EuroIntervention 2019;15:857-866

Residual challenges in TAVI: moving forward

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KEYWORDS

- aortic stenosis
- bicuspid aortic valve
- coronary access
- prosthesis
- TAVR
- valve-in-valve

Abstract

Transcatheter aortic valve implantation (TAVI) has, in less than 20 years, become the dominant interventional treatment for aortic stenosis in developed countries. Its development has been characterised by the growth of procedural expertise and device improvement. Every aspect of this therapy has been investigated, increasing clinical evidence and leading to continued optimisation. The purpose of this review article is to provide an overview of the rapidly changing field of TAVI therapy, briefly describing key past achievements and discussing residual challenges.

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SUBMITTED ON 27/08/2019 - REVISION RECEIVED ON 03/10/2019 - ACCEPTED ON 07/10/2019

DOI: 10.4244/EIJ-D-19-00788

Introduction

In less than 20 years, transcatheter aortic valve implantation (TAVI) has taken an incredible journey, characterised by an extraordinary growth of procedural expertise, device improvement, and increasing clinical evidence[1,2]. This innovative therapy is now established as the dominant interventional treatment for aortic stenosis in many developed countries[3-6]. Many researchers and operators have investigated every aspect of this therapy, providing fundamental elements for further optimisation and development[1]. The cultural ferment is evident from the extremely high number of scientific articles on the field of TAVI that have crowded first-tier cardiology journals in the last two decades.

The purpose of this review article is to provide an overview of the rapidly changing field of TAVI therapy, briefly describing key past achievements and discussing residual challenges. In the interest of simplicity, the discussion has been subdivided into three areas: preprocedural, procedural and post-procedural challenges.

Preprocedural challenges

WHO SHOULD PERFORM TAVI?

Everyone wants to perform TAVI! Since severe aortic stenosis is the most common valvular heart disease affecting elderly patients in developed countries[7], providing access to this procedure is a key issue[8]. When discussing TAVI penetration rates, there are several aspects that should be understood. National economic indices (i.e., healthcare expenditure per capita, sources of healthcare funding, and reimbursement strategies) are a major factor but will not be discussed in this article. However, at least two important questions have raised the interest of the clinical community. 1) Should TAVI be performed in centres without on-site cardiac surgery? 2) What is the minimum number of TAVI procedures that should be performed in a centre to ensure optimal outcomes?

The 2017 Valvular Heart Disease Guidelines of the European Society of Cardiology (ESC) mandate that TAVI should be restricted to hospitals with both cardiology and cardiac surgery on-site[4]. The permanent accessibility of both specialties in the same institution is considered optimal to ensure appropriate patient selection by the Heart Team as well as to prompt management of potential severe complications during TAVI, many of which require emergency cardiac surgery[9] **(Figure 1)**. Interestingly, recent data extracted from the Society of Thoracic Surgeons/American College of Cardiology (ACC) Transcatheter Valve Therapy (TVT) Registry demonstrated that the rate of surgical bail-out during TAVI was fairly stable over a period of four years (1.17% for the period 01/12-02/13, and 1.04% for the period 06/14-09/14)[10]. The lack of endorsement for TAVI at hospitals without on-site cardiac surgery stems from perceptions of inappropriate patient selection and poor outcomes at such sites, even in the absence of supportive data. However, it is undeniable that this represents the only practical way to avoid uncontrolled and indiscriminate adoption of the procedure in low-volume and low-experience centres. Of course, the lack of a cardiac surgery department is not synonymous with low levels of expertise. Here lies the "bug". At some

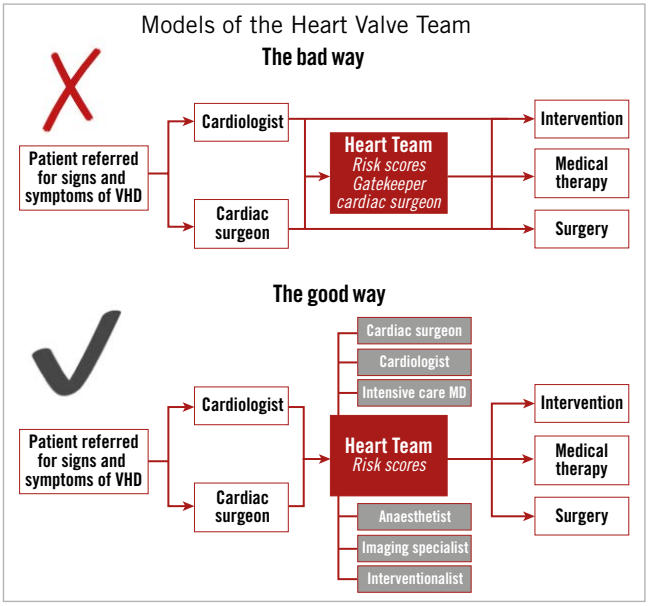

Figure 1. *Examples of heart valve team dynamics. The upper panel shows a bad model, in which patients are referred to either cardiologists or cardiac surgeons and then treated without collegial assessment. In the context of the Heart Team discussion, when this is involved, the cardiac surgeon acts as a gatekeeper. In the lower algorithm, a good example of a Heart Team model is shown, in which every patient is discussed by the Heart Team, composed of a cardiologist, a cardiac surgeon and other specialists (if needed), and therefore undergoes the best treatment according to clinical and anatomical features.*

hospitals without on-site cardiac surgery, the Heart Team approach (a key prerequisite for TAVI) has been adopted by in-house cardiologists and visiting cardiac surgical teams from external, collaborating hospitals[11]. Preliminary data on the experience with this Heart Team approach in small numbers of patients undergoing TAVI at sites without on-site cardiac surgery have suggested favourable outcomes, supporting its feasibility and safety[12,13]. The German Quality Assurance Registry on Aortic Valve Replacement (AQUA), a prospective registry of all TAVI and surgical aortic valve replacement (SAVR) procedures performed in Germany, compared patient characteristics, complications and outcomes of patients undergoing TAVI in hospitals with and without an on-site cardiac surgery department[14]. Among 17,919 patients undergoing TAVI from 2013 to 2014, 1,332 (7.4%) underwent the procedure at hospitals without an on-site cardiac surgery department. Although these patients were older (82.1±5.8 vs 81.1±6.1 years, $p<0.001$) and at higher procedural risk (logistic EuroSCORE I 23.2±15.8 vs 21.0±15.4%, $p<0.001$), major complication rates (including strokes [2.6 vs 2.3%, $p=0.452$], vascular complications [10.1 vs 8.9%, $p=0.161$] and in-hospital mortality [3.8 vs 4.2%, $p=0.396$]) were not statistically different[14].

More recently, an analysis of the prospective multicentre Austrian TAVI registry included consecutive high-risk and inoperable patients with severe symptomatic aortic stenosis undergoing

transfemoral TAVI (n=1,822), of whom 15.9% were treated at hospitals without cardiac surgery departments, with no difference in propensity-matched periprocedural and post-procedural survival rates up to one year[15]. However, this study carries several important limitations. First, patients were not truly matched for all baseline factors. Second, there are issues other than survival such as pacemaker rates, vascular complications, stroke, appropriate device selection, paravalvular leak (PVL), duration of hospital stay, discharge home as opposed to another facility, resource use and cost, that should be considered. Third, there is also the issue of who did not undergo TAVI: the question is whether low-volume or non-surgical centres offered the procedure to all appropriate patients. These findings require validation in a randomised study given the small number of patients undergoing TAVI at hospitals without an on-site cardiac surgery department. However, besides the inherent limitations of self-reported registries (where underreporting and heterogeneity in outcomes among centres cannot be excluded), the AQUA and the Austrian registry findings raise the important question of whether there is a real and contemporary unmet clinical need that may justify extending TAVI to institutions without cardiac surgery departments (especially outside Germany). At this time, based on current guidelines and pending additional data, we believe that clinicians should strongly avoid performing TAVI procedures at hospitals without on-site cardiac surgery[4,5,16]. TAVI is more than just a procedure. It is part of a comprehensive treatment programme that embraces team-based care by experienced clinicians with shared decision making and access to all treatment options.

An expanding body of literature supports the observation that outcomes of interventional or surgical procedures improve with increasing centre volume – commonly referred to as the "volume–outcomes relationship"[17-20]. Although numerous studies (including some focused on TAVI) have attempted to define this relationship[19-24], findings have been conflicting and much remains to be understood.

