

I would like to highlight the paper by Salinas et al. because it provides a comprehensive and exhaustive review on the state of the art of transcatheter aortic valve implantation (TAVI). During the last decade TAVI has revolutionised the cardiovascular field and currently represents a well-established treatment strategy for selected 'high-risk' patients with severe aortic stenosis. Now the burning question is "Where to go from here?" as, based on the excellent results currently obtained in clinical practice, the indications of this exciting procedure may be rapidly expanding.

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## STATE OF THE ART OF AORTIC VALVE IMPLANTATION: INDICATIONS, OUTCOMES, AND CONTROVERSIES

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### ABSTRACT

During the last decade, transcatheter aortic valve implantation (TAVI) has become a revolution in the treatment of high-risk severe aortic stenosis (AS). Current guidelines provide a Class I indication for TAVI in inoperable AS and Class IIa indication for TAVI as an alternative to surgical repair in high-risk patients. A large amount of retrospective, prospective, and randomised data has been published covering almost every angle of the procedure. Improved patient evaluation and selection, new devices, and technical refinements will reduce procedural complications and improve long-term outcomes. With a growing elderly population segment in the Western countries, the procedure has a bright perspective. The purpose of this review is to summarise the state of the art of TAVI procedures, including current indications, and describe procedural characteristics, as well as short and long-term outcomes. Controversial issues such as paravalvular regurgitation and stroke are discussed, as well as off-label indications. A shift towards intermediate risk AS patients, approval of some of the off-label indications, and device versus device competition are some of the future directions of the technique.

**Keywords:** Transcatheter aortic valve implantation, transcatheter aortic valve replacement, transcatheter valve, aortic valve stenosis, aortic stenosis, review.

### INTRODUCTION

Senile or calcified aortic stenosis (AS) is the end-stage of a degenerative-inflammatory process with risk factors and physiopathology that, while not completely understood, is somewhat similar to atherosclerosis.<sup>1</sup> After a long asymptomatic period, when AS becomes haemodynamically

severe and symptoms appear, the mortality suddenly rises if a valve replacement is not performed.<sup>2,3</sup> Several surgical techniques competed in the 60<sup>th</sup> and 70<sup>th</sup> decades (valvotomy, valve replacement with homograft) but eventually, surgical aortic valve replacement (SAVR) with a mechanical or biological prosthesis became the standard of treatment.<sup>4,5</sup> Although no randomised

or systematic trials were performed, SAVR showed a clear improved survival compared to non-operated controls.<sup>6,7</sup> SAVR procedures increased along with the ageing of the population to become the most frequent valvular heart surgery in adults today.<sup>8</sup> However, almost one-in-three SAVR candidates were not eventually operated on due to surgical contraindications, advanced age, and/or comorbidities.<sup>9,10</sup> Initially designed to overcome this treatment gap in symptomatic severe AS, from the first-in-man implantation in 2002, transcatheter aortic valve implantation (TAVI) has become a revolution in the approach to valvular heart disease.<sup>11</sup> A huge amount of retrospective, prospective, and randomised data has been published in the last decade, covering almost any angle of the procedure, and finally finding a place in the American and European Guidelines 10 years later.<sup>12,13</sup> At this moment, >125,000 TAVI implants have been performed worldwide, and the number of procedures approximately duplicates each year.<sup>14</sup> The purpose of this review is to provide an up-to-date overview of TAVI indications, outcomes, controversies, and future perspectives.

## INDICATIONS AND OUTCOMES

Two transcatheter valves (Edwards SAPIEN from Edwards Lifesciences Corp. and CoreValve from Medtronic, Inc.) built the core of the evidence in the past 12 years. For this reason, most of the data discussed in this paper is applicable to these valves, although for educational purposes we will generalise the speaking of 'TAVI procedure', and stating specific differences if necessary. The balloon expandable Edwards SAPIEN (ES) valve was commercially approved in 2007 for the European Union (EU) and in 2012 for the United States (US), and its last evolution has recently been released (Sapien 3). The self-expandable Medtronic CoreValve (CoVa) was commercially approved in 2007 (EU) and in 2014 (US), and has also recently presented its last version (Evolut R). Many other TAVI devices have been or will soon be commercially approved in the EU:<sup>15</sup> Acurate (Symetis SA), Centera (Edwards Lifesciences Corp), Direct Flow (Direct Flow Medical Inc.), Engager (Medtronic Inc), Jenavalve (Jenavalve Technology), Lotus (Boston Scientific), Portico (St. Jude Medical Inc, commercialisation temporarily suspended). However, experience with these devices is still limited (Figure 1).

