortness of breath on exertion, angina, dizziness, or syncope) is very important for right patient management. The characteristic systolic murmur draws attention and guides further diagnostic work in the right direction.

**Echocardiography** is the key diagnostic tool [7]. It discriminates the degree of valve calcification, LV function, and wall thickness; helps to identify other associated valve diseases or aortic pathology; and provides prognostic information. The severity of the stenotic lesion can be defined with Doppler echocardiographic measurements. Transoesophageal echocardiography (TOE) provides additional evaluation of concomitant mitral valve abnormalities, and become useful when transthoracic visualization is poor [8]. TOE has gained importance in the assessment and intraprocedure guidance and after TAVI or surgical interventions.

Three-dimensional TOE offers a more detailed examination of valve anatomy than two-dimensional echocardiography and is useful for the assessment and planning of complex valve problems [8]. AS severity could be graded on the basis of a variety of hemodynamic and natural history data as shown in **Table 1**.

Multislice computed tomography (MSCT) and cardiac magnetic resonance (CMR) give additional data on the assessment of the ascending aorta when it is enlarged or to quantifying the valve area, coronary calcification, size and shape of the aortic valve annulus, and its distance to the coronary ostia, which aids in evaluation and prognosis. It is essential to evaluate the feasibility of the various access routes for TAVI, as this provides information on minimal luminal diameters, atherosclerotic plaque burden, the presence of aneurysms or thrombi, etc. [8]. MSCT plays an important role in the diagnostic work-up before transcatheter aortic valve implantation. The risk of radiation exposure—and of renal failure due to contrast injection—should, however, be taken into consideration.

Peak velocity (m/s)	$\geq 4$
Mean gradient (mmHg)	$\geq 40$
Indexed AVA ( $\text{cm}^2/\text{m}^2$ )	$< 0.6$
AVA ( $\text{cm}^2$ )	$< 1$
Velocity ratio	$< 0.25$

*Based on the recommendations on the echocardiographic assessment of aortic valve stenosis: a focused update from the European Association of Cardiovascular Imaging and the American Society of Echocardiography [9].*

**Table 1.**

*Severe aortic stenosis measurement by echocardiography. The definitions apply only in the presence of normal flow conditions.*

In patients with inadequate echocardiographic quality or discrepant results, CMR should be used to assess the severity of valvular lesions and to assess ventricular volumes and systolic function [8].

In physically active patients, an **exercise testing** could be recommended for unmasking symptoms and for risk stratification of asymptomatic patients [10]. Also, exercise stress echocardiography may give prognostic information in asymptomatic severe aortic stenosis [10, 11]. In some patients, it may be necessary to proceed with cardiac catheterization and coronary angiography at the time of initial evaluation [7].

**Biomarkers.** Several studies [12–15] report that biomarkers such as B-type natriuretic peptide (BNP) have been shown to be related to functional class and prognosis, particularly in AS and MR. Natriuretic peptides have been shown to predict symptom-free survival and outcome in normal- and low-flow severe AS and may be useful in asymptomatic patients, helping to discriminate those patients who can benefit from an early intervention [13–15]. In fact, in the last ESC/EACTS guidelines for the management of valvular heart disease, natriuretic peptides may be of value for risk stratification and timing of intervention, particularly in asymptomatic patients (“markedly elevated BNP levels (>threefold age- and sex-corrected normal range) confirmed by repeated measurements without other explanations”) [8].

#### 4. Indications for intervention

Here, we have to take notice of the patient’s status in order to choose the type of intervention and the correct timing of it. **Early valve intervention should be strongly recommended in all symptomatic patients with severe AS, because it is the only effective treatment.** “As long as the mean gradient remains >40 mmHg, there is virtually no lower ejection fraction limit for intervention, whether surgery or TAVI” [8].

However, patients with severe comorbidities indicating a survival of <1 year and patients in whom is unlikely that the intervention will improve quality of life or survival should be excluded from further interventions.