Recent data extracted from the Society of Thoracic Surgeons/ACC-TVT Registry support the need for careful continued examination of TAVI volume requirements[24]. Vemulapalli and colleagues analysed 113,662 TAVI procedures performed at 555 hospitals by 2,960 operators from 2015-2017 in the USA. Procedural volume at hospital level (for both transfemoral and non-transfemoral TAVI) was inversely associated with 30-day risk-adjusted mortality (3.19% [lowest-volume quartile; 95% CI: 2.78-3.67] vs 2.66% [highest-volume quartile; 95% CI: 2.48-2.85]; OR 1.21; p=0.02), even after excluding a hospital's first year of cases to account for a potential learning curve (3.10% vs 2.61%; OR 1.19; 95% CI: 1.01-1.40). These findings contrast with a previous study that only included cases performed with the SAPIEN 3 valve (Edwards Lifesciences, Irvine, CA, USA)[25], but are consistent with prior analyses (including one examining earlier data from the TVT Registry)[26].

Both operator and hospital volumes were taken into account in this interesting analysis, highlighting the fact that multiple skills and a functional team are needed to achieve optimal TAVI outcomes, as in many other areas of modern interventional cardiology. Importantly, the lowest 30-day mortality rates are associated with operator volumes as low as 40 TAVI procedures/year, a volume that should be achievable relatively easily within functioning TAVI networks[25].

NEXT STEPS IN TRANSCATHETER HEART VALVE SIZING

Although some TAVI-related complications can be attributed to patient characteristics or operator expertise, some arise from specific device-host interactions. Amongst the latter, the most significant and impactful are: 1) incomplete and/or non-circular frame expansion due to the presence of aortic calcification leading to PVL, and 2) unexpected movement of calcified cusps leading to coronary obstruction or aortic root rupture despite appropriate valve size selection[27-29]. Although current three-dimensional computed tomography (CT) reconstructions are highly accurate, device-host interactions are difficult to predict owing to wide variation in the geometry and dimensions of the aortic root and differing volume and distribution of calcium among patients[30]. The increasing number and spectrum of TAVI patients (and increasing variety of available valve types) will necessitate patient-specific tools to predict device-host interaction for case selection and procedural planning (i.e., selection of the valve that best fits the individual patient). Finite element computer simulation of a TAVI procedure (based upon integration of patient-specific anatomy, physical and mechanical valve properties, and biomechanical characteristics of the aortic root) may help to define *in vivo* device-host interactions, thereby enhancing the safety of TAVI[31]. To date, this extremely interesting field remains poorly explored. Schultz et al attempted to predict the *in vivo* morphology of two TAVI devices (CoreValve® [Medtronic, Minneapolis, MN, USA] and SAPIEN XT [Edwards Lifesciences]) and displacement of the calcified aortic leaflets immediately after implantation, by comparing the findings derived from a patient-specific cardiovascular computer model with those from CT performed after TAVI[32]. Although they were able to demonstrate high agreement between the predicted and observed dimensions of the valve frame, the model slightly overestimated the dimensions at all levels (except the commissures). These observations are promising, but at the same time demonstrate that these tools need significant improvement.

Procedural challenges

BICUSPID AORTIC VALVE

Bicuspid aortic valve (BAV) is a complex disease spectrum including several anatomical variants, ranging from true type 0 bicuspid valve (with no raphe) to forms in which three cusps can be identified (with variably located raphes [type 1 and type 2]) **(Figure 2)**. Approximately 2-6% of TAVI patients have a BAV[33,34] and give rise to several major concerns **(Figure 3)**.

– Asymmetric shape and calcification may impair adequate prosthesis expansion, function and durability
– Associated aortopathy may increase the risk of aortic dissection and annular rupture
– Device sizing techniques have yet to be refined.

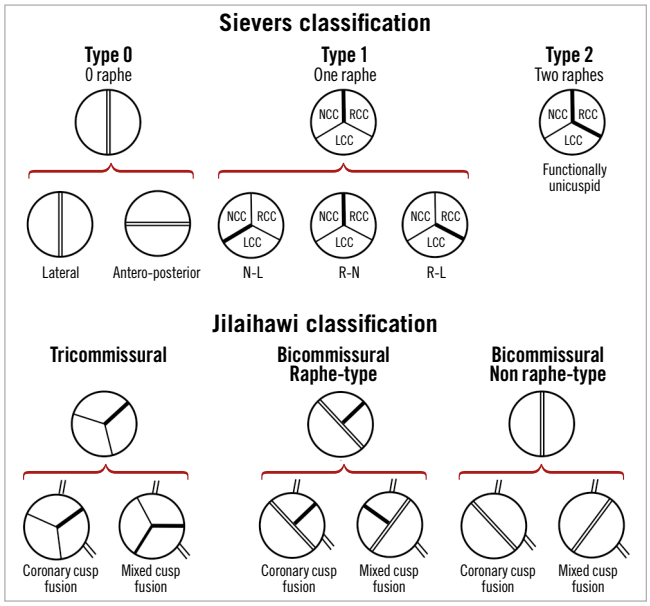

Figure 2. *Schematic representation of bicuspid aortic valve morphologies according to Sievers' and Jilaihawi's classifications. LCC: left coronary cusp; NCC: non-coronary cusp; RCC: right coronary cusp*

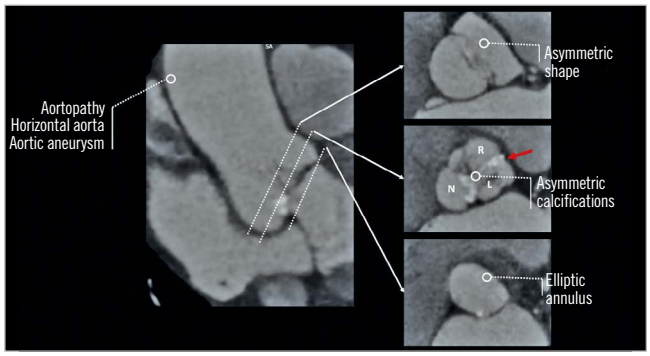

Figure 3. *Computed tomography images of a type 1 R-L bicuspid aortic stenosis. The image summarises the current issues of TAVI therapy in bicuspid aortic valves. The red arrow indicates the raphe. L: left coronary cusp; N: non-coronary cusp; R: right coronary cusp*

Despite these concerns, many patients affected by BAV have already been treated with TAVI over the years. In a large multicentre study, outcomes of 546 matched pairs of patients with BAV and tricuspid aortic stenosis were compared[35]. Overall, BAV was associated with a higher rate of conversion to surgery (2.0% vs 0.2%, p=0.006) (mainly due to aortic root injury), the need for a second valve (4.8% vs 1.5%, p=0.002) and ≥moderate PVL (10.4% vs 6.8%, p=0.04). However, in spite of these procedural pitfalls, no difference in survival was observed at 30-day or two-year follow-up. Of note, the increased rate of procedural complications in BAV patients was only observed in those who received older-generation devices[36]. Specifically, aortic rupture was observed more frequently with the SAPIEN XT, whereas second valve need and PVL were more frequent with the CoreValve. Conversely, results were markedly better in patients who received new-generation devices (in particular, the SAPIEN 3 and Lotus™ [Boston Scientific, Marlborough, MA, USA]), even though there was a numerical trend highlighting the problems related to TAVI in BAV (conversion to surgery 1.3% vs 0%, second valve need 1.3% vs 0.4%, PVL 2.7% vs 1.8%, all p>0.05)[35].

More recently, Makkar et al reported a sub-analysis of the ACC/TVT Registry including 2,691 propensity score-matched pairs of bicuspid and tricuspid aortic stenosis. They found that patients with bicuspid versus tricuspid aortic stenosis had no significant difference in 30-day (2.6% vs 2.5%; HR 1.04 [95% CI: 0.74-1.47]) or one-year (10.5% vs 12.0%; HR 0.90 [95% CI: 0.73-1.10]) mortality and moderate or severe PVL at 30 days (2.0% vs 2.4%; absolute risk difference, 0.3% [95% CI: -1.3% to 0.7%]), but had increased 30-day risk for stroke (2.5% vs 1.6%; HR 1.57 [95% CI: 1.06-2.33])[36].