## Indications

Beyond a large amount of observational data and multicentre registries, current indications come from three randomised trials. The PARTNER trial showed non-inferiority of TAVI with ES valve compared to SAVR in high surgical risk AS patients (PARTNER cohort A),<sup>16</sup> and better survival compared to medical treatment including balloon aortic valvuloplasty in inoperable patients (PARTNER cohort B).<sup>17</sup> In the CoVa pivotal trial, TAVI with CoVa was superior to SAVR in terms of all-cause death at 1 year in high-risk patients.<sup>18</sup>

The 2012 European Society of Cardiology Guidelines gave a I-B recommendation for TAVI in patients with life expectancy of >1 year if unsuitable for SAVR; a IIa-B recommendation for considering TAVI over SAVR in high-risk patients; and propose that a multidisciplinary 'Heart Team' including cardiologist, cardiac surgeons, and other specialists should guide the decisions (I-C).<sup>12</sup> The 2014 American Heart Association/American College of Cardiology Guidelines gives a I-B recommendation for TAVI if there is a prohibitive surgical risk and expected post-TAVI survival >12 month; a IIa-B recommendation for TAVI as an alternative to SAVR in high surgical risk patients; and also advocates case-by-case discussion in a Heart Team (I-C).<sup>13</sup> High risk is usually considered as logistic EuroSCORE  $\geq 20\%$  or Society of Thoracic Surgeons (STS) score  $\geq 10$ , but taking into account other factors such as frailty, porcelain aorta, patent coronary bypass grafts, or history of chest radiation.<sup>19</sup> Extreme or prohibitive risk patients are those with an estimated >50% risk of morbidity or mortality, considered inoperable by at least two cardiovascular surgeons from a tertiary centre of excellence.<sup>20</sup>

In the recent years, patient selection has shifted from absence of TAVI contraindications in SAVR-rejected patients in the early days of TAVI to a careful and collaborative candidate evaluation to choose between SAVR, TAVI, or medical treatment. Issues such as cognitive function, poor functional outcome, frailty, quality of life (QoL), and futility are variables that are currently discussed in this setting.<sup>21</sup> In the high-risk subset, the global trend in TAVI is towards a high 'but not so high risk', and some ongoing trials are exploring TAVI versus SAVR in intermediate risk patients (PARTNER II;<sup>22</sup> and SURTAVI<sup>23</sup>). In the inoperable scenario the concept of futility has emerged and has been embraced by the guidelines, proposing that, after

a careful evaluation of patients, medical treatment should be offered if no benefit from correction of AS is expected (no-benefit recommendation, III-B, for TAVI).<sup>13,24</sup> Characteristics related to poor outcome after TAVI (defined as death, low or worsening from baseline score in a QoL scale) were low body weight, low mean aortic gradient, oxygen-dependent lung disease, and poor baseline functional and cognitive status.<sup>24</sup>