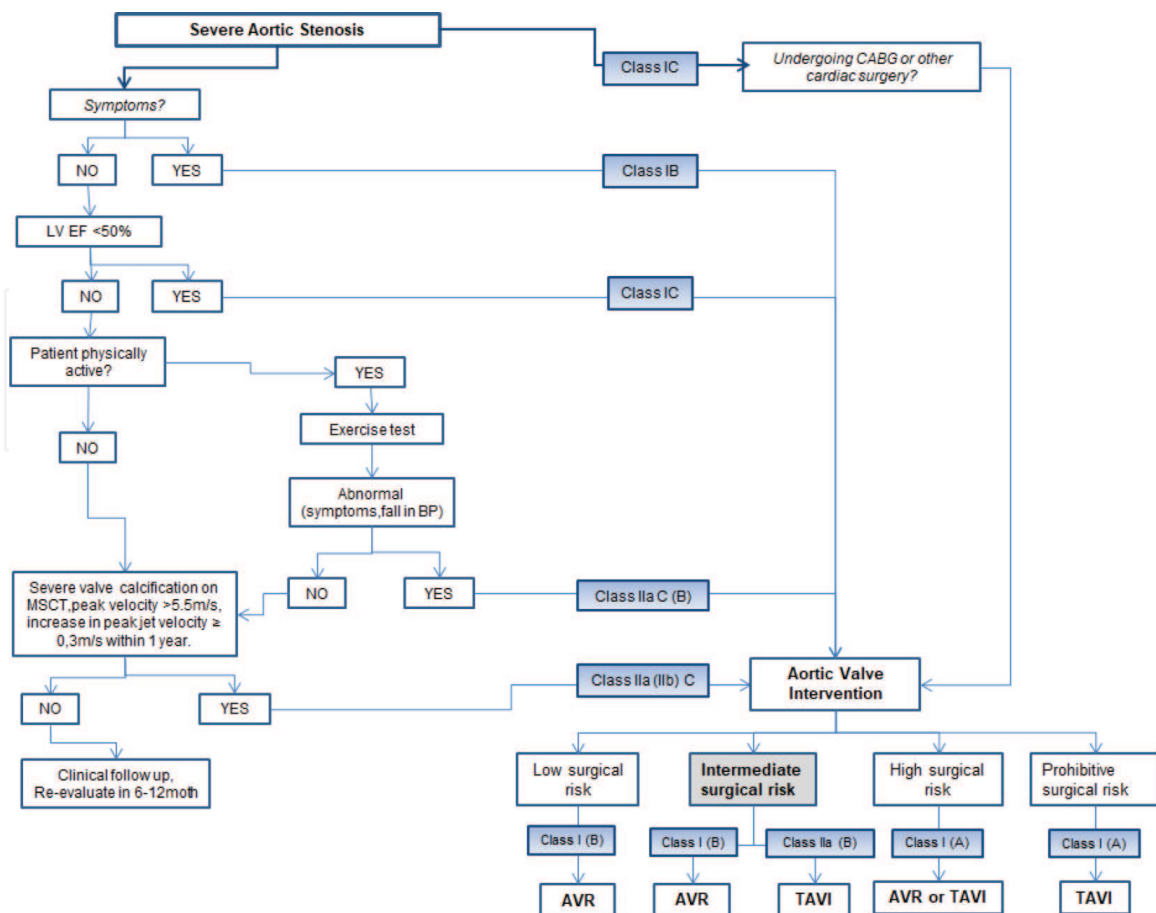
**Asymptomatic patients.** There is some disagreement about the optimal timing of surgery in asymptomatic patients, and the decision to operate on this kind of patient requires careful weighing of the benefits against the risks.