The number of treated cases is still limited; more experience is needed to clarify fully the role of TAVI in BAV disease, particularly in younger and lower-risk patients. Furthermore, there are no randomised controlled trials comparing TAVI and SAVR in this specific anatomical subset. However, results with new-generation devices demonstrate promisingly low complication rates, similar to conventional tricuspid aortic stenosis[35,36]. As a general rule, cautious preprocedural screening and procedural performance remain necessary in BAV patients, in order to minimise aortic root trauma and avoid excessive prosthesis oversizing (even allowing some downsizing). In conclusion, BAV in itself is not an absolute contraindication to TAVI. Instead, the anatomy of each single case should be carefully assessed prior to the procedure to rule out possible issues (concomitant root dilatation, valve size, location of calcification, horizontal aorta) and choose the best type of prosthesis for the specific anatomy.

VALVE-IN-VALVE PROCEDURES

All surgical bioprostheses have limited durability and usually fail within 10-15 years[37,38]. Similarly, transcatheter heart valve (THV) durability up to six years is already a well-established reality, with low rates of structural valve dysfunction (SVD) demonstrated in large rigorous studies[39,40]. However, data concerning clinical outcomes and THV integrity beyond six years remain scarce[41]. Patients with failed surgical or transcatheter bioprosthetic valves are commonly at high surgical risk because of comorbidities, old age, and the need for repeat thoracotomy in patients with surgical valves[42]. In this context, implantation of a THV inside the failed aortic bioprosthetic valve (valve-in-valve [ViV]) has emerged as an effective and less invasive treatment for degenerated aortic bioprostheses[43].

Successful ViV procedures require a detailed understanding of the anatomical and fluoroscopic appearances of the surgical heart valve, and knowledge of THV design and sizing for ideal implantation position of the chosen THV within the existing bioprosthesis. Although procedural success is achieved in the vast majority of patients, these TAVI-ViV procedures are associated with several

potential complications, including THV-surgical heart valve mismatch, immediate or delayed THV migration and embolisation, high residual gradients, and coronary occlusion (especially amongst particular types of aortic bioprosthesis)[43].

Coronary occlusion has poor prognosis and remains one of the major concerns of TAVI-ViV procedures[43-47] despite its low frequency (TVT Registry 0.5%; Valve-in-Valve International Data [VIVID] registry 2.3%)[45,46]. Avoidance requires meticulous procedural planning to choose the correct prosthesis type and size. However, the main predisposing factor in ViV procedures is the proximity of a coronary ostium to the anticipated final position of the displaced bioprosthetic leaflets after THV implantation[48]. The virtual THV to coronary distance (VTC) is a CT-obtained predictor of the proximity of the coronary ostia to the anticipated final position of the displaced bioprosthetic leaflets after THV implantation[48]. The VTC combines the height of the coronary ostia, sinus width and THV size, and also simulates THV tilt in the annulus (coronary occlusion risk: maximum <4 mm, borderline 4-6 mm, low >6 mm)[48]. Predictors of coronary occlusion after ViV implantation include anatomical factors (low coronary ostia, narrow sinuses of Valsalva and sinotubular junction, bulky leaflets), bioprosthetic valve factors (supra-annular position, high leaflet profile, internal stent frame [e.g., Mitroflow (Sorin Group, Milan, Italy), Trifecta™ (St. Jude Medical, St. Paul, MN, USA)] or no stent frame [homograft, stentless valve]), and THV factors (extended sealing cuff, high implantation)[49] **(Figure 4)**. Coronary protection should be used in high-risk cases to allow swift restoration of coronary flow and improve clinical outcome[49]. Furthermore, intentional laceration of the bioprosthetic aortic scallop to prevent iatrogenic coronary artery obstruction – the BASILICA procedure – is emerging as an effective method to prevent coronary occlusion[50].

Residual aortic stenosis is a major drawback of TAVI-ViV procedures. In the VIVID Registry, elevated mean gradients (≥20 mmHg) were recorded in 27% of patients[45] and are especially common in patients receiving balloon-expandable THVs in small surgical valves (label size ≤21 mm)[51]. In such cases, expansion of the THV frame is constrained by the bioprosthetic surgical valve ring, with consequent underexpansion of the THV leaflets, greater obstruction to flow and suboptimal haemodynamics[50]. Potential solutions include (a) optimal positioning of the THV within the surgical bioprosthesis[52], (b) implantation of the THV in a supra-annular position[52], or (c) bioprosthetic valve ring fracture (BVF) using high-pressure non-compliant balloons (Atlas® GOLD or TRUE® balloons; Bard Peripheral Vascular Inc., Tempe, AZ, USA) before or after THV implantation[53]. Surgical valves with a metallic frame (Hancock® II [Medtronic], Trifecta and older-generation PERIMOUNT or Carpentier-Edwards [Edwards Lifesciences]) cannot be fractured using currently available balloons[50]. The procedural and haemodynamic outcomes of patients treated with ViV and BVF have been reported in two case series encompassing 30 cases[53]. In 15 cases in which BVF was performed after TAVI-ViV, mean gradient was reduced from 41.9 mmHg to 20.5 mmHg with ViV, and further reduced to 6.7 mmHg following BVF ($p<0.001$)[53].

In contrast with redo valve surgery, preliminary data suggest that redo TAVI (so called THV-in-THV) procedures are safe, with low periprocedural complication rates and midterm survival and prosthesis performance comparable to recent TAVI series[54]. However, this concept is associated with several potential concerns. First, it is unknown whether the presence of two THVs could affect long-term durability. Second, it could be argued that patients with double THVs may be more prone to leaflet thrombosis, although this was not apparent in one small series (albeit without systematic CT assessment). Third, coronary access may be challenging, particularly after implantation of two THVs that extend into the ascending aorta (e.g., CoreValve/Evolut™ [Medtronic])[54]. Finally, it can be argued that a number of patients would not be able to have repeat TAVI due to the risk of coronary "occlusion" due to supra-annular THV-in-THV **(Figure 5)**. This has implications for THV selection and positioning in younger low-risk patients.

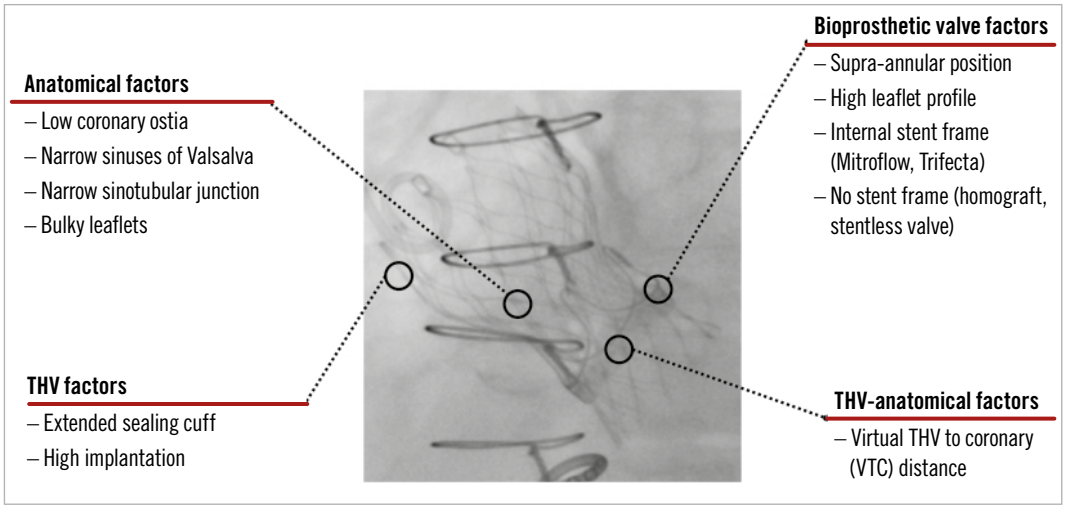

Figure 4. *Predictors of coronary occlusion after valve-in-valve TAVI procedures.*