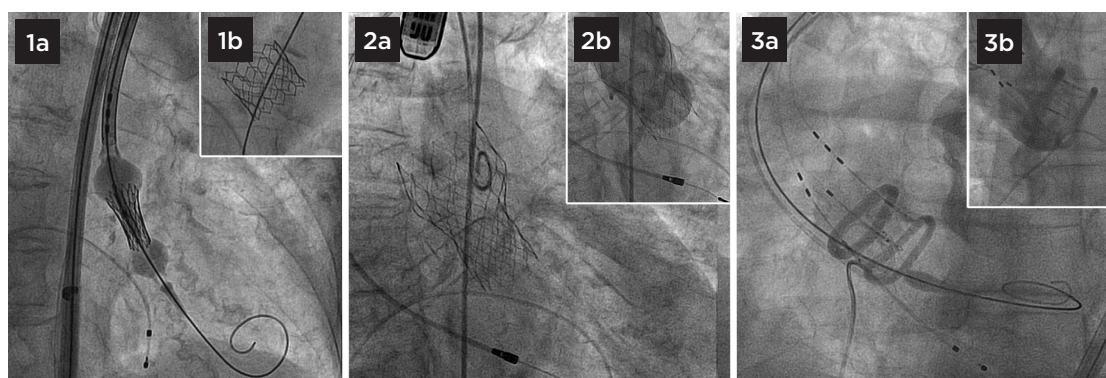
## Procedural Characteristics

Retrograde transfemoral is the current standard transfemoral approach (although the first TAVI procedures were performed anterogradely through the atrial septum).<sup>11,25</sup> Vascular closure is usually obtained with percutaneous closure devices, but some groups use surgical dissection and direct arterial closure. The transapical (ES) and subclavian (CoVa) accesses followed shortly for patients with inadequate lower limb arterial tree.<sup>26,27</sup> Lately, a direct transaortic approach through a mini-sternotomy has become popular among surgeons performing TAVI.<sup>28</sup> Although alternative approaches are regularly used in patients that have a more unfavourable risk profile, the transfemoral approach is generally associated with better outcomes, even after multivariate analysis.<sup>29</sup> There is no consensus on the best TAVI approach, so a case-by-case decision is made taking into account local experience and patient's anatomy.

Pre-procedural assessment includes clinical evaluation, transthoracic and transoesophageal echocardiography, computed tomography, and cardiac catheterisation. Annulus measurement is

crucial to optimising valve sizing, which is critical in preventing complications (annular rupture) and achieving good immediate and long-term results (paravalvular regurgitation).<sup>30,31</sup> Multimodality 3D cardiac imaging is encouraged as it showed improved accuracy compared to 2D assessments.<sup>32,33</sup> The procedure may be performed in a hybrid operating room or in the catheterisation laboratory, and is usually (although not mandatory) monitored by transoesophageal echocardiography. General anaesthesia was preferred in the early experience, but now many centres are using local anaesthesia and conscious sedation. A few studies have compared these approaches and preliminary data show similar outcomes and reduced resource consumption without general anaesthesia.<sup>34,35</sup>

Concomitant coronary artery disease is present or detected during pre-procedural coronary catheterisation in approximately 60% of TAVI candidates.<sup>36</sup> EU guidelines for myocardial revascularisation provide a IIa-C recommendation for percutaneous coronary intervention (PCI) of stenosis >70% in proximal coronary segments in patients undergoing TAVI.<sup>37</sup> The timing, completeness, and impact of PCI is discussed separately (see controversies). Standard post-procedural medical treatment is aspirin plus clopidogrel for 3-6 months and aspirin alone thereafter. The hypothesis of aspirin alone after TAVI is supported by a small randomised study<sup>38</sup> and is currently tested in the larger ARTE trial.<sup>39</sup> Patients on warfarin are empirically treated with warfarin alone or warfarin plus aspirin or clopidogrel depending on thrombotic and bleeding risks.



**Figure 1: New generation TAVI devices. 1: Sapien 3 (Edwards Lifesciences) during the implantation (a) and after the valve deployment (b). 2: Corevalve Evolut R (Medtronic) in the final position (a) and during simultaneous angiography (b), showing the smaller portion of the valve inside the left ventricular outflow tract of this version. 3: DirectFlow device (DirectFlow Medical) during implantation with the three positioning wires (a) and testing the final position with angiography before deployment (b).**