*The available studies do not provide convincing data to support the general recommendation of early SAVR, even in patients with asymptomatic and very severe aortic stenosis, and TAVI is not recommended in asymptomatic patients* [7, 8]. However, subclinical adverse remodeling can precede the development of symptoms and LV dysfunction [16]. Musa et al. performed cardiac magnetic resonance (CMR) in 674 patients who had severe AS and were scheduled for surgical or transcatheter AVR. Myocardial fibrosis (scar) demonstrated by late gadolinium enhancement (LGE) on CMR was common (51%). In a median follow-up of 3.6 years (interquartile range, 2.6–5.9 years), 21.5% of patients had died. In multivariable analysis, scar (LGE positivity) was independently associated with all-cause and cardiovascular mortality (hazard ratios, 2.39 and 3.14, respectively). The elevated mortality was independent of whether the patients underwent surgical or transcatheter AVR and was similar in patients with infarct and noninfarct scar patterns. These findings raise the possibility that adverse remodeling has irreversible effects before symptoms develop: We may be waiting too long to treat these patients. The authors suggest that physicians might use scar burden to optimize the timing of intervention, a hypothesis currently being evaluated in a randomized trial (EVOLVED-AS) [16].

**Early elective surgery is indicated in asymptomatic patients with [8]:**

- depressed LV function not due to other causes and in patients who develop symptoms during exercise testing
- abnormal exercise test showing symptoms on exercise clearly related to aortic stenosis
- abnormal exercise test showing a decrease in blood pressure below baseline
- predictors of symptom development and adverse outcomes: clinical characteristics (older age, presence of atherosclerotic risk factors), echocardiographic parameters (valve calcification, peak aortic jet velocity, LVEF, rate of hemodynamic progression, increase in mean gradient >20 mmHg with exercise, excessive LV hypertrophy, abnormal longitudinal LV function, and pulmonary hypertension), and biomarkers (>threefold age- and sex-corrected normal range).
- When early elective surgery is considered in patients with normal exercise performance because of the presence of such outcome predictors, the operative risk should be low. In patients without predictive factors, watchful waiting appears safe and early surgery is unlikely to be beneficial.

An update of proposed management strategy for patients with severe AS by Leal et al. [17] is shown in **Figure 1**, based on the ESC/EACTS and ACC/ AHA guidelines on the management of valvular heart disease [8, 18].



**Figure 1.** Management of severe aortic stenosis [8, 17, 18]. ACC/AHA recommendations have been shown in parentheses.

## 5. Risk stratification

Risk stratification applies to any sort of intervention and is required for weighing the risk of intervention against the expected natural history of VHD as a basis for decision making [8]. Nowadays, the STS score and logistic EuroSCORE II are the most commonly used. **The EuroSCORE I** overestimates operative mortality and its calibration of risk is poor, and *it should no longer be used to guide decision making*, but it has been used in many TAVI studies/registries and may still be useful to identify the subgroups of patients for decision between intervention modalities and to predict 1-year mortality [8]. **The EuroSCORE II** and the **Society of Thoracic Surgeons (STS)** scores more accurately discriminate high- and low-risk surgical patients and show better calibration to predict postoperative outcome after valvular surgery [8]. Current models do not include some risk factors that may be particularly important in the prediction of outcomes, including frailty, pulmonary hypertension (PH), porcelain aorta, and the presence of hepatic dysfunction.

New scores have been developed to estimate the risk of 30-day mortality in patients undergoing TAVI, with better accuracy and discrimination, but not without certain limitations by a lack of consideration of frailty, disability, and cognitive function [19]. Examples of those are: FRANCE-2 risk score [20], the STS/ACC TVT registry predictive model [21], and the TAVR risk score based on data from the German aortic valve registry [22]. A new tool based on the STS/ACC TVT Registry™ is an application for from the STS/ACC TVT Registry™ an application for mobile devices and web, call “**TAVR in-hospital mortality Risk app**” [23], in order to inform physicians of the estimated risk of in-hospital mortality.

It remains essential not to rely on a single risk score figure when assessing patients or to determine unconditionally the indication and type of intervention.