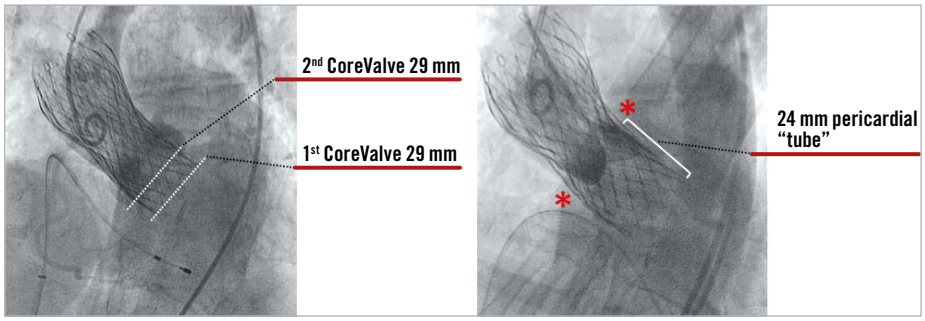

Figure 5. *Case example of a THV-in-THV procedure. A degenerated 29 mm CoreValve treated with redo TAVI using a 29 mm CoreValve. The second THV was implanted approximately 6 mm higher than the first one. After 20 minutes, the progressive expansion of the second CoreValve created a covered cylinder of 24 mm that occluded the sinuses of Valsalva with a complete obliteration of the coronary ostia.*

Post-procedural challenges

TRANSCATHETER HEART VALVE DURABILITY

TAVI is now being offered to younger and lower-risk patients. In this cohort, life expectancy will exceed that of the initial TAVI candidates, which makes the question of long-term prosthesis durability crucially important. Several limitations prevent robust evaluation of TAVI durability. First, TAVI is a relatively young technology given that its wider adoption started following CE mark approval in 2007 and US Food and Drug Administration approval in 2011. Thus, there are few data concerning valve durability beyond 10 years. Second, current data on long-term outcomes beyond five years relate to first-generation TAVI devices. Finally, the major limitation of long-term durability evaluation is the older age of the TAVI population, most of whom are affected by multiple comorbidities with high-risk profiles and limited life expectancy. A paucity of patients (usually <50% of the initial population) therefore remain alive at very long-term follow-up. In the past few years, results of several TAVI studies with more than five-year follow-up data have been published. The Placement of AoRTic TraNscathetER Valve Trial (PARTNER-1 trial) showed no evidence of SVD at five-year follow-up[55,56]. Moreover, the PARTNER-1A substudy demonstrated similar echocardiographic performance of both transcatheter and surgical valves, with a mean transvalvular gradient of 10.7 and 10.6 mmHg, and aortic valve area of 1.6 and 1.5 cm^2, respectively[55,56]. This evaluation confirmed the satisfactory haemodynamic profile of transcatheter aortic valves up to five years post implantation, even if moderate or severe aortic regurgitation caused by PVL (excluded in the SVD definition) was more common in the TAVI group.

Following introduction of EAPCI/ESC/EACTS standardised criteria of SVD in 2017[57], an increasing number of studies have reported outcomes after TAVI with either SAPIEN or CoreValve THVs up to seven and eight years[41,58-62] **(Table 1)**. Three single-centre studies demonstrated stable transprosthetic gradients over time and rates of severe THV dysfunction of 2.4%, 3.2% and 3.6%[41,58,59]. Holy et al analysed long-term outcomes of 152 consecutive patients who had undergone TAVI with the self-expanding CoreValve between 2007 and 2011[60]. Echocardiographic follow-up was undertaken at 6.3±1.0 years (5.0-8.9 years) and was 88% complete (60/68 participants who survived beyond five years). No case of SVD was reported and five patients (3.3%) had undergone redo TAVI or surgery due to PVL[60]. A similar analysis by Deutsch et al demonstrated an overall crude cumulative incidence of SVD of 14.9% seven years after TAVI (CoreValve 11.8% vs SAPIEN 22.6%; p=0.01)[61]. Further reports from national registries confirm low rates of THV dysfunction at long-term follow-up. Data from the French Aortic National CoreValve and Edwards (FRANCE-2) registry showed an incidence of severe and moderate/severe SVD of 2.5% and 13.3%, respectively, in patients surviving five years beyond the procedure[63], while Blackman et al reported a 10-year incidence of severe and moderate SVD of 0.4% and 8.7%, respectively, in the UK TAVI Registry[64]. Finally, a recent analysis from the Nordic Aortic Valve Intervention (NOTION) trial reported lower rates of moderate-to-severe SVD after TAVI compared with surgery (4.8% vs 24% for TAVI and surgical aortic valve replacement, respectively), with no difference in bioprosthetic valve failure (6.7% vs 7.5%)[39].

CORONARY ACCESS

As TAVI edges towards consideration in younger, lower-risk patients, it is important to address not only the clinical outcomes following initial implantation, but also longer-term considerations for future interventions such as percutaneous coronary intervention (PCI). Furthermore, the prevalence of coronary artery disease (CAD) in patients with severe aortic stenosis is high and there is no doubt that the presence of a THV in the aortic position may present an important challenge for coronary re-access (particularly those devices that extend into the ascending aorta). Whilst this has been particularly relevant for the CoreValve prosthesis for many years, the SAPIEN 3 valve (with a higher frame) has introduced potential issues with coronary re-engagement after balloon-expandable THV. In this context, the ACURATE *neo*™ bioprosthesis (Symetis SA/Boston Scientific, Ecublens, Switzerland) carries the important feature of a high frame, but with very large cells (stabilisation arches) that potentially minimise interference with coronary ostia re-access after THV deployment[65]. However, with limited

Table 1. Long-term durability after transcatheter aortic valve implantation using EAPCI/ESC/EACTS definitions.

Author	Year	N	Prosthesis type	Mean FU (years)	SVD (%)	BVF, n (%)
Deutsch et al	2018	300	CoreValve and Edwards SAPIEN	7.14	7-year: 22.7% (moderate and severe SVD)	7-year: 11%
Eltchaninoff et al	2018	378	PVT, Cribier-Edwards, Edwards SAPIEN and SAPIEN XT	3.1	8-year: 12.8% (moderate and severe SVD)	8-year: 0.58%
Barbanti et al	2018	288	CoreValve and SAPIEN XT	6.7	8-year: 2.5% (severe SVD)	8-year: 4.5%
Holy et al	2018	152	CoreValve	6.3	NR	8-year: 4.5%
Panico et al	2018	278	CoreValve	6.8	NR	3.1%
Didier et al	2018	4,201	CoreValve, Edwards SAPIEN and SAPIEN XT	5.0	Moderate SVD: 12.4% between 4 and 5 years Severe SVD: 2.9% between 4 and 5 years	
Søndergaard et al	2019	139	CoreValve	NR	6-year: 3.6% (moderate SVD) 6-year: 0.7% (severe SVD)	6-year: 7.5%
Blackman et al	2019	241	CoreValve, Edwards SAPIEN and SAPIEN XT	6.1 5.3	8.7% (moderate SVD) 0.4% (severe SVD)	
Durand et al	2019	1,403	CoreValve and SAPIEN XT	3.9	7-year: 7.0% (moderate SVD) 7-year: 4.2% (severe SVD)	7-year: 1.9%

published studies, it is nearly impossible to estimate the incidence, feasibility, and success rates of coronary angiography and PCI in this patient population. In the largest observational study investigating this issue, Zivelonghi et al[66] reported the feasibility of angiography in 66 patients immediately after TAVI (CoreValve Evolut, n=25; SAPIEN 3, n=41). Selective angiography required guidewire positioning in 4% of vessels; only one artery could not be engaged due to high Evolut™ R implantation (possibly because the leaflet base of the supra-annular valve was located at the level of origin of the coronary ostium). PCI was successful in all 17 patients (including six with Evolut R). In conclusion, factors that could theoretically make coronary re-access challenging after TAVI are: 1) THV with closer cells landing above the origin of the coronary ostia, 2) high THV implant placing the base of the prosthetic leaflets in front of the coronary ostia; 3) narrow sinus of Valsalva and sinotubular junction; 4) commissure of the THV directly in front of the coronary ostia.