**Table 1: Short and mid-term results of main multicentre registries and randomised or controlled trials. Complication rates are given at 30 days.**

	n	Device	Years	Access	Implantation success	Stroke	Permanent Pacemaker	Major vasc. complication	MI	Surgical conversion	PVR >2+	30-day mortality	1-year mortality
SOURCE registry <sup>96,97</sup>	1,038	ES	2007 - 08	463 TF/575 TA	93.8%	2.5%	7%	7%	0.6%	2.7%	1.9%	8.5%	23.9%
UK registry <sup>64</sup>	870	217 ES/452 CoVa	2007 - 09	599 TF/271 non TF	97.2%	4.1%	16.3%	6.3%	1.3%	0.7%	13.6%	7.1%	21.4%
Tamburino et al. <sup>98</sup>	663	CoVa	2007 - 09	599 TF/64 TS	98%	1.2%	16.6%	2%	0%	0.8%	21%	5.4%	15%
GARY registry <sup>99 a</sup>	697	109 ES/588 CoVa	2009	666 TF/33 non TF	98.4%	1.8%	20.8%	12.3%	0.2%	1.6%	0.4%	12.4%	-
FRANCE 2 registry <sup>29</sup>	3,195	2,107 ES/1,043 CoVa	2010 - 11	2,361 TF/834 non TF	96.9%	3.4%	15.6%	4.7%	1.2%	0.4%	0.8%	9.7%	24%
Spanish registry <sup>100</sup>	1,416	806 ES/610 CoVa	2010 - 11	1,114 TF/302 TA	94%	3%	10%	3%	1%	1%	6%	9%	16 - 9% <sup>b</sup>
TCVT EU registry <sup>55</sup>	4,571	2,604 ES/1,967 CoVa	2011 - 12	3,392 TF/1,179 non TF	96.5%	1.8%	13.2%	3.1%	0.9%	4.2%	1.3%	-	-
TVT US registry <sup>101,102</sup>	7,710	ES	2011 - 13	4,972 TF/2,738 non TF	92%	2%	6.6%	6.4%	0.8%	1%	8.5%	7.6% <sup>c</sup>	26.2% <sup>c</sup>
PARTNER A (TAVI arm) <sup>16</sup>	348	ES	2007 - 09	244 TF/104 TA	-	4.7%	3.8%	11%	0% <sup>d</sup>	2.6%	12.2%	3.4% <sup>e</sup>	24.2% <sup>f</sup>
PARTNER B (TAVI arm) <sup>17</sup>	179	ES	2007 - 09	TF	-	6.7%	3.4%	16.2%	0% <sup>d</sup>	0%	11.8%	6.4% <sup>e</sup>	30.7% <sup>f</sup>
CoVa Pivotal (TAVI arm) <sup>18 d</sup>	390	CoVa	2011 - 12	323 TF/67 non TF	99.7%	4.9%	19.8%	5.9%	0.8%	0.5%	7.8%	3.3%	14.2%
CoVa Extreme risk <sup>103 d</sup>	506	CoVa	2011 - 12	TF	-	4%	21.6%	8.2%	1.2%	-	11.4%	8.4%	24.3%

a) Data of complications was provided separately for TF and TA patients in the original population, for this table average percentages are provided from the complete TAVI population. b) One-year mortality was 16% for CV and 19% for ES. c) Follow-up data from 3,528 patients (30-day mortality), and 5,980 (1-year mortality). d) The PARTNER Trial excluded patients with substantial coronary artery disease requiring revascularisation. e) A-treated analysis. f) Intention-to-treat analysis.

MI: myocardial infarction; PVR: paravalvular regurgitation; ES: Edwards-SAPIEN; CoVa: CoreValve; TF: transfemoral; TA: transapical; TS: transsubclavian; TAVI: transcatheter aortic valve implantation; vasc.: vascular.

**Table 2: Long-term mortality after TAVI. The original procedures of these studies were performed in 2007–2012 with earlier versions of current devices.**

	n	Valve	Follow-up Max. / Mean	Median survival	1-year Mort.	2-year Mort.	3-year Mort.	4-year Mort.	5-year Mort.	Valve Re-op.
Ussia et al. <sup>60</sup>	181	CoVa	-/3.4 years	-	23.6%	30.3%	34.8%	-	-	0%
D'Onofrio et al. <sup>104</sup>	774	ES	3.6/1 years	-	18.3%	23.9%	32.4%	-	-	0%
UK registry <sup>63,64</sup>	870	217 ES/ 452 CoVa	7.1/- years	-	21.4%	26.3%	38.8%	-	54.5%	0.8%
Rodés-Cabau et al. <sup>59</sup>	339	ES	4/3.5 years	-	24%	33%	49%	57%	-	0.6%
Toggweiler et al. <sup>68 a</sup>	88	ES	-/5 years	3.4 years	17%	26%	47%	58%	65%	1.1%
Doss et al. <sup>105</sup>	100	ES	5/3.8 years	-	8%	-	10%	-	13.0%	1%
EI-Mawardy et al. <sup>69</sup>	61	CoVa	-/5 years	-	11.5%	21.3%	26.2%	39.3%	52.5%	-
PARTNER A (TAVI arm) <sup>106,107 b</sup>	348	ES	-/3 years	-	24.2%	33.7%	44.2%	-	-	0% <sup>c</sup>
PARTNER B (TAVI arm) <sup>61,108 b</sup>	179	ES	-/5 years	2.5 years	30.7%	43%	53.9%	64.1%	71.8%	1.1% <sup>c</sup>