*The role of the heart team* is essential to take all of these data into account and adopt a final decision on the best treatment strategy. It is important to take into account patient's life expectancy, expected quality of life, and patient preference, as well as local resources, in order to do a proper planning of intervention. There is a growing interest in the assessment of frailty, an overall marker of impairment of functional, cognitive, and nutritional status. Frailty is associated with increased morbidity and mortality after surgery and TAVI [24].

Finally, the patient and family should be thoroughly informed and assisted in their decision on the best treatment option.

Actual **AHA/ACC guideline** classifies patients with severe AS into *four global risk categories*: [19].

1. Low risk: STS <4% with no frailty, no comorbidity, and no procedure-specific impediments.
2. **Intermediate risk: STS 4-8%** with no more than mild frailty or one major organ system compromise not to be improved postoperatively and minimal procedure-specific impediments.
3. High risk: STS >8%, or moderate-severe frailty, no more than two major organ systems compromise not to be improved postoperatively, or a possible procedure-specific impediment.
4. Prohibitive risk: preoperative risk of mortality and morbidity >50% at 1 year or ≥three major organ systems compromises not to be improved postoperatively or severe frailty or severe procedure-specific impediments.

Thus, the current **ESC/EACTS guidelines** for the management of valvular heart disease [8] consider *two global risk categories*:

1. Low surgical risk (STS or EuroSCORE II < 4% or logistic EuroSCORE I < 10% and no other risk factors not included in these scores, such as frailty, porcelain aorta, and sequelae of chest radiation).
2. Increased surgical risk (STS or EuroSCORE II >4% or logistic EuroSCORE I > 10% or other risk factors not included in these scores such as frailty, porcelain aorta, and sequelae of chest radiation).

A resume of risk categories is shown in **Table 2**.

Risk category	Risk assessment tool		
	STS score	EuroScore II	EuroScore
Low risk	<4%	<4%	<10%
Intermediate risk	4–8%	>4–7%*	>10–20%*
High risk	>8%	>7*	>20%*
Prohibitive risk	>50%		

*\*ESC/EACTS guidelines consider two categories (low and increased surgical risk).  
Based on 2017 ACC Expert Consensus Decision Pathway for Transcatheter Aortic Valve Replacement in the Management of Adults with Aortic Stenosis and the 2017 ESC/EACTS Guidelines for the management of valvular heart disease [8, 19, 25].*

**Table 2.**  
*Risk assessment tools.*

In conclusion, the decision to proceed with AVR or TAVI requires careful weighing of the potential for improved symptoms and survival and the morbidity and mortality of surgery and should be made by the heart team according to the individual patient characteristics. Checklist for choice of therapeutic intervention option (**Table A1**) could be consulted and printed from the additional material, in order to provide aspects that should be considered for the individual decision, based on the current recommendation of de ESC/EACTS guidelines.

## 6. Interventional therapeutic options

### 6.1 Surgical approach

#### 6.1.1 Conventional AVR

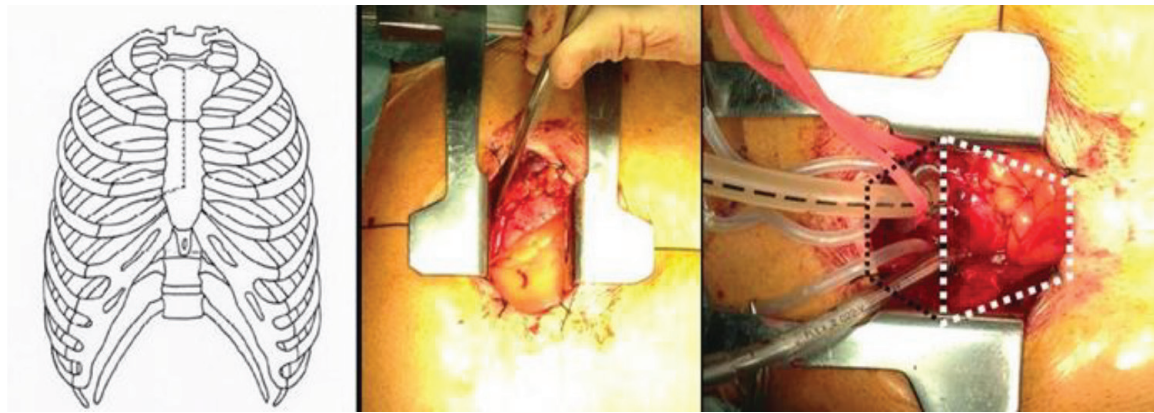
The conventional approach to AVR consists of a mid-line incision and full sternotomy, which provide a complete and comfortable access to the heart. Since it was first successfully carried out by Harken and Starr in 1960 [26, 27], there has been a continuous innovation in prosthetic technology and surgical techniques. All these collective efforts have resulted in improvements in both operative and long-term results [17]. Regardless of surgical approach, elected AVR is the gold standard for the treatment of severe AS. Several studies have shown short- and long-term outcomes,