This last possibility has raised the attention of researchers. To date, there has been no reliable and consistent way to assess the position of the THV commissures in relation to those of the native aortic valve. In a pilot study, Tang et al reported techniques to reduce the severity of overlap of the THV commissures with one or both coronary ostia, suggesting that it may be possible to achieve a more ideal final position of the self-expanding Evolut R and Evolut™ PRO devices[67]. Using the C-tab as a marker, they co-registered valve positioning to the pre-TAVI CT scan using imaging software to orientate the valve commissures and their proximity to the left main and right coronary arteries. When the black capsule "hat" marker on the valve catheter was positioned at the inner curve/centre back of the aortic root during initial deployment, severe overlap of the neo-commissures with the left main and right coronary artery was common (63.9% and 52.8%, respectively). Conversely, when the capsule hat marker was positioned on the outer curve/centre front of the aortic root, overlap occurred in only 19.5% and 6.1% of cases, respectively[67].

Conclusion

TAVI has revolutionised the management of patients with symptomatic severe aortic stenosis and indications are expanding towards younger patients with lower-risk profiles. Although many aspects of this innovative therapy have been deeply studied and clarified, several issues and challenges remain. Rigorous studies and ongoing technological development will help in providing patients with severe aortic stenosis with the most reliable and effective solution for their pathology.

Conflict of interest statement

M. Barbanti is a consultant for Edwards Lifesciences and an advisory board member for Biotronik. J.G. Webb is a consultant to, and has received research funding from Edwards Lifesciences, Abbott Vascular, Boston Scientific and ViVitro Labs. D. Dvir is a consultant for Edwards Lifesciences, Medtronic, and St. Jude Medical. B. Prendergast has received unrestricted educational and research grants from Edwards Lifesciences and speaker fees from Edwards Lifesciences.

References

1. Barbanti M, Webb JG, Gilard M, Capodanno D, Tamburino C. Transcatheter aortic valve implantation in 2017: state of the art. *EuroIntervention.* 2017;13: AA11-21.

2. Siontis GCM, Overtchouk P, Cahill TJ, Modine T, Prendergast B, Praz F, Pilgrim T, Petrinic T, Nikolakopoulou A, Salanti G, Søndergaard L, Verma S, Jüni P, Windecker S. Transcatheter aortic valve implantation vs. surgical aortic valve replacement for treatment of symptomatic severe aortic stenosis: an updated meta-analysis. *Eur Heart J.* 2019;40:3143-53.

3. Mylotte D, Osnabrugge RLJ, Windecker S, Lefèvre T, de Jaegere P, Jeger R, Wenaweser P, Maisano F, Moat N, Søndergaard L, Bosmans J, Teles RC, Martucci G, Manoharan G, Garcia E, Van Mieghem NM, Kappetein AP, Serruys PW, Lange R, Piazza N. Transcatheter aortic valve replacement in Europe: adoption trends and factors influencing device utilization. *J Am Coll Cardiol.* 2013;62:210-9.

4. Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, Iung B, Lancellotti P, Lansac E, Rodriguez Muñoz D, Rosenhek R, Sjögren J, Tornos

Mas P, Vahanian A, Walther T, Wendler O, Windecker S, Zamorano JL; ESC Scientific Document Group. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J.* 2017;38:2739-91.

5. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Fleisher LA, Jneid H, Mack MJ, McLeod CJ, O'Gara PT, Rigolin VH, Sundt TM 3rd, Thompson A. 2017 AHA/ACC focused update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation.* 2017;135:e1159-95.

6. Barbanti M, Buccheri S, Rodés-Cabau J, Gulino S, Genereux P, Pilato G, Dvir D, Picci A, Costa G, Tamburino C, Leon MB, Webb JG. Transcatheter aortic valve replacement with new-generation devices: a systematic review and meta-analysis. *Int J Cardiol.* 2017;245:83-9.

7. Lindroos M, Kupari M, Heikkilä J, Tilvis R. Prevalence of aortic valve abnormalities in the elderly: an echocardiographic study of a random population sample. *J Am Coll Cardiol.* 1993;21:1220-5.

8. Webb JG, Barbanti M. Transcatheter aortic valve adoption rates. *J Am Coll Cardiol.* 2013;62:220-1.

9. Eggebrecht H, Vaquerizo B, Moris C, Bossone E, Lämmer J, Czerny M, Zierer A, Schröfel H, Kim WK, Walther T, Scholtz S, Rudolph T, Hengstenberg C, Kempfert J, Spaziano M, Lefevre T, Bleiziffer S, Schofer J, Mehilli J, Seiffert M, Naber C, Biancari F, Eckner D, Cornet C, Lhermusier T, Philippart R, Siljander A, Giuseppe Cerillo A, Blackman D, Chieffo A, Kahlert P, Czerwinska-Jelonkiewicz K, Szymanski P, Landes U, Kornowski R, D'Onofrio A, Kaulfersch C, Søndergaard L, Mylotte D, Mehta RH, De Backer O; European Registry on Emergent Cardiac Surgery during TAVI (EuRECS-TAVI). Incidence and outcomes of emergent cardiac surgery during transfemoral transcatheter aortic valve implantation (TAVI): insights from the European Registry on Emergent Cardiac Surgery during TAVI (EuRECS-TAVI). *Eur Heart J.* 2018;39:676-84.

10. Pineda AM, Harrison JK, Kleiman NS, Rihal CS, Kodali SK, Kirtane AJ, Leon MB, Sherwood MW, Manandhar P, Vemulapalli S, Beohar N. Incidence and Outcomes of Surgical Bailout During TAVR: Insights From the STS/ACC TVT Registry. *JACC Cardiovasc Interv.* 2019;12:1751-64.

11. Torzewski J, Zimmermann O, Paula J, Fiedermutz M, Li K, Ito W, Karch M, Liu Z, Ruland A, Hüttner I, Osberghaus M, Doll N. In-hospital results of transcatheter aortic valve implantation (TAVI) in a district hospital--an approach to treat TAVI patients in rural areas. *Int J Cardiol.* 2013;168:4845-6.

12. Eggebrecht H, Mehta RH, Haude M, Sack S, Mudra H, Hein R, Brachmann J, Gerckens U, Kuck KH, Zahn R, Sechtem U, Richardt G, Schneider S, Senges J. Transcatheter aortic valve implantation (TAVI) by centres with and without an on-site cardiac surgery programme: preliminary experience from the German TAVI registry. *EuroIntervention.* 2014;105:602-8.

13. Gafoor S, Sirotina M, Doss M, Franke J, Piayda K, Lam S, Bertog S, Vaskelyte L, Hofmann I, Sievert H. Safety of transcatheter aortic valve implantation in a hospital with visiting on-site cardiac surgery. *J Interv Cardiol.* 2015;28:76-81.

14. Eggebrecht H, Bestehorn M, Haude M, Schmermund A, Bestehorn K, Voigtländer T, Kuck KH, Mehta RH. Outcomes of transfemoral transcatheter aortic valve implantation at hospitals with and without on-site cardiac surgery department: insights from the prospective German aortic valve replacement quality assurance registry (AQUA) in 17 919 patients. *Eur Heart J.* 2016;37:2240-8.

15. Egger F, Zweiker D, Freynhofer MK, Löffler V, Rohla M, Geppert A, Farhan S, Vogel B, Falkensammer J, Kastner J, Pichler P, Vock P, Lamm G, Luha O, Schmidt A, Scherr D, Hammerer M, Hoppe UC, Maurer E, Grund M, Lambert T, Tkalec W, Sturmberger T, Zeindlhofer E, Grabenwöger M, Huber K; Austrian TAVI Group. Impact of On-Site Cardiac Surgery on Clinical Outcomes After Transfemoral Transcatheter Aortic Valve Replacement. *JACC Cardiovasc Interv.* 2018;11:2160-7.

16. Holmes DR Jr, Mack MJ, Kaul S, Agnihotri A, Alexander KP, Bailey SR, Calhoon JH, Carabello BA, Desai MY, Edwards FH, Francis GS, Gardner TJ, Kappetein AP, Linderbaum JA, Mukherjee C, Mukherjee D, Otto CM, Ruiz CE, Sacco RL, Smith D, Thomas JD. 2012 ACCF/AATS/SCAI/STS expert consensus document on transcatheter aortic valve replacement. *J Am Coll Cardiol.* 2012;59:1200-54.

17. Luft HS. The relation between surgical volume and mortality: an exploration of causal factors and alternative models. *Med Care.* 1980;18:940-59.

18. Luft HS, Bunker JP, Enthoven AC. Should operations be regionalized? The empirical relation between surgical volume and mortality. *N Engl J Med.* 1979;301:1364-9.