a) Selected population, excluding implantation failure or dead before 30 days. Complete follow-up in 84 out of 88 patients.

b) Intention-to treat analysis. Crossover patients were censored at the moment of crossover.

c) Re-operation data were reported at 2 years of follow-up.

Max: maximum; Mort: mortality; Re-op: re-operation of the transcatheter valve; ES: Edwards-SAPIEN; CoVa: CoreValve; TAVI: transcatheter aortic valve implantation.

Triple antithrombotic therapy is rarely prescribed except for concomitant PCI. Factors such as new antithrombotic drugs, atrial fibrillation (AF), or concomitant PCI suggest the need for individualised therapy and further investigation on the optimal post-TAVI antithrombotic regime.<sup>40</sup>

## Procedural Outcomes

Rigorous clinical research has been a feature of TAVI development, but until 2011 outcome data was somewhat heterogeneous. Eventually, definition of endpoints related to TAVI procedures were standardised in a position paper from the Valve Academic Research Consortium (VARC),<sup>41</sup> and revised posteriorly in the current, second version.<sup>19</sup> Successful TAVI implantation is reported in 90–95% of procedures. Device success is a VARC composite

endpoint defined as implantation of one valve in the correct anatomical position without death or valve dysfunction; and is currently obtained in >80% of TAVI cases.<sup>42</sup> The VARC combined 30-day safety endpoint (including all-cause mortality, major stroke, life-threatening bleeding, acute kidney injury (AKI), peri-procedural myocardial infarction, major vascular complication, or repeated procedure) was met in average in 32.7% of procedures in a recent meta-analysis.<sup>42</sup> Short-term outcomes from most relevant multicentre studies are summarised in Table 1. Both symptoms and QoL improvements in short and mid-term have been reported after TAVI.<sup>16,17,43,44</sup>

Most frequent TAVI complications are: a) vascular complications, with a great range of severity (from small haematomas or femoral pseudoaneurysm, to

arterial dissection/rupture and need for covered stents or emergent surgery), are reported in 1-19% of TAVI procedures.<sup>45</sup> Reductions in vascular complications and related bleedings have been uniformly reported with the downsizing of delivery catheters and increased experience;<sup>46,47</sup> b) severe bleeding, usually related to access site complications is frequent (15-32%),<sup>48,49</sup> but lower than SAVR procedures<sup>50</sup> - blood transfusion after TAVI is associated with a worse prognosis;<sup>51</sup> c) cardiac tamponade (due to temporary pacemaker catheter or high-support guidewire) is contemporarily reduced to <5% of cases but it was identified as the most frequent cause of procedural mortality;<sup>52</sup> d) permanent pacemaker implantation (<10% with ES and 10-35% with CoVa); e) AKI, with a reported incidence of 12-28%, and related in several studies to increased mortality.<sup>53,54</sup>

Paravalvular regurgitation (PVR) and stroke are discussed separately (see controversies). In the largest multinational European registry, conversion to open heart surgery was needed in 4.26% of patients.<sup>55</sup> Rare complications (0.5-2%) are aortic annulus (AA) rupture, damage to mitral valve (MV), valve embolisation, or coronary obstruction.<sup>56</sup> The rate of procedural complications has declined over the years, due to improvements in device designs, better candidate selection, more accurate anatomical screening, and local experience.<sup>57</sup> The learning curve has been reported as an independent predictor of survival.<sup>58</sup>