as well as improved quality of life. Operative outcomes following AVR were still improving in the past decade. Wu et al. [28], determined the economic value of the additional life given to patients undergoing AVR, and concluded that AVR is cost-effective for all ages, and still worthwhile in octogenarian and nonagenarian patients.

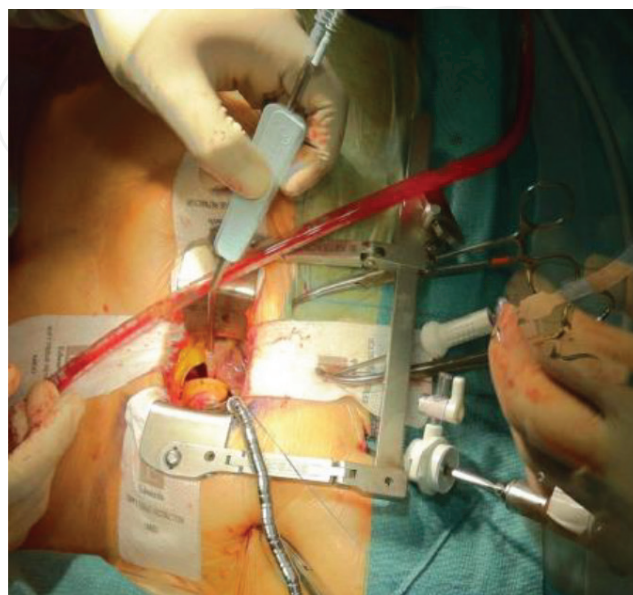
### 6.1.2 Minimally invasive surgical (MIS) approaches

Minimally invasive surgery aims to minimize the degree of surgical intrusiveness. Currently, there are several surgical approaches. The partial sternotomy and right anterior minithoracotomy are the most frequently used incisions for a minimally invasive approach to the aortic valve. The choice of interventional approach depends on the patient's anatomy as observed in preoperative imaging studies such as CT.

The “J” incision is the most widely used approach among the partial upper hemisternotomy approach (**Figure 2**). **Figure 3** shows the access view through right anterior minithoracotomy.



**Figure 2.**  
*Partial upper hemisternotomy approach. Operative field distribution from surgeon view [17].*



**Figure 3.**  
*Right anterior thoracotomy through 2 or 3° intercostal space [17].*



### *6.1.2.1 Advantages and disadvantages of MIS approaches in aortic stenosis*

Benefits have been observed in certain aspects such as:

- reduction in bleeding and use of hemoderivatives
- reduction in the pain perceived by the patient, which results in reduced consumption of analgesic [29–31]
- less respiratory complications such as atelectasis by maintaining the integrity of the thorax [32]
- better esthetic results, due to the reduced size of the surgical incisions and their relocation to less visible areas [33]
- reduction of the surgical wound infections [34]
- reduction on duration of hospitalization and time spent in intensive care units, which results on less expensive cost of the process.