19. Birkmeyer JD, Siewers AE, Finlayson EV, Stukel TA, Lucas FL, Batista I, Welch HG, Wennberg DE. Hospital volume and surgical mortality in the United States. *N Engl J Med.* 2002;346:1128-37.

20. Nathens AB, Jurkovich GJ, Maier RV, Grossman DC, MacKenzie EJ, Moore M, Rivara FP. Relationship between trauma center volume and outcomes. *JAMA.* 2001;285:1164-71.

21. Khera S, Kolte D, Gupta T, Goldsweig A, Velagapudi P, Kalra A, Tang GHL, Aronow WS, Fonarow GC, Bhatt DL, Aronow HD, Kleiman NS, Reardon M, Gordon PC, Sharaf B, Abbott JD. Association Between Hospital Volume and 30-Day Readmissions Following Transcatheter Aortic Valve Replacement. *JAMA Cardiol.* 2017;2:732-41.

22. Wassef AWA, Rodes-Cabau J, Liu Y, Webb JG, Barbanti M, Muñoz-García AJ, Tamburino C, Dager AE, Serra V, Amat-Santos IJ, Alonso Briales JH, San Roman A, Urena M, Himbert D, Nombela-Franco L, Abizaid A, de Brito FS Jr, Ribeiro HB, Ruel M, Lima VC, Nietlispach F, Cheema AN. The Learning Curve and Annual Procedure Volume Standards for Optimum Outcomes of Transcatheter Aortic Valve Replacement: Findings From an International Registry. *JACC Cardiovasc Interv.* 2018;11:1669-79.

23. Salemi A, Sedrakyan A, Mao J, Elmously A, Wijeysundera H, Tam DY, Di Franco A, Redwood S, Girardi LN, Fremes SE, Gaudino M. Individual Operator Experience and Outcomes in Transcatheter Aortic Valve Replacement. *JACC Cardiovasc Interv.* 2019;12:90-7.

24. Vemulapalli S, Carroll JD, Mack MJ, Li Z, Dai D, Kosinski AS, Kumbhani DJ, Ruiz CE, Thourani VH, Hanzel G, Gleason TG, Herrmann HC, Brindis RG, Bavaria JE. Procedural Volume and Outcomes for Transcatheter Aortic-Valve Replacement. *N Engl J Med.* 2019;380:2541-50.

25. Russo MJ, McCabe JM, Thourani VH, Guerrero M, Genereux P, Nguyen T, Hong KN, Kodali S, Leon MB. Case volume and Outcomes After TAVR With Balloon-Expandable Prostheses: Insights From TVT Registry. *J Am Coll Cardiol.* 2019;73:427-40.

26. Carroll JD, Vemulapalli S, Dai D, Matsouaka R, Blackstone E, Edwards F, Masoudi FA, Mack M, Peterson ED, Holmes D, Rumsfeld JS, Tuzcu EM, Grover F. Procedural Experience for Transcatheter Aortic Valve Replacement and Relation to Outcomes: The STS/ACC TVT Registry. *J Am Coll Cardiol.* 2017;70:29-41.

27. Barbanti M, Yang TH, Rodès Cabau J, Tamburino C, Wood DA, Jilaihawi H, Blanke P, Makkar RR, Latib A, Colombo A, Tarantini G, Raju R, Binder RK, Nguyen G, Freeman M, Ribeiro HB, Kapadia S, Min J, Feuchtner G, Gurtvich R, Alqoofi F, Pelletier M, Ussia GP, Napodano M, de Brito FS Jr, Kodali S, Norgaard BL, Hansson NC, Pache G, Canovas SJ, Zhang H, Leon MB, Webb JG, Leipsic J. Anatomical and procedural features associated with aortic root rupture during balloon-expandable transcatheter aortic valve replacement. *Circulation.* 2013;128:244-53.

28. Hansson NC, Nørgaard BL, Barbanti M, Nielsen NE, Yang TH, Tamburino C, Dvir D, Jilaihawi H, Blanke P, Makkar RR, Latib A, Colombo A, Tarantini G, Raju R, Wood D, Andersen HR, Ribeiro HB, Kapadia S, Min J, Feuchtner G, Gurvitch R, Alqoofi F, Pelletier M, Ussia GP, Napodano M, Sandoli de Brito F Jr, Kodali S, Pache G, Canovas SJ, Berger A, Murphy D, Svensson LG, Rodés-Cabau J, Leon MB, Webb JG, Leipsic J. The impact of calcium volume and distribution in aortic root injury related to

balloon-expandable transcatheter aortic valve replacement. *J Cardiovasc Comput Tomogr.* 2015;9:382-92.

29. Barbanti M, Leipsic J, Binder R, Dvir D, Tan J, Freeman M, Norgaard B, Hansson N, Cheung A, Ye J, Yang TH, Maryniak K, Raju R, Thompson A, Blanke P, Lauck S, Wood D, Webb J. Underexpansion and ad hoc post-dilation in selected patients undergoing balloon-expandable transcatheter aortic valve replacement. *J Am Coll Cardiol.* 2014;63:976-81.

30. Blanke P, Weir-McCall JR, Achenbach S, Delgado V, Hausleiter J, Jilaihawi H, Marwan M, Norgaard BL, Piazza N, Schoenhagen P, Leipsic JA. Computed tomography imaging in the context of transcatheter aortic valve implantation (TAVI) / transcatheter aortic valve replacement (TAVR): An expert consensus document of the Society of Cardiovascular Computed Tomography. *J Cardiovasc Comput Tomogr.* 2019;13:1-20.

31. Bianchi M, Marom G, Ghosh RP, Rotman OM, Parikh P, Gruberg L, Bluestein D. Patient-specific simulation of transcatheter aortic valve replacement: impact of deployment options on paravalvular leakage. *Biomech Model Mechanobiol.* 2019;18:435-51.

32. Schultz C, Rodriguez-Olivares R, Bosmans J, Lefèvre T, De Santis G, Bruining N, Collas V, Dezutter T, Bosmans B, Rahhab Z, El Faquir N, Watanabe Y, Segers P, Verhegghe B, Chevalier B, van Mieghem N, De Beule M, Mortier P, de Jaegere P. Patient-specific image-based computer simulation for theprediction of valve morphology and calcium displacement after TAVI with the Medtronic CoreValve and the Edwards SAPIEN valve. *EuroIntervention.* 2016;11:1044-52.

33. Mack MJ, Brennan JM, Brindis R, Carroll J, Edwards F, Grover F, Shahian D, Tuzcu EM, Peterson ED, Rumsfeld JS, Hewitt K, Shewan C, Michaels J, Christensen B, Christian A, O'Brien S, Holmes D; STS/ACC TVT Registry. Outcomes following transcatheter aortic valve replacement in the United States. *JAMA.* 2013;310:2069-77.

34. Yoon SH, Ahn JM, Hayashida K, Watanabe Y, Shirai S, Kao HL, Yin WH, Lee MK, Tay E, Araki M, Yamanaka F, Arai T, Lin MS, Park JB, Park DW, Kang SJ, Lee SW, Kim YH, Lee CW, Park SW, Muramatsu T, Hanyu M, Kozuma K, Kim HS, Saito S, Park SJ; Asian TAVR Investigators. Clinical Outcomes Following Transcatheter Aortic Valve Replacement in Asian Population. *JACC Cardiovasc Interv.* 2016;9:926-33.

35. Yoon SH, Bleiziffer S, De Backer O, Delgado V, Arai T, Ziegelmueller J, Barbanti M, Sharma R, Perlman GY, Khalique OK, Holy EW, Saraf S, Deuschl F, Fujita B, Ruile P, Neumann FJ, Pache G, Takahashi M, Kaneko H, Schmidt T, Ohno Y, Schofer N, Kong WKF, Tay E, Sugiyama D, Kawamori H, Maeno Y, Abramowitz Y, Chakravarty T, Nakamura M, Kuwata S, Yong G, Kao HL, Lee M, Kim HS, Modine T, Wong SC, Bedgoni F, Testa L, Teiger E, Butter C, Ensminger SM, Schaefer U, Dvir D, Blanke P, Leipsic J, Nietlispach F, Abdel-Wahab M, Chevalier B, Tamburino C, Hildick-Smith D, Whisenant BK, Park SJ, Colombo A, Latib A, Kodali SK, Bax JJ, Søndergaard L, Webb JG, Lefèvre T, Leon MB, Makkar R. Outcomes in Transcatheter Aortic Valve Replacement for Bicuspid Versus Tricuspid Aortic Valve Stenosis. *J Am Coll Cardiol.* 2017;69:2579-89.