### Long-Term Outcomes

Long-term data are still scarce (mainly due to the relative youthfulness of the technique), but a few studies have available data up to 4-5 years of follow-up (Table 2). The long-term mortality in these studies is high, reaching generally 50% at 4-5 years. Nevertheless it must be reminded that these studies were performed in an elderly, comorbid population, with older versions of the valve devices and in the early stages of each centre's experience. The studies that have addressed causes of death in the follow-up show that more than half of the mortality is non-cardiovascular, suggesting the importance of candidate selection and multidisciplinary medical follow-up.<sup>59-61</sup> Main predictors of long-term mortality are: PVR, AKI and chronic kidney disease, stroke, chronic obstructive pulmonary disease, AF, major bleeding, left ventricular dysfunction, low stroke volume, frailty, and risk scores (STS, EuroSCORE).<sup>59-64</sup>

Immediate haemodynamic recovery of aortic valve parameters are obtained,<sup>17</sup> as well as other echocardiographic parameters that improve in the mid-term: left ventricular ejection fraction improvement,<sup>65</sup> pulmonary pressure decrease,<sup>66</sup> and even a reduction in the concomitant degree of mitral regurgitation may be obtained.<sup>67</sup> Valve durability is one of the questioned issues of this technique. The rate of need for replacement after a TAVI procedure is very low across studies (<1.5%, see Table 2). Haemodynamic benefits are sustained during follow-up, with available data for up to 4-5 years of follow-up.<sup>59-61,68,69</sup>

## OFF-LABEL USE

The use of transcatheter aortic valves outside the boundaries of manufacturer recommendations and/or current indications is difficult to quantify because of its ambiguous definition, but represents at least 10% of current TAVI procedures. The most common (and probably next-to-be an accepted indication) is the 'valve-in-valve' procedure for the treatment of dysfunctional aortic bioprostheses. In a large multinational registry, a 7.6% 1-month and 16.8% 1-year mortality was reported.<sup>70</sup> Bicuspid AVD with severe AS has been successfully treated with TAVI without differences in major outcomes compared to tricuspid anatomy, but higher risk of PVR.<sup>71</sup> On pure aortic regurgitation (AR), TAVI procedure has been used with reasonable survival results (30 day survival 90.7% and 1-year survival 78.6%) but a higher rate of PVR that raised the need for a second valve to 18.6% in a multicentric experience.<sup>72</sup> In a different multicentre registry TAVI for AR found less device success and reduced survival (69% at 12 months) compared to TAVI for AS.<sup>73</sup> Other occasional off-label use is the deployment of a transcatheter valve in degenerated rings, conduits, or bioprosthesis in tricuspid, pulmonary, or mitral positions.<sup>74-77</sup>

## CONTROVERSIES

### Coronary Artery Disease Management

Contrary to coronary artery bypass grafting on top of SAVR, PCI among patients undergoing TAVI seems feasible and safe in the short term.<sup>78-80</sup> Despite of the lack of randomised data (ongoing ACTIVATION trial is randomising TAVI patients with stable coronary artery disease to PCI or medical treatment; ISRCTN 75836930), routine

practice in most centres is PCI at least on severe proximal lesions, whereas some centres aim for complete revascularisation.<sup>78,81</sup> The timing of the PCI is controversial, but both concomitant PCI and TAVI procedures, and staged procedures are valid strategies.<sup>78,82,83</sup> The long-term impact of concomitant coronary artery disease and PCI is still controversial. A meta-analysis of observational studies showed no differences in mortality after a median follow-up of 452 days; but a large single centre registry found that patients in the highest tertiles of SYNTAX score received less complete revascularisation and had a higher risk of death and cardiovascular events.<sup>79,80</sup>

### Device Versus Device Comparison

There are no obvious differences in short or long-term mortality between the most studied ES and CoVa devices, however, most data come from indirect comparisons on large registries.<sup>29,55,64,84</sup> The main acknowledged difference is a 4-5-fold increased rate of pacemaker implantation with CoVa.<sup>55,64</sup> Methods like no or moderate predilatation, and less deep implantation of the device could help to reduce conduction disturbances in CoVa implantation.<sup>85,86</sup> Annular rupture, a rare but life-threatening complication is usually reported with oversized ES implantations.<sup>30,87</sup> The only randomised trial (CHOICE<sup>88</sup>) to date showed greater VARC device success with ES compared to CoVa, mainly driven by a higher rate of AR assessed immediately by angiography. Besides some study flaws, major clinical endpoints at 1 year are eagerly expected, and whether this increase in short-term AR is clinically relevant remains to be demonstrated.