A certain consensus exists around the benefits mentioned above. There is also a question of the impact of MIS on duration of surgery. There is disparity in the results found in the literature. Once the learning curve has been overcome, these times tend to equal out, and there is no significant difference to be observed between the different approaches.

### *6.1.3 Rapid deployment prostheses*

Their use in association with MIS approaches, providing a reduction in surgical aggression in addition to the reduction in ECC and aortic clamping time. These designs have the common feature of being expandable, anchoring themselves to the aortic ring in a similar way to the devices used in TAVI. To date, there are two commercially available models: Perceval (LivaNova) and Intuity (Edwards Lifesciences). Those prostheses differ from each other in a few characteristics.

- **Perceval** (LivaNova): it is useful on patients in which a reduction in surgery time may have a paramount impact, or those where it is necessary to carry out mixed procedures [35, 36]. A recent multicenter study reports a reduction on mean crossclamp and cardiopulmonary bypass times, and a significant improvement in clinical status was observed postoperatively in the majority of patients [37]. The Perceval valve implantation could be easily performed by offering a significant reduction in crossclamping and CPB times compared with both the traditional valve prostheses and the other sutureless prostheses available on the market, even when performed via a minimally invasive approach [37]. It remains important for the continuation of the patient's follow-up, in order to provide further assessment of long-term valve performance [37].
- **Intuity** (Edwards Lifesciences): it is made by the conjunction between the Edwards Perimount bioprosthesis, the clinical and hemodynamic results of which are widely known, and the experience in the development of the Sapien transcatheter prosthesis. The mode of implantation for this prosthesis

allows the aortic clamping and extracorporeal circulation times to be reduced. Reports of early outcomes have shown an important reduction in aortic crossclamp and cardiopulmonary bypass (CPB) [38, 39]. These findings were confirmed in both the European TRITON [40] and the US TRANSFORM trials [41]. Even more important, these times were reduced significantly in combined cardiac procedures [38].

#### *6.1.4 Transcatheter aortic valve implantation (TAVI)*

TAVI was developed as an alternative to AVR in the very or extremely high-risk patient population, and its first implantation in man was performed by Cribier [42] in 2002. Since then, there has been a nonstop development of less invasive strategies with lower mortality, lower morbidity, and less invasiveness [43].

##### *6.1.4.1 Implantation techniques*

TAVI is currently carried out using two main approaches, **transfemoral** and **transapical**. If this is not feasible, then the other two main approaches could be used namely trans-axillary artery or transaortic approaches. It is, therefore, highly recommended to perform an adequate preoperative assessment of the degree of peripheral arterial disease through imaging studies such as CT.

##### *6.1.4.2 TAVI results*

The results of the PARTNER I Cohort A trial also have important implications. The primary endpoint of the trial was met, with TAVI found not to be inferior to aortic valve replacement for all-cause mortality at 1 year. Death at 30 days was lower than expected in both arms of the trial: TAVI mortality (3.4%) was the lowest reported in any series, despite an early generation device and limited previous operator experience. Aortic valve replacement mortality (6.5%) was lower than the expected operative mortality (11.8%). On 2015, the 5-year follow-up result of the PARTNER I trial was published [44]; they screened 3105 patients, of whom 699 were enrolled (348 assigned to TAVR, 351 assigned to SAVR). At 5 years, risk of death was 67.8% in the TAVR group compared with 62.4% in the SAVR group (hazard ratio 1.04, 95% CI 0.86–1.24;  $p = 0.76$ ). They recorded no structural valve deterioration requiring surgical valve replacement in either group. Moderate or severe aortic regurgitation occurred in 40 (14%) of 280 patients in the TAVR group and two (1%) of 228 in the SAVR group ( $p < 0.0001$ ), and was associated with the increased 5-year risk of mortality in the TAVR group [44].