36. Makkar RR, Yoon SH, Leon MB, Chakravarty T, Rinaldi M, Shah PB, Skipper ER, Thourani VH, Babaliaros V, Cheng W, Trento A, Vemulapalli S, Kapadia SR, Kodali S, Mack MJ, Tang GHL, Kaneko T. Association Between Transcatheter Aortic Valve Replacement for Bicuspid vs Tricuspid Aortic Stenosis and Mortality or Stroke. *JAMA.* 2019;321:2193-202.

37. Gao G, Wu YX, Grunkemeier GL, Furnary AP, Starr A. Durability of pericardial versus porcine aortic valves. *J Am Coll Cardiol.* 2004;44:384-8.

38. David TE, Ivanov J, Armstrong S, Feindel CM, Cohen G. Late results of heart valve replacement with the Hancock II bioprosthesis. *J Thorac Cardiovasc Surg.* 2001;121:268-77.

39. Søndergaard L, Ihlemann N, Capodanno D, Jørgensen TH, Nissen H, Kjeldsen BJ, Chang Y, Steinbrüchel DA, Olsen PS, Petronio AS, Thyregod HGH. Durability of Transcatheter and Surgical Bioprosthetic Aortic Valves in Patients at Lower Surgical Risk. *J Am Coll Cardiol.* 2019;73:546-53.

40. Costa G, Criscione E, Todaro D, Tamburino C, Barbanti M. Long-term Transcatheter Aortic Valve Durability. *Interv Cardiol.* 2019;14:62-9.

41. Barbanti M, Costa G, Zappulla P, Todaro D, Picci A, Rapisarda G, Di Simone E, Sicuso R, Buccheri S, Gulino S, Pilato G, La Spina K, D'Arrigo P, Valvo R, Indelicato A, Giannazzo D, Immè S, Tamburino C, Patanè M, Sgroi C, Giuffrida A, Trovato D, Monte IP, Deste W, Capranzano P, Capodanno D, Tamburino C. Incidence of Long-Term Structural Valve Dysfunction and Bioprosthetic Valve Failure After Transcatheter Aortic Valve Replacement. *J Am Heart Assoc.* 2018;7:e008440.

42. Naji P, Griffin BP, Sabik JF, Kusunose K, Asfahan F, Popovic ZB, Rodriguez LL, Lytle BW, Grimm RA, Svensson LG, Desai MY. Characteristics and Outcomes of Patients With Severe Bioprosthetic Aortic Valve Stenosis Undergoing Redo Surgical Aortic Valve Replacement. *Circulation.* 2015;132:1953-60.

43. Dvir D, Webb JG, Bleiziffer S, Pasic M, Waksman R, Kodali S, Barbanti M, Latib A, Schaefer U, Rodés-Cabau J, Treede H, Piazza N, Hildick-Smith D, Himbert D, Walther T, Hengstenberg C, Nissen H, Bekeredjian R, Presbitero P, Ferrari E, Segev A, de Weger A, Windecker S, Moat NE, Napodano M, Wilbring M, Cerillo AG, Brecker S, Tchetche D, Lefèvre T, De Marco F, Fiorina C, Petronio AS, Teles RC, Testa L, Laborde JC, Leon MB, Kornowski R; Valve-in-Valve International Data Registry Investigators. Transcatheter aortic valve implantation in failed bioprosthetic surgical valves. *JAMA.* 2014;312:162-70.

44. Ribeiro HB, Webb JG, Makkar RR, Cohen MG, Kapadia SR, Kodali S, Tamburino C, Barbanti M, Chakravarty T, Jilaihawi H, Paradis JM, de Brito FS Jr, Canovas SJ, Cheema NA, de Jaegere PP, del Valle R, Chiam PT, Moreno R, Pradas G, Ruel M, Salgado-Fernandez J, Sarmento-Leite R, Toeg HD, Velianou JL, Zajarias A, Babaliaros V, Cura F, Dagar AE, Manoharan G, Lerakis S, Pichard AD, Radhakrishnan S, Perin MA, Dumont E, Larose E, Pasian SG, Nombela-Franco L, Urena M, Tuzcu EM, Leon MB, Amat-Santos IJ, Leipsic J, Rodés-Cabau J. Predictive factors, management, and clinical outcomes of coronary obstruction following transcatheter aortic valve implantation: insights from a large multicenter registry. *J Am Coll Cardiol.* 2013;62:1552-62.

45. Holmes DR Jr, Nishimura RA, Grover FL, Brindis RG, Carroll JD, Edwards FH, Peterson ED, Rumsfeld JS, Shahian DM, Thourani VH, Tuzcu EM, Vemulapalli S, Hewitt K, Michaels J, Fitzgerald S, Mack MJ; STS/ACC TVT Registry. Annual Outcomes With Transcatheter Valve Therapy: From the STS/ACC TVT Registry. *J Am Coll Cardiol.* 2015;66:2813-23.

46. Ribeiro HB, Rodés-Cabau J, Blanke P, Leipsic J, Kwan Park J, Bapat V, Makkar R, Simonato M, Barbanti M, Schofer J, Bleiziffer S, Latib A, Hildick-Smith D, Presbitero P, Windecker S, Napodano M, Cerillo AG, Abdel-Wahab M, Tchetche D, Fiorina C, Sinning JM, Cohen MG, Guerrero ME, Whisenant B, Nietlispach F, Palma JH, Nombela-Franco L, de Weger A, Kass M, Sandoli de Brito F Jr, Lemos PA, Kornowski R, Webb J, Dvir D. Incidence, predictors, and clinical outcomes of coronary obstruction following transcatheter aortic valve replacement for degenerative bioprosthetic surgical valves: insights from the VIVID registry. *Eur Heart J.* 2018;39:687-95.

47. Jabbour RJ, Tanaka A, Finkelstein A, Mack M, Tamburino C, Van Mieghem N, de Backer O, Testa L, Gatto P, Purita P, Rahhab Z, Veulemans V, Stundl A, Barbanti M, Nerla R, Sinning JM, Dvir D, Tarantini G, Szerlip M, Scholtz W, Scholtz S, Tchetche D, Castriota F, Butter C, Søndergaard L, Abdel-Wahab M, Sievert H, Alfieri O, Webb J, Rodés-Cabau J, Colombo A, Latib A. Delayed Coronary Obstruction After Transcatheter Aortic Valve Replacement. *J Am Coll Cardiol.* 2018;71:1513-24.

48. Dvir D, Leipsic J, Blanke P, Ribeiro HB, Kornowski R, Pichard A, Rodes-Cabau J, Wood DA, Stub D, Ben-Dor I, Maluenda G, Makkar RR, Webb JG. Coronary obstruction in transcatheter aortic valve-in-valve implantation: preprocedural evaluation, device selection, protection, and treatment. *Circ Cardiovasc Interv.* 2015 Jan;8(1).

49. Barbanti M. Avoiding Coronary Occlusion and Root Rupture in TAVI - The Role of Pre-procedural Imaging and Prosthesis Selection. *Interv Cardiol.* 2015; 10:94-7.

50. Dvir D, Khan J, Kornowski R, Komatsu I, Chatriwalla A, Mackenson GB, Simonato M, Ribeiro H, Wood D, Leipsic J, Webb J, Mylotte D. Novel strategies in aortic valve-in-valve therapy including bioprosthetic valve fracture and BASILICA. *EuroIntervention.* 2018;14:AB74-82.

51. Bleiziffer S, Erlebach M, Simonato M, Pibarot P, Webb J, Capek L, Windecker S, George I, Sinning JM, Horlick E, Napodano M, Holzhey DM, Petursson P, Cerillo A, Bonaros N, Ferrari E, Cohen MG, Baquero G, Jones TL, Kalra A, Reardon MJ, Chhatriwalla A, Gama Ribeiro V, Alnasser S, Van Mieghem NM, Rustenbach CJ, Schofer J, Garcia S, Zeus T, Champagnac D, Bekeredjian R, Kornowski R, Lange R, Dvir D. Incidence, predictors and clinical outcomes of residual stenosis after aortic valve-in-valve. *Heart.* 2018; 104:828-34.