### PVR

The rate of PVR has been heterogeneously reported because of different imaging modalities and different time to assessment (PVR is at its maximum immediately after the procedure and tends to decrease thereafter). Generally, moderate-to-severe PVR at discharge is reported in a range from 0-24%.<sup>89</sup> The grade of PVR is linearly related to increased short and long-term mortality, especially in cases with moderate-to-severe PVR.<sup>89</sup> PVR was one of the first identified flaws of TAVI procedures and has, in the last 5 years, been challenged with several improvements in valve designs (new or extended 'skirts' to seal the AA), deployment technique, and anatomical considerations (multimodality imaging of AA, optimised valve sizing).<sup>90</sup> As a result, a reduction

in PVR rate has been reported in the preliminary results of new-generation devices.<sup>91</sup>

### Stroke

In a meta-analysis of 10,037 TAVI patients, a relatively small rate of peri-procedural (<24 hour) stroke was found (1.5%), but increased to a 30-day 3.3% all stroke rate. Moreover, it was associated with 30-day mortality.<sup>92</sup> The stroke risk is persistent during follow-up with a cumulative 5-year combined (haemorrhagic and ischaemic) stroke rate of 17%.<sup>68</sup> TAVI and stroke have a complex relationship, with multiple identified factors that usually coexist in the same patient: aortic calcification, diabetes, operator experience, pre-existent and new-onset AF and/or intra-procedural thrombus, or debris embolisation.<sup>93-95</sup> Several cerebral protective devices have been developed and are currently under clinical research. Another important matter of research is the post-TAVI antithrombotic treatment, which is largely empirical at this moment.<sup>40</sup> Comparison with SAVR is controversial with higher stroke rates in the TAVI arm of PARTNER trial, but no differences in a meta-analysis, and a trend towards fewer strokes in the randomised US CoVa pivotal trial.<sup>16,18,50</sup> Stroke has been incorporated as a co-primary endpoint in the intermediate risk TAVI trials.

## FUTURE PERSPECTIVES

Long-term valve durability data, up to 10 years, will become available, as some of the early experience patients will survive to be assessed. Results of randomised TAVI versus SAVR trials in intermediate risk patients are eagerly expected (PARTNER II<sup>22</sup> and SURTAVI,<sup>23</sup> with STS between 4-8%). Additional indications that currently are considered off-label will probably be embraced by the guidelines; especially valve-in-valve procedures for degenerated bioprosthesis and selected cases of combined aortic valve disease (AVD) with predominance of AR. New devices will be incorporated in daily practice and will help the refinement of the technique. Many accessories designed for the procedures such as delivery catheters, femoral and transapical closure devices, cerebral protection devices, and combined imaging modalities will help to improve procedural outcomes. The most audacious are looking into low-risk patients with bioprosthesis indication, selected severe asymptomatic AS patients, and TAVI superiority over SAVR in some candidates. Although not related to AVD, the experience with

TAVI will also promote advancements in other percutaneous valve therapies, such as tricuspid and MV diseases.

In summary, TAVI is now a suitable alternative to SAVR in high-risk patients and has a clear mortality benefit when compared to medical treatment in inoperable patients. A shift towards lower risk candidates and a withdrawal of any invasive treatment in extreme risk patients with no expected benefit from TAVI is happening. Better patient

selection, device evolutions, and worldwide experience will probably further improve short and long-term TAVI results. Open issues like PVR, and stroke are a cause for concern but also are areas of intense investigation. With the currently acknowledged underutilisation of the technique, and a progressively ageing population in developed countries, the number of TAVI procedures is deemed to keep increasing. Existing registries, ongoing randomised trials and future investigation will ensure a solid future for the technique.

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