## **7. Intermediate risk patients: who are they? And how do we have to manage them?**

As we described before, currently AHA/ACC guideline for the management of patients with valvular heart disease [7, 19] defines the intermediate-risk patients as those who has an STS 4–8% with no more than mild frailty or one major organ system compromise not to be improved postoperatively and minimal procedure-specific impediments. In the other hand, the European guidelines define such patient as at “increased surgical risk” (STS or EuroSCORE II  $>4\%$  or logistic EuroSCORE I  $> 10\%$  or other risk factors not included in these scores such as frailty, porcelain aorta, and sequelae of chest radiation) [8].

***This cohort of patients has two therapeutic options, surgical AVR or TAVI, and the decision pathway goes through the accurate interpretation of all data by the Heart Team.***

Nowadays, increased operator experience and enhanced transcatheter valve systems have led to a worldwide trend to use TAVI in patients who are at low or intermediate risk [45]. This tendency has been evaluated in small observational studies, but since most patients who are currently recommended for surgery are at low or intermediate risk, the expansion of the use of TAVI demands more rigorous clinical-trial validation [46]. The intermediate-surgical-risk trials were approved comparing TAVI to surgery, with the balloon-expandable SAPIEN XT valve (PARTNER 2 trial) and the self-expandable CoreValve (SURgical Replacement and Transcatheter Aortic Valve Implantation trial (SURTAVI trial)) [46, 47].

**The PARTNER 2 trial** [46] was a multicenter, randomized control trial conducted, which enrolled 2032 patients with severe symptomatic aortic stenosis and intermediate-surgical-risk, and randomized them in a 1:1 fashion across the TAVI arm and the surgical arm [48]. After 2 years, the all-cause mortality or disabling stroke was similar in the TAVI group and the SAVR group (19.3 vs. 21.1%,  $p = 0.33$  and  $p = 0.001$  for **noninferiority**). In the transfemoral access cohort, TAVI demonstrated a lower mortality and disabling stroke (hazard ratio = 0.79; 95% CI = 0.62–1.00;  $p = 0.05$ ). TAVI resulted in larger aortic valve areas, lower rates of acute kidney injury, severe bleeding, and new-onset atrial fibrillation; SAVR resulted in fewer major vascular complications and less paravalvular aortic leak [49]. As a result of the PARTNER 2 trial, the current guideline from the American Heart Association and American College of Cardiology recommended TAVI as an alternative to surgery in patients at intermediate surgical risk [18, 48].

**The SURTAVI trial** [47] analyzes the self-expanding CoreValve in intermediate-risk patients and was a randomized, multicenter control trial, which recruited a total of 1746 patients [46]. The combined primary endpoint (all-cause mortality or disabling stroke) at 24 months was 12.6% in the TAVI group and 14.0% in the surgery group. Residual aortic regurgitation and need for pacemaker implantation were more frequent among TAVI patients. In the other hand, SAVR was associated with the higher rates of atrial fibrillation, acute kidney injury, and transfusion requirements. The TAVI resulted in lower mean gradients and larger aortic valve areas than surgery did. Structural valve deterioration at 24 months did not occur in either group. SURTAVI revealed that CoreValve TAVI was not inferior to surgery in patients with intermediate surgical risk [49].

**Bicuspid aortic valves:** the extreme and asymmetrical calcification noted with bicuspid valves can prevent adequate expansion of the valve frame of TAVI valves, affecting valve hemodynamics, and leading to higher aortic valve gradients and more paravalvular leaks [48].

**Prostheses thrombosis:** the Portico Re-sheathable Transcatheter Aortic Valve System U.S. Investigational Device Exemption (PORTICO IDE) study evaluates TAVI with either a Portico valve (St. Jude Medical) or a commercially available valve. Computed tomography (CT) was performed in a subgroup of patients to assess the stent frame of the implanted valve. A finding of reduced leaflet motion on CT in a patient who had had a stroke after TAVI and similar findings in an asymptomatic patient at one clinical site led to a closer look of this observation. Additional CT review by the core laboratory revealed that this finding was not isolated, which prompted a more extensive investigation. This findings encourage to create two registries to evaluate the prostheses thrombosis (SAVORY registry and RESOLVE registry), and find out that therapeutic anticoagulation with warfarin,

but not therapy with antiplatelet drugs, prevented and effectively treated this phenomenon. Better characterization of this observation is needed to determine its frequency and evaluate its clinical effect [50].