52. Simonato M, Azadani AN, Webb J, Leipsic J, Kornowski R, Vahanian A, Wood D, Piazza N, Kodali S, Ye J, Whisenant B, Gaia D, Aziz M, Pasala T, Mehilli J, Wijeysundera HC, Tchetche D, Moat N, Teles R, Petronio AS, Hildick-Smith D, Landes U, Windecker S, Arbel Y, Mendiz O, Makkar R, Tseng E, Dvir D. In vitro evaluation of implantation depth in valve-in-valve using different transcatheter heart valves. *EuroIntervention.* 2016;12:909-17.

53. Chhatriwalla AK, Allen KB, Saxon JT, Cohen DJ, Aggarwal S, Hart AJ, Baron SJ, Dvir D, Borkon AM. Bioprosthetic Valve Fracture Improves the Hemodynamic Results of Valve-in-Valve Transcatheter Aortic Valve Replacement. *Circ Cardiovasc Interv.* 2017;10:e005216.

54. Barbanti M, Webb JG, Tamburino C, Van Mieghem NM, Makkar RR, Piazza N, Latib A, Sinning JM, Won-Keun K, Bleiziffer S, Bedogni F, Kapadia S, Tchetche D, Rodés-Cabau J, Fiorina C, Nombela-Franco L, De Marco F, de Jaegere PP, Chakravarty T, Vaquerizo B, Colombo A, Svensson L, Lange R, Nickenig G, Möllmann H, Walther T, Della Rosa F, Elhmidi Y, Dvir D, Brambilla N, Immè S, Sgroi C, Gulino S, Todaro D, Pilato G, Petronio AS, Tamburino C. Outcomes of Redo Transcatheter Aortic Valve Replacement for the Treatment of Postprocedural and Late Occurrence of Paravalvular Regurgitation and Transcatheter Valve Failure. *Circ Cardiovasc Interv.* 2016 Sep;9(9).

55. Mack MJ, Leon MB, Smith CR, Miller DC, Moses JW, Tuzcu EM, Webb JG, Douglas PS, Anderson WN, Blackstone EH, Kodali SK, Makkar RR, Fontana GP, Kapadia S, Bavaria J, Hahn RT, Thourani VH, Babaliaros V, Pichard A, Herrmann HC, Brown DL, Williams M, Akin J, Davidson MJ, Svensson LG; PARTNER 1 trial investigators. 5-year outcomes of transcatheter aortic valve replacement or surgical aortic valve replacement for high surgical risk patients with aortic stenosis (PARTNER 1): a randomised controlled trial. *Lancet.* 2015;385:2477-84.

56. Douglas PS, Leon MB, Mack MJ, Svensson LG, Webb JG, Hahn RT, Pibarot P, Weissman NJ, Miller DC, Kapadia S, Herrmann HC, Kodali SK, Makkar RR, Thourani VH, Lerakis S, Lowry AM, Rajeswaran J, Finn MT, Alu MC, Smith CR, Blackstone EH; PARTNER Trial Investigators. Longitudinal Hemodynamics of Transcatheter and Surgical Aortic Valves in the PARTNER Trial. *JAMA Cardiol.* 2017;2:1197-206.

57. Capodanno D, Petronio AS, Prendergast B, Eltchaninoff H, Vahanian A, Modine T, Lancellotti P, Sondergaard L, Ludman PF, Tamburino C, Piazza N, Hancock J, Mehilli J, Byrne RA, Baumbach A, Kappetein AP, Windecker S, Bax J, Haude M. Standardized definitions of structural deterioration and valve failure in assessing long-term durability of transcatheter and surgical aortic bioprosthetic valves: a consensus statement from the European Association of Percutaneous Cardiovascular Interventions (EAPCI) endorsed by the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J.* 2017;38:3382-90.

58. Eltchaninoff H, Durand E, Avinée G, Tron C, Litzler PY, Bauer F, Dacher JN, Werhlin C, Bouhzam N, Bettinger N, Candolfi P, Cribier A. Assessment of structural valve deterioration of transcatheter aortic bioprosthetic balloon-expandable valves using the new European consensus definition. *EuroIntervention.* 2018;14:e264-71.

59. Panico RA, Giannini C, De Carlo M, Angelillis M, Spontoni P, Pieroni A, Costa G, Bertini P, Guarracino F, Petronio AS. Long-term results and durability of the CoreValve transcatheter aortic bioprosthesis: outcomes beyond five years. *EuroIntervention.* 2019;14:1639-47.

60. Holy EW, Kebernik J, Abdelghani M, Stämpfli SF, Hellermann J, Allali A, El-Mawardy M, Sachse S, Lüscher TF, Tanner FC, Richardt G, Abdel-Wahab M. Long-term durability and haemodynamic performance of a self-expanding transcatheter heart valve beyond five years after implantation: a prospective observational study applying the standardised definitions of structural deterioration and valve failure. *EuroIntervention.* 2018;14:e390-6.

61. Deutsch MA, Erlebach M, Burri M, Hapfelmeier A, Witt OG, Ziegelmueller JA, Wottke M, Ruge H, Krane M, Piazza N, Bleiziffer S, Lange R. Beyond the five-year horizon: long-term outcome of high-risk and inoperable patients undergoing TAVR with first-generation devices. *EuroIntervention.* 2018;14:41-9.

62. Durand E, Sokoloff A, Urena-Alcazar M, Chevalier B, Chassaing S, Didier R, Tron C, Litzler PY, Bouleti C, Himbert D, Hovasse T, Bar O, Avinée G, Iung B, Blanchard D, Gilard M, Cribier A, Lefevre T, Eltchaninoff H. Assessment of Long-Term Structural Deterioration of Transcatheter Aortic Bioprosthetic Valves Using the New European Definition. *Circ Cardiovasc Interv.* 2019;12:e007597.

63. Didier R, Eltchaninoff H, Donzeau-Gouge P, Chevreul K, Fajadet J, Leprince P, Leguerrier A, Lièvre M, Prat A, Teiger E, Lefevre T, Tchetché D, Carrié D, Himbert D, Albat B, Cribier A, Sudre A, Blanchard D, Rioufol G, Collet F, Houel R, Dos Santos P, Meneveau N, Ghostine S, Manigold T, Guyon P, Cuisset T, Le Breton H, Delepine S, Favereau X, Souteyrand G, Ohlmann P, Doisy V, Lognoné T, Gommeaux A, Claudel JP, Bourlon F, Bertrand B, Iung B, Gilard M. Five-Year Clinical Outcome and Valve Durability After Transcatheter Aortic Valve Replacement in High-Risk Patients. *Circulation.* 2018;138:2597-607.

64. Blackman DJ, Saraf S, MacCarthy PA, Myat A, Anderson SG, Malkin CJ, Cunnington MS, Somers K, Brennan P, Manoharan G, Parker J, Aldalati O, Brecker SJ, Dowling C, Hoole SP, Dorman S, Mullen M, Kennon S, Jerrum M, Chandrala P, Roberts DH, Tay J, Doshi SN, Ludman PF, Fairbairn TA, Crowe J, Levy RD, Banning AP, Ruparelia N, Spence MS, Hildick-Smith D. Long-Term Durability of Transcatheter Aortic Valve Prostheses. *J Am Coll Cardiol.* 2019;73:537-45.

65. Barbanti M, Todaro D. Midterm Outcomes With the Self-expanding ACURATE neo Aortic Bioprosthesis: The "Bumblebee Paradox" in Transcatheter Aortic Valve Replacement. *JACC Cardiovasc Interv.* 2018;11:1375-6.

66. Zivelonghi C, Pesarini G, Scarsini R, Lunardi M, Piccoli A, Ferrero V, Gottin L, Vassanelli C, Ribichini F. Coronary Catheterization and Percutaneous Interventions After Transcatheter Aortic Valve Implantation. *Am J Cardiol.* 2017;120:625-31.

67. Tang GHL, Zaid S, Gupta E, Ahmad H, Patel N, Khan M, Khan A, Kovacic JC, Lansman SL, Dangas GD, Sharma SK, Kini A. Impact of Initial Evolut Transcatheter Aortic Valve Replacement Deployment Orientation on Final Valve Orientation and Coronary Reaccess. *Circ Cardiovasc Interv.* 2019;12:e008044.