

Transcatheter aortic valve update 2013

Christos V. Bourantas¹, MD, PhD; Nicolas M. Van Mieghem¹, MD; Osama Soliman², MD, PhD; Carlos A. M. Campos¹, MD; Javaid Iqbal¹, MRCP, PhD; Patrick W. Serruys^{1*}, MD, PhD

1. ThoraxCenter; Erasmus Medical Center, Rotterdam, The Netherlands; 2. Cardialysis Imaging Core Lab, Rotterdam, The Netherlands

KEYWORDS

- aortic stenosis
- cardiovascular imaging
- prognosis
- transcatheter aortic valve implantation

Abstract

Cumulative evidence has demonstrated that transcatheter aortic valve implantation (TAVI) constitutes an effective treatment option for patients with severe symptomatic aortic stenosis and a high operative risk. New valve designs and TAVI-enabling devices have simplified the procedure, reduced the risk of complications, and broadened the applications of this treatment. The global adoption of TAVI allows us to appreciate the advantages, potentialities and caveats of the technology, identify patients who would benefit from TAVI and stratify more accurately the risk of complications. The focus of this article is to discuss the advances in this field, present the current evidence, and highlight the developments and strategies proposed to address the limitations of TAVI treatment.

*Corresponding author: Interventional Cardiology Department, Erasmus MC, 's-Gravendijkwal 230, 3015 CE Rotterdam, The Netherlands. E-mail: p.w.j.c.serruys@erasmusmc.nl

Introduction

Transcatheter aortic valve implantation (TAVI) was introduced over a decade ago by Cribier and colleagues and has revolutionised the treatment of symptomatic severe aortic stenosis (AS). Its less invasive nature, compared to surgical aortic valve replacement (SAVR), appeared particularly attractive for the treatment of high-risk or inoperable patient cohorts. Multiple prospective registries and the randomised Placement of AoRTic TraNscatheter Valves (PARTNER) trial support the broad application of this treatment in patients with a (very) high operative risk¹.

The global adoption of TAVI allowed us to appreciate its potential, refine patient selection and optimise device and treatment strategies so as to reduce the risk of complications. In recent years several trials have been organised to explore the efficacy of TAVI in different populations and a considerable effort has been made towards the development of new more effective valves and TAVI-enabling devices that would simplify the procedure, increase safety, and permit treatment of patients with a complex valve anatomy. In this review article we present the current evidence stemming from registries and clinical trials, cite the upcoming or ongoing clinical studies, discuss the limitations of TAVI treatment and provide an update about the recent advances in the field.

Clinical evidence

Three randomised controlled trials have examined the efficacy of TAVI in different populations. The PARTNER Cohort B trial demonstrated a 20% absolute reduction in all-cause mortality at one-year follow-up and a better quality of life in inoperable patients undergoing TAVI as compared to those receiving optimal medical therapy, including balloon valvuloplasty¹. The PARTNER Cohort A trial randomised patients at high operative risk to TAVI or SAVR and showed no difference in mortality between the two groups at two-year follow-up. TAVI patients experienced more neurological events or major vascular complications whereas SAVR patients had more bleeding complications². The STAC-CATO trial randomised elderly low-risk patients (>75 years old) to transapical TAVI or SAVR. The study was prematurely ended after enrolling only 70 patients as there was an increased event rate in the TAVI arm³.

Results from large national registries such as the United Kingdom, the French, and the German registries confirmed the findings of the randomised trials, underscored a high success rate and an acceptable periprocedural event rate, and provided additional data about the short and mid-term efficacy of TAVI treatment⁴⁻⁶. Although there is robust evidence to support the short- and mid-term effectiveness of TAVI, there is limited data about the long-term efficacy of the implanted devices. The first report that assessed the long-term performance of TAVI, included 70 patients implanted with an Edwards SAPIEN THV prosthesis (Edwards Lifesciences, Irvine, CA, USA) who were followed-up for 3.5 years and had serial echocardiographic evaluation and computed tomographic (CT) imaging at three-year follow-up⁷. Only one patient had a re-operation because of endocarditis.

Echocardiography demonstrated stable prosthesis function with only a minor decrease in the aortic valve area (by 0.06 cm²/year, $p < 0.001$) and no deterioration in the reported aortic regurgitation, while CT did not show evidence of leaflet thickening, fusion or calcification nor frame fracture. Similar were the results of the Italian CoreValve registry which showed no significant changes in the transaortic valve gradient or the reported aortic insufficiency at three-year follow-up⁸. Recently Rodes-Cabau provided further insights into valve durability presenting the five-year follow-up data of the Canadian Multicenter Experience study⁹. A total of 333 patients underwent TAVI with an Edwards SAPIEN THV device. Serial echocardiography demonstrated a gradual decrease in the aortic valve area at two-year follow-up (from 1.62±0.38 cm² to 1.44±0.33 cm² at one year, and 1.38±0.35 cm² at two years, $p < 0.007$) which did not change at three-year (1.36±0.38 cm²) and four-year follow-up (1.35±0.37 cm²). These findings however, require further confirmation as in this study only 50 patients had echocardiographic evaluation at 3-year, and 28 patients at 4-year follow-up.

The Medtronic CoreValve® U.S. Pivotal Trial (NCT01240902) randomising AS patients at high operative risk to TAVI with the Medtronic CoreValve® (Medtronic, Minneapolis, MN, USA) or SAVR and also exploring TAVI with the Medtronic CoreValve in inoperable patients (not randomised) has recently completed enrolment and the results are anticipated in due course. Two randomised clinical trials are exploring TAVI vs. SAVR in patients at intermediate operative risk: the PARTNER II Cohort A (ClinicalTrials.gov, number NCT01314313) and the SURGical and Transcatheter Aortic Valve Implantation (SURTAVI) trial (ClinicalTrials.gov, number NCT01586910). PARTNER II Cohort A will randomise about 2,000 patients and SURTAVI 2,500. Both are non-inferiority studies and will include patients with coronary artery disease amenable by percutaneous coronary intervention (**Figure 1**). Finally, the Percutaneous Coronary Intervention prior to transcatheter aortic Valve implantation (ACTIVATION) trial has recently commenced and aims to randomise 310 patients with ischaemic coronary artery disease to direct TAVI and percutaneous coronary intervention before TAVI on a 1:1 basis so as to examine the effect of revascularisation on clinical outcomes at one-year follow-up.

Complications in TAVI

Stroke, vascular complications, a dysfunctional prosthesis (i.e., device malapposition and migration or paravalvular leak), and conduction abnormalities are the most frequent complications associated with TAVI, whereas aortic dissection and rupture, coronary ostium obstruction, periaortic haematoma, tamponade and mitral injury are rare but potentially fatal acute complications. The definitions of these complications have recently been standardised by the Valve Academic Research Consortium-2 consensus document¹⁰. New valve designs and TAVI-enabling devices have been developed to simplify the procedure, reduce the risk of adverse events and allow the use of this treatment in complex anatomies and a broader number of patients.

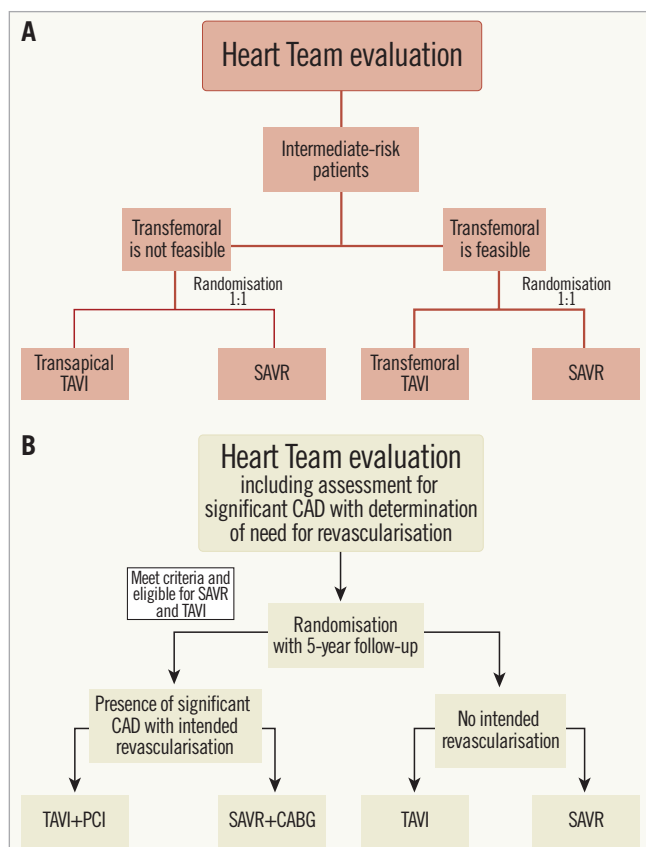


Figure 1. Flow chart of the PARTNER II Cohort A (A) and the SURTAVI trials (B). TAVI: transcatheter aortic valve implantation; CAD: coronary artery disease; PCI: percutaneous coronary intervention; SAVR: surgical aortic valve replacement

CEREBROVASCULAR EVENTS

Cerebrovascular events (CVE) negatively impact survival and quality of life in patients treated with TAVI. Recent studies have provided additional evidence about the incidence and timing of these events and showed that most of the CVE occur within the first 24 hours post procedure and that their incidence remains high for the first two months after device implantation. Multiple manipulations during implantation such as repositioning and post-dilation of the prosthesis appear to augment the risk for CVE¹¹.

Magnetic resonance imaging and transcranial Doppler studies have shown that TAVI is associated with new cerebral lesions, supporting the hypothesis that most of the CVE have embolic aetiology; while recently van Mieghem et al investigated the histopathology of the embolised material and demonstrated that most of the debris that travels to the brain derives either from the native aortic valve or the aortic wall^{12,13}. Brain hypoperfusion during device deployment has also been considered as a potential cause of stroke, whereas new onset atrial fibrillation is associated with the CVE occurring between the first 24 hours and the first two months post-procedure¹⁴.

To reduce the risk of CVE, three cerebral embolic protection devices have been developed which were tested in small clinical studies (Table 1)^{13,15,16}. Direct implantation of the valve without balloon predilation is also likely to decrease the risk of CVE. The SIMPLIFY TAVI trial has recently commenced and aims to randomise 110 patients with severe AS and an ejection fraction <35% to TAVI with and without predilation and compare the 30-day event rate (all-cause mortality, stroke, non-fatal myocardial infarction, acute kidney injury, and pacemaker implantation) in the two groups (ClinicalTrials.gov, number NCT01539746).




Antiplatelet treatment is strongly recommended for patients undergoing TAVI but there is a lack of evidence about the optimal regimen and the duration of treatment¹⁷. According to the recently published ACCF/AATS/SCAI/STS guidelines dual antiplatelet treatment with aspirin and clopidogrel should be initiated in all the patients, but the dose and the duration of the treatment has not been specified. Of note, a small-scale randomised trial that included 90 patients undergoing TAVI showed no difference in the prognosis between patients treated with dual antiplatelet treatment and those receiving only aspirin¹⁸. Further evidence is expected from the Aspirin versus aspirin and clopidogrel following Transcatheter Aortic Valve Implantation (ARTE) trial that is currently underway and aims to randomise 200 patients to aspirin versus aspirin and clopidogrel in order to compare the efficacy of these therapies in the prevention of major ischaemic events (ClinicalTrials.gov, number NCT01559298).

VASCULAR COMPLICATIONS

Vascular complications and major bleeding are significant limitations of TAVI. Their incidence is increased when TAVI is performed through the transfemoral route, which nonetheless constitutes the preferred access owing to its less invasive nature. Evaluation of the iliofemoral anatomy with multislice computed tomography (MSCT) and, more specifically, assessment of the vessel size, degree of calcification, plaque burden and tortuosity, allow identification of the patients who are suitable for transfemoral TAVI and reduce the risk of vascular complications. In a recent study, Van Mieghem et al examined the incidence, predictors, and implications of access-site complications in almost 1,000 patients implanted through the transfemoral approach¹⁹. They found that only the size of the sheath was a predictor of vascular complications, while major bleeding was independently related to female gender, larger sheaths, a history of peripheral vascular disease and percutaneous access and closure. Vascular complications and major bleeding were associated with worse outcomes.

Appreciating the effect of a sheath's dimensions on vascular adverse events, an effort has been made in recent years to reduce the size of the delivery systems and improve the crossing profile of the new-generation valves. Edwards Lifesciences has recently introduced a low profile (16 Fr) expandable sheath called eSheath that expands transiently when it is in the aorta to allow the passage of the mounted valve and then returns to its natural dimensions. Terumo (Terumo Corporation, Somerset, NJ, USA) has also developed a less traumatic sheath SoloPath® with an even lower crossing

Table 1. Design, advantages and disadvantages of the currently available cerebral protection devices.

Cerebral protection devices	Design	Advantages	Limitations
 <p>Claret Pro</p>	<p>Has two filters, a proximal that consists of a nitinol frame, and a polyurethane filter with 140 µm diameter pores which is attached to a 100 cm catheter and a non-proprietary distal filter. The proximal filter is placed to the right brachiocephalic artery whereas the distal filter is placed to the left common carotid artery</p>	<p>Requires a small sheath (6 Fr). Is able to capture the debris delivered during the procedure</p>	<p>Can be implanted only through the right radial/brachial artery and not through an alternative access. The device has to be removed post procedure. Does not protect the left vertebral artery and in a small feasibility study it was possible to deploy the distal filter in only 73% of the patients studied. Small-scale studies have shown that the device can capture debris derived from the aorta and the aortic valve during TAVI; however, there is no clinical evidence in the context of a randomised control trial to support the use of the device during TAVI</p>
 <p>Triguard</p>	<p>Consists of a nitinol mesh that is fixed onto a nitinol frame and is used to deflect the debris, 2 stabilisers that provide fixation of the device on the aortic arch, and a tail end that connects the device with the delivery system</p>	<p>It can be implanted through both the left and right femoral arteries. Permits full coverage of the supra-aortic trunk. Can be left in the aortic arch for days</p>	<p>It is a deflector device that redirects debris away from the brain towards the descending aorta. Requires a relatively large sheath (9 Fr). Although it has been tested in a small feasibility study there are no robust randomised clinical data to support its use in everyday practice.</p>
 <p>Embrella embolic deflector</p>	<p>Incorporates a heparin-coated polyurethane membrane that is mounted on a nitinol frame which is attached to a 110 cm catheter. The device has three radiopaque markers which facilitate the correct positioning of the device</p>	<p>Requires a small sheath (6 Fr)</p>	<p>Cannot be deployed through an alternative access point. Does not protect always the left vertebral artery. It is a deflector device that redirects emboli away from the brain towards the peripheral arteries. There is a lack of evidence to support the value of the device in a clinical setting</p>

TAVI: transcatheter aortic valve implantation.

profile (diameter of the distal tip of 13 Fr) that can be used for the deployment of the Medtronic CoreValve. SoloPath is also expanded in the aorta with the use of a balloon to allow passage and deployment of the valve. The performance of this low-profile sheath was recently tested in a small feasibility study that included 27 patients with a complex, borderline iliofemoral anatomy. The vascular complications rate in this high-risk population was 18% which is comparable to the event rate reported in studies conducted in unselected patients, highlighting the potential value of this device in the management of patients with an unfavourable iliofemoral anatomy²⁰.











The smaller size of the new sheaths has permitted the development of closure devices for a controlled and safe sealing of the access site. To date, three devices have been tested in a clinical setting: the Prostar[®] (Abbott Vascular, Santa Clara, CA, USA) and the ProGlide (Abbott Vascular, Santa Clara, CA, USA) for the transfemoral and the APICA ASC (APICA Cardiovascular, Galway, Ireland) for the transapical approach, while others such as the ProMed (Promed, Santa Clara, CA, USA) and the InSeal (InSeal Medical, Caesarea, Israel), for the transfemoral access and the Permaseal[™] (Micro Intervention Devices, Bethlehem, PA, USA) for the transapical route are currently undergoing first-in-man studies²¹. Finally, two devices, the VasoStitch (VasoStitch Inc., Danville, CA, USA) for the transfemoral and the CardioClose (Entourage Medical, Menlo Park, CA, USA) for the transapical approach, are under preclinical evaluation.

PROSTHESIS DYSFUNCTION

Suboptimal valve positioning is a common problem seen in TAVI. The first-generation valves, i.e., the Edwards SAPIEN THV, the Edwards SAPIEN XT (Edwards Lifesciences, Irvine, CA, USA) and the CoreValve[®] could not be retrieved after positioning and thus, in case of an erroneous placement, the operator had to deploy a second device or refer the patient for urgent SAVR. To overcome this limitation several new valve systems have been developed that can be repositioned or even be retrieved if needed. Some of them have been tested in a clinical setting and a few have already acquired Conformité Européenne (CE) mark approval such as: the Direct Flow Medical valve (Direct Flow Medical Inc., Santa Rosa, CA, USA) that is both retrievable and repositionable, the JenaValve (JenaValve, Munich, Germany) and the Portico (St. Jude Medical, St Paul, MN, USA) that are both retrievable until being fully deployed, the Engager that is only repositionable (Medtronic, Minneapolis, MN, USA), and the Symetis[®] Acurate[™] (Symetis SA, Ecublens, Switzerland) that has a self-seating and self-sealing design that conforms with the native anatomy potentially leading to a lower incidence of paravalvular leak (**Table 2**).

Paravalvular aortic regurgitation after TAVI has been attributed to suboptimal device sizing and positioning. Two recently published studies have provided convincing evidence about the prognostic implications of a significant ($\geq 2/4$) aortic regurgitation²²⁻²³. Accurate evaluation of valve anatomy and sizing of the prosthesis

Table 2. Features and technological advances introduced in the second-generation valves to reduce the risk of complications. Images were obtained with permission from Bourantas et al³⁴.

Second-generation valves	Features of the second-generation valves
Direct Flow Medical 	Repositionable Retrievable after being fully deployed Low frame height designed to minimise conduction disturbances Bovine pericardial leaflets for increased durability
Jena 	Repositionable Anchoring system that facilitates optimal deployment Tactile feedback during deployment Low placement of the leaflets of the valve to minimise frame protrusion in the left ventricular outflow tract Large stent design to reduce the risk of coronary ostium obstruction Markers to facilitate device deployment
Engager 	Repositionable Anchoring system that facilitates optimal deployment Tactile feedback during deployment Markers to facilitate device deployment Bovine pericardial leaflets and anticalcification technology for increased durability
Portico 	Repositionable Low placement of the leaflets of the valve to minimise frame protrusion in the left ventricular outflow tract Large stent design to reduce the risk of coronary ostium obstruction Markers to facilitate device deployment Bovine pericardial leaflets and anticalcification technology for increased durability
Acurate 	Repositionable Anchoring system to facilitate optimal positioning Low placement of the leaflets of the valve to minimise frame protrusion in the left ventricular outflow tract Tactile feedback during deployment Markers to facilitate device deployment Additional cuff to reduce the risk of paravalvular leak Anticalcification technology for increased durability
CoreValve Evolut R 	Repositionable Retrievable after being fully deployed Low delivery profile Large stent design to reduce the risk of coronary ostium obstruction Markers to facilitate device deployment Extended skirt and modified cell geometry to reduce the risk of paravalvular leak Anticalcification technology for increased durability
Sapien III 	Incorporates a distal flex mechanism and fine positioning control for accurate placement Low delivery profile Low frame height designed to minimise conduction disturbances Circular deployment at the annulus for optimal haemodynamics Additional cuff to reduce the risk of paravalvular leak Bovine pericardial leaflets and anticalcification technology for increased durability
Lotus 	Repositionable Retrievable after being fully deployed Tactile feedback during deployment Low placement of the leaflets of the valve to minimise frame protrusion in the left ventricular outflow tract Additional cuff to reduce the risk of paravalvular leak Markers to facilitate device deployment Bovine pericardial leaflets and anticalcification technology for increased durability
Centera 	Repositionable Low delivery profile Motorised handle with touch deployment allows precise device placement Contoured frame designed for optimal seating and sealing in the annulus Low frame height designed to minimise conduction disturbances Bovine pericardial leaflets and anticalcification technology for increased durability
Heart leaflet technology 	Repositionable Markers to facilitate device deployment Additional cuff to reduce the risk of paravalvular leak

appear to reduce the risk of paravalvular regurgitation. Today, several imaging modalities are available for this purpose including 2-dimensional (2-D), 3-D and transoesophageal echocardiography, MSCT, x-ray aortography and magnetic resonance imaging. These modalities also allow assessment of the distance between aortic valve annulus and left main stem ostium, which is important for a successful procedure (i.e., a low origin of the left main stem has been associated with an increased risk of left main obstruction), evaluation of the calcification in the leaflets and annulus that can affect

treatment planning, and assessment of the take-off of the ascending aorta (i.e., horizontal or vertical take-off) which is important as a horizontal take-off may hinder correct and coaxial device deployment (**Figure 2**)²⁴.

Recent advances in imaging and image processing technology have allowed the development of new systems and data fusion techniques that permit comprehensive, real-time visualisation of the aortic valve anatomy and can be used in the catheterisation laboratory to guide treatment. The C-THV Paieon (Paieon Inc, New York, NY, USA), the

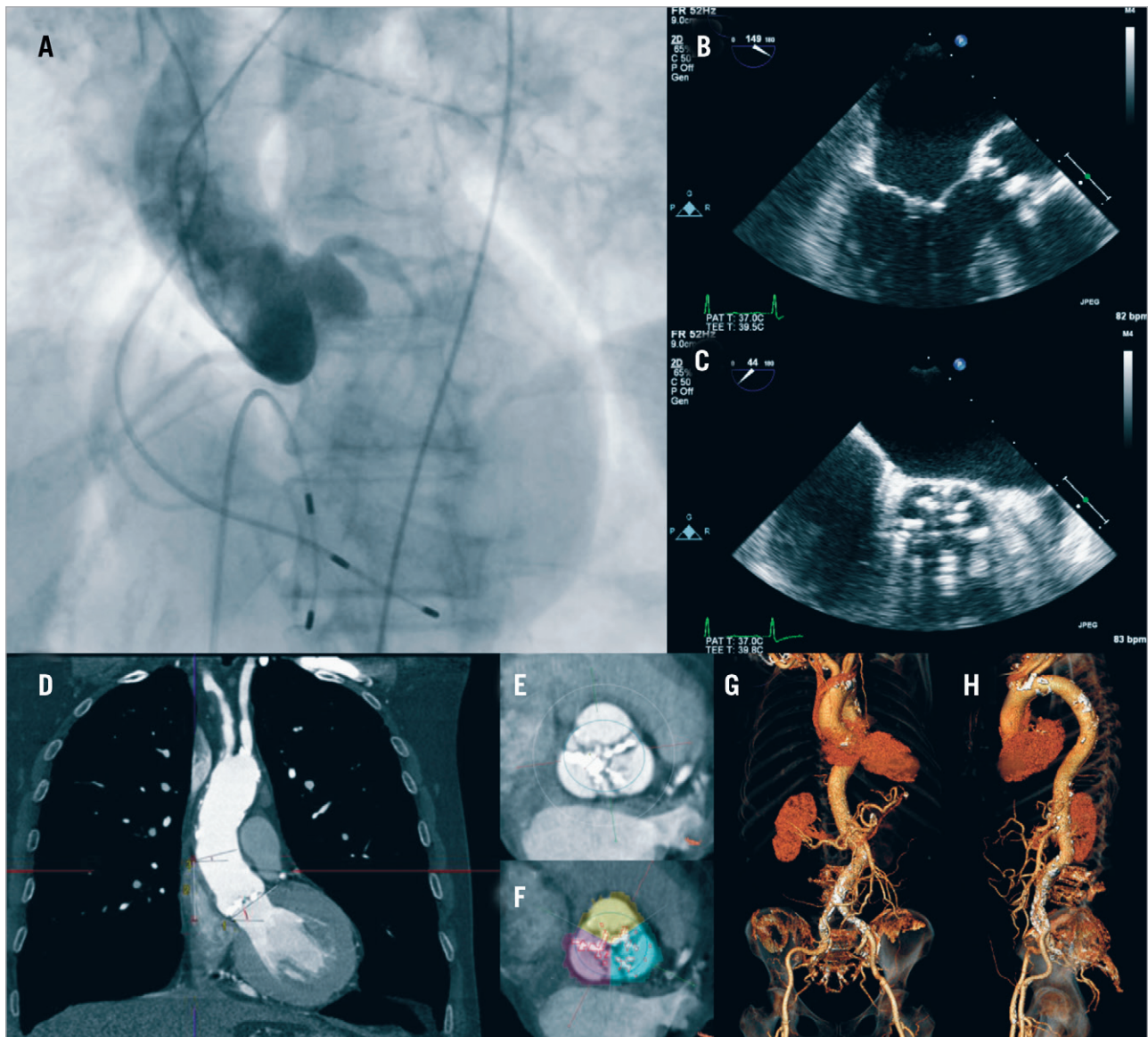


Figure 2. Imaging modalities used in the SURTAVI study to assess patients' suitability and procedural planning. (A) x-ray angiography is used to assess coronary anatomy and the morphology of the aorta; (B, C) transoesophageal echocardiography allows evaluation of aortic valve anatomy measurement of its dimensions and quantification of the severity of the aortic stenosis; (D-F) multislice computed tomography (MSCT) provides comprehensive images that permit accurate evaluation of the take-off of the aorta, and of the ostium of the left main stem and right coronary artery, assessment of the dimensions of the aortic root and valve and quantification of the calcification of the valve; (G-H) in addition MSCT provides detailed visualisation of the iliofemoral arteries and of the descending aorta, assessment of vessels' tortuosity and measurement of their dimensions.

3mensio valve™ system (3mensio Medical Imaging, Bilthoven, NL), the Phillips heart navigator (Phillips, Best, NL), and the DynaCT (Siemens AG, Erlangen, Germany) are software that can process angiographic or MSCT data to reconstruct coronary anatomy and define the best angiographic projection for treatment planning. Recent proof-of-concept studies validating these systems demonstrated a reduction in the paravalvular regurgitation in patients treated with the use of these software^{25,26}.

CONDUCTION DISTURBANCES

Conduction abnormalities are common complications seen during TAVI, especially in patients implanted with the self-expanding systems that are deployed deeper in the left ventricular outflow tract and exert a long-lasting radial force that can injure the conduction system of the heart. Although there is evidence that conduction abnormalities, which often require pacemaker implantation, may affect left ventricular systolic function and functional status, their effect on prognosis is questionable with most of the recently published studies showing no association between conduction abnormalities and prognosis and one study demonstrating increased mortality in the patients who develop left bundle branch block during TAVI²⁷⁻²⁹.

To reduce the risk of conduction abnormalities the second-generation self-expanding valves have a low frame height or a low placement of their leaflets in their frame that permit a minimal protrusion of the valves in the left ventricular outflow tract.

New developments in TAVI technology

Apart from the devices mentioned above that have already acquired CE mark approval, several other valves have been designed that are currently undergoing clinical evaluation such as: the Sapien III (Edwards Lifesciences, Irvine, CA, USA) which incorporates an additional cuff that covers the frame of the valve and is anticipated to reduce the incidence of paravalvular leak; the Lotus valve that is both retrievable and repositionable (Boston Scientific, Natick, MA, USA), the CoreValve Evolut R (Medtronic, Minneapolis, MN, USA) that has a low delivery profile; the self-expanding Centera (Edwards Lifesciences, Irvine, CA, USA) valve which has a low frame height to reduce the risk of conduction disturbances; as well as the HLT™ (HLT Inc., Maple Grove, MN, USA) valve that was initially implanted in humans in 2009 where it was found to be associated with an increased risk of complications. This last device has recently been redesigned and currently there is a plan for clinical evaluation (Table 2).

To reduce the risk of pericardial effusion, or ventricular perforation, caused by the stiff guidewires used in TAVI procedures Roy et al have introduced a dedicated TAVI guidewire³⁰. The proposed device is made of stainless steel that tapers gradually towards its tip, which is covered by polytetrafluoroethylene,

and has a pre-shaped curve that performs at least one revolution. This design is anticipated to reduce the local force that the other wires often exert to the left ventricle during prosthesis implantation. The proposed guidewire was evaluated in a small study that included 39 patients. In all cases the guidewire was successfully positioned into the left ventricle and none of the patients experienced guidewire-related procedural complications.

Future trends in TAVI

Several small-scale studies have provided evidence that TAVI has a value for the treatment of complex patients with a failed surgically implanted bioprosthesis³¹. It is unclear what sizing, positioning and deployment principles should be followed during device implantation but it seems that valve-in-valve TAVI is gradually establishing itself as a valid alternative.

A bicuspid aortic valve anatomy and a dysfunctional aortic valve with severe aortic regurgitation were considered as contraindications for TAVI. However, recent small-scale studies have shown that TAVI may be an effective alternative for the treatment of severe symptomatic aortic regurgitation or AS in patients with a bicuspid valve³²⁻³³. Although the small number of patients included in these studies does not allow us to draw firm conclusions, it is likely that in the future the applications of TAVI will expand.

Conclusions

TAVI has changed the landscape of interventional cardiology, introducing an attractive, less invasive option for the treatment of symptomatic AS. Growing evidence from large registries and randomised controlled trials has underscored the efficacy of TAVI and supported its use in selected populations, while the technological advances in valve design and TAVI-enabling devices have facilitated the procedure, reduced the risk of complications and broadened the applications of this treatment. Although there has been a tremendous evolution in this field in recent years, further research is required to confirm the long-term efficacy of the implanted devices, identify the patients who will benefit from this treatment, stratify more accurately the risk of complications, minimise periprocedural adverse events and optimise post-procedural management.

Funding

C.V. Bourantas is funded by the Hellenic Cardiological Society, Athens, Greece.

Conflict of interest statement

The authors have no conflicts of interest to declare.

Online data supplement

References

- Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Brown DL, Block PC, Guyton RA, Pichard AD, Bavaria JE, Herrmann HC, Douglas PS, Petersen JL, Akin JJ, Anderson WN, Wang D, Pocock S. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med.* 2010;363:1597-607.
- Kodali SK, Williams MR, Smith CR, Svensson LG, Webb JG, Makkar RR, Fontana GP, Dewey TM, Thourani VH, Pichard AD, Fischbein M, Szeto WY, Lim S, Greason KL, Teirstein PS, Malaisrie SC, Douglas PS, Hahn RT, Whisenant B, Zajarias A, Wang D, Akin JJ, Anderson WN, Leon MB. Two-year outcomes after transcatheter or surgical aortic-valve replacement. *N Engl J Med.* 2012;366:1686-95.
- Nielsen HH, Klaaborg KE, Nissen H, Terp K, Mortensen PE, Kjeldsen BJ, Jakobsen CJ, Andersen HR, Egeblad H, Krusell LR, Thuesen L, Hjortdal VE. A prospective, randomised trial of transapical transcatheter aortic valve implantation vs. surgical aortic valve replacement in operable elderly patients with aortic stenosis: the STACCATO trial. *EuroIntervention.* 2012;8:383-9.
- Zahn R, Gerckens U, Linke A, Sievert H, Kahlert P, Hambrecht R, Sack S, Abdel-Wahab M, Hoffmann E, Schiele R, Schneider S, Senges J. Predictors of one-year mortality after transcatheter aortic valve implantation for severe symptomatic aortic stenosis. *Am J Cardiol.* 2013 Apr 8. [Epub ahead of print]
- Gilard M, Eltchaninoff H, Lung B, Donzeau-Gouge P, Chevreul K, Fajadet J, Leprince P, Leguerrier A, Lievre M, Prat A, Teiger E, Lefevre T, Himbert D, Tchetché D, Carrie D, Albat B, Cribier A, Rioufol G, Sudre A, Blanchard D, Collet F, Dos Santos P, Meneveau N, Tirouvanziam A, Caussin C, Guyon P, Bosch J, Le Breton H, Collart F, Houel R, Delpine S, Souteyrand G, Favereau X, Ohlmann P, Doisy V, Grollier G, Gommeaux A, Claudel JP, Bourlon F, Bertrand B, Van Belle E, Laskar M. Registry of transcatheter aortic-valve implantation in high-risk patients. *N Engl J Med.* 2012;366:1705-15.
- Moat NE, Ludman P, de Belder MA, Bridgewater B, Cunningham AD, Young CP, Thomas M, Kovac J, Spyt T, McCarthy PA, Wendler O, Hildick-Smith D, Davies SW, Trivedi U, Blackman DJ, Levy RD, Brecker SJ, Baumbach A, Daniel T, Gray H, Mullen MJ. Long-term outcomes after transcatheter aortic valve implantation in high-risk patients with severe aortic stenosis: the U.K. TAVI (United Kingdom Transcatheter Aortic Valve Implantation) Registry. *J Am Coll Cardiol.* 2011;58:2130-8.
- Gurvitch R, Wood DA, Tay EL, Leipsic J, Ye J, Lichtenstein SV, Thompson CR, Carere RG, Wijesinghe N, Nietlisbach F, Boone RH, Lauck S, Cheung A, Webb JG. Transcatheter aortic valve implantation: durability of clinical and hemodynamic outcomes beyond 3 years in a large patient cohort. *Circulation.* 2010;122:1319-27.
- Ussia GP, Barbanti M, Petronio AS, Tarantini G, Etori F, Colombo A, Violini R, Ramondo A, Santoro G, Klugmann S, Bedogni F, Maisano F, Marzocchi A, Poli A, De Carlo M, Napodano M, Fiorina C, De Marco F, Antonucci D, de Cillis E, Capodanno D, Tamburino C. Transcatheter aortic valve implantation: 3-year outcomes of self-expanding CoreValve prosthesis. *Eur Heart J.* 2012;33:969-76.
- Rodes-Cabau J, Webb JG, Cheung A, Ye J, Dumont E, Osten M, Feindel CM, Natarajan MK, Velianou JL, Martucci G, DeVarenes B, Chisholm R, Peterson M, Thompson CR, Wood D, Toggweiler S, Gurvitch R, Lichtenstein SV, Doyle D, DeLarochelliere R, Teoh K, Chu V, Bainey K, Lachapelle K, Cheema A, Latter D, Dumesnil JG, Pibarot P, Horlick E. Long-term outcomes after transcatheter aortic valve implantation: insights on prognostic factors and valve durability from the Canadian multicenter experience. *J Am Coll Cardiol.* 2012;60:1864-75.
- Kappetein AP, Head SJ, Genereux P, Piazza N, van Mieghem NM, Blackstone EH, Brott TG, Cohen DJ, Cutlip DE, van Es GA, Hahn RT, Kirtane AJ, Krucoff MW, Kodali S, Mack MJ, Mehran R, Rodes-Cabau J, Vranckx P, Webb JG, Windecker S, Serruys PW, Leon MB. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. *EuroIntervention.* 2012;8:782-95.
- Stortecky S, Windecker S, Pilgrim T, Heg D, Buellesfeld L, Khattab AA, Huber C, Gloekler S, Nietlisbach F, Mattle H, Juni P, Wenaweser P. Cerebrovascular accidents complicating transcatheter aortic valve implantation: frequency, timing and impact on outcomes. *EuroIntervention.* 2012;8:62-70.
- Kahlert P, Al-Rashid F, Dottger P, Mori K, Plicht B, Wendt D, Bergmann L, Kottenberg E, Schlamann M, Mummel P, Holle D, Thielmann M, Jakob HG, Konorza T, Heusch G, Erbel R, Eggebrecht H. Cerebral embolization during transcatheter aortic valve implantation: a transcranial Doppler study. *Circulation.* 2012;126:1245-55.
- Van Mieghem NM, Schipper ME, Ladich E, Faqiri E, van der Boon R, Randjgari A, Schultz C, Moelker A, van Geuns RJ, Otsuka F, Serruys PW, Virmani R, de Jaegere PP. Histopathology of embolic debris captured during transcatheter aortic valve replacement. *Circulation.* 2013;127:2194-201.
- Nombela-Franco L, Webb JG, de Jaegere PP, Toggweiler S, Nuis RJ, Dager AE, Amat-Santos IJ, Cheung A, Ye J, Binder RK, van der Boon RM, Van Mieghem N, Benitez LM, Perez S, Lopez J, San Roman JA, Doyle D, Delarochelliere R, Urena M, Leipsic J, Dumont E, Rodes-Cabau J. Timing, predictive factors, and prognostic value of cerebrovascular events in a large cohort of patients undergoing transcatheter aortic valve implantation. *Circulation.* 2012;126:3041-53.
- Rodes-Cabau J. Procedural and early neurological outcomes in the PROTAVI-C pilot study. EuroPCR 2013, Paris, France, May, 2013.

16. Mullen M. First report of the DEFLECT I trial: a prospective, single arm feasibility study to evaluate the safety and performance of the Keystone Heart TriGard embolic deflection device in patients undergoing TAVI. *EuroPCR* 2013, Paris, France, May, 2013.
17. Rodes-Cabau J, Dauerman HL, Cohen MG, Mehran R, Small EM, Smyth SS, Costa MA, Mega JL, O'Donoghue ML, Ohman EM, Becker RC. Antithrombotic treatment in transcatheter aortic valve implantation: insights for cerebrovascular and bleeding events. *J Am Coll Cardiol*. 2013 Apr 10. [Epub ahead of print]
18. Ussia GP, Scarabelli M, Mule M, Barbanti M, Sarkar K, Cammalleri V, Imme S, Aruta P, Pistrutto AM, Gulino S, Deste W, Capodanno D, Tamburino C. Dual antiplatelet therapy versus aspirin alone in patients undergoing transcatheter aortic valve implantation. *Am J Cardiol*. 2011;108:1772-6.
19. Van Mieghem NM, Tchetché D, Chieffo A, Dumonteil N, Messika-Zeitoun D, van der Boon RM, Vahdat O, Buchanan GL, Marcheix B, Himbert D, Serruys PW, Fajadet J, Colombo A, Carrie D, Vahanian A, de Jaegere PP. Incidence, predictors, and implications of access site complications with transfemoral transcatheter aortic valve implantation. *Am J Cardiol*. 2012;110:1361-7.
20. Piva T, Nicolini E, Gabrielli G, Mucaj A, Serenelli M, Rescigno G, Pangrazi A, Perna G. Balloon-expandable sheath for borderline vascular access in transfemoral TAVI. *EuroIntervention*. 2012;8:Q125.
21. Blumenstein J, Kempfert J, Van Linden A, Arsalan M, Schmidt SK, Mollmann H, Kim WK, Thourani V, Walther T. First-in-man evaluation of the transapical APICA ASC access and closure device: the initial 10 patients. *Eur J Cardiothorac Surg*. 2013 Apr 5. [Epub ahead of print]
22. Gotzmann M, Korten M, Bojara W, Lindstaedt M, Rahlmann P, Muge A, Ewers A. Long-term outcome of patients with moderate and severe prosthetic aortic valve regurgitation after transcatheter aortic valve implantation. *Am J Cardiol*. 2012;110:1500-6.
23. Hayashida K, Lefevre T, Chevalier B, Hovasse T, Romano M, Garot P, Bouvier E, Farge A, Donzeau-Gouge P, Cormier B, Morice MC. Impact of post-procedural aortic regurgitation on mortality after transcatheter aortic valve implantation. *JACC Cardiovasc Interv*. 2012;5:1247-56.
24. Schultz C, Rossi A, van Mieghem N, van der Boon R, Papadopoulou SL, van Domburg R, Moelker A, Mollet N, Krestin G, van Geuns RJ, Nieman K, de Feyter P, Serruys PW, de Jaegere P. Aortic annulus dimensions and leaflet calcification from contrast MSCT predict the need for balloon post-dilatation after TAVI with the Medtronic CoreValve prosthesis. *EuroIntervention*. 2011;7:564-72.
25. Poon KK, Crowhurst J, James C, Campbell D, Roper D, Chan J, Incani A, Clarke A, Tesar P, Aroney C, Raffel OC, Walters DL. Impact of optimising fluoroscopic implant angles on paravalvular regurgitation in transcatheter aortic valve replacements - utility of three-dimensional rotational angiography. *EuroIntervention*. 2012;8:538-45.
26. Binder RK, Leipsic J, Wood D, Moore T, Toggweiler S, Willson A, Gurvitch R, Freeman M, Webb JG. Prediction of optimal deployment projection for transcatheter aortic valve replacement: angiographic 3-dimensional reconstruction of the aortic root versus multidetector computed tomography. *Circ Cardiovasc Interv*. 2012;5:247-52.
27. Urena M, Mok M, Serra V, Dumont E, Nombela-Franco L, DeLarochelliere R, Doyle D, Igual A, Larose E, Amat-Santos I, Cote M, Cuellar H, Pibarot P, de Jaegere P, Philippon F, Garcia del Blanco B, Rodes-Cabau J. Predictive factors and long-term clinical consequences of persistent left bundle branch block following transcatheter aortic valve implantation with a balloon-expandable valve. *J Am Coll Cardiol*. 2012;60:1743-52.
28. Testa L, Latib A, De Marco F, De Carlo M, Agnifili M, Latini RA, Petronio AS, Etori F, Poli A, De Servi S, Ramondo A, Napodano M, Klugmann S, Ussia GP, Tamburino C, Brambilla N, Colombo A, Bedogni F. Clinical impact of persistent left bundle-branch block after transcatheter aortic valve implantation with CoreValve Revalving System. *Circulation*. 2013;127:1300-7.
29. Houthuizen P, Van Garsse LA, Poels TT, de Jaegere P, van der Boon RM, Swinkels BM, Ten Berg JM, van der Kley F, Schalijs MJ, Baan J Jr, Cocchieri R, Brueren GR, van