**Durability:** intermediate surgical-risk patients are expected to survive longer after TAVI when compared to higher-risk patients; the broad application of TAVI in low-risk patients should be limited until in vivo durability results are available for the TAVI prostheses [48]. While structural valve deterioration in surgically replaced valves has been thoroughly investigated, long-term follow-up data for TAVI valves implanted in patients remain sparse [48].

## 8. Conclusions

Nowadays, the patients with intermediate risk are in the frontier of TAVI and surgical AVR, and more than ever, the heart team has to be more accurate to choose between the different treatment options available. Current expansion of TAVI into lower surgical risk patients encourages the need to remain cautious about unbridled expansion into those patients, as many questions remain about valve durability, leaflet thrombosis, and higher rates of paravalvular leak and permanent pacemakers [48]. Meanwhile, the surgical approach has improved and evolved to a reduction in surgical aggression. TAVI and minimally invasive aortic valve replacement [51] have become alternatives to surgical aortic valve replacement via median sternotomy (SAVR) to treat severe aortic stenosis (AS). Despite increased interest and utilization, few studies have directly compared TAVI and miniAVR. MiniAVR maintains potential advantages over SAVR, including the implantation of a durable prosthesis and low rates of perioperative myocardial infarction and paravalvular leak. It is associated with longer aortic crossclamp and cardiopulmonary bypass (CPB) times; however, the use of rapid deployment valves can circumvent this. Studies comparing TAVI and miniAVR demonstrate decreased postoperative mortality, valvular regurgitation, and incidence of stroke in the miniAVR cohorts [51].

From economic point of view, it is clear that for high-risk operable patients, TAVI is currently a more expensive therapy and probably a less effective alternative to surgical AVR, with an incremental cost-effectiveness ratio (ICER) that may be acceptable for high-income countries, but definitely not for the moderate- or low-income countries [52]. When use of TAVI is extended to include a larger number of moderate- to low-risk patients suitable for AVR, overall economic results become less favorable. When manufacturers reduce the exuberant cost of the valve and its accessories, TAVI may become the predominant therapy for patients with severe aortic stenosis. [52].

Finally, it is clear that both strategies will be the cornerstones in the modern AVR era, but the situations in which to apply each strategy have not yet been clearly delineated. More studies are needed to compare TAVI and miniAVR in low- and intermediate-risk patients. However, the current practice guidelines give a good pathway to choose the adequate therapeutic option in each individual case.

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## Appendix

	Favor TAVI	Patient	Favor AVR	Patient
<i>Clinical characteristic</i>				
STS/EuroScore II < 4% (EuroScore I < 10%)			+	
STS/EuroScore II > 4% (EuroScore I > 10%)	+			
Severe comorbidities	+			
Age <75 years			+	
Age >75 years	+			
Previous cardiac surgery	+			
Frailty	+			
Restricted mobility	+			
Suspicion of Endocarditis			+	
<i>Anatomical and technical aspects</i>				
Favorable access for transfemoral TAVI	+			
Unfavorable access for TAVI			+	
Sequelae of chest radiation	+			
Porcelain aorta	+			
Pervious and permeable CABG	+			
Expected patient-prosthesis mismatch	+			
Severe chest deformation	+			
Short distance between coronary ostia and aortic valve annulus			+	
Aortic root morphology unfavorable for TAVI (Bicuspid valve, severe calcification)			+	
Undergoing CABG or another cardiac surgery			+	

*Based on 2017 ESC/EACTS guidelines for the management of valvular heart disease [8].*

**Table A1.**  
*Checklist for choice of therapeutic intervention option.*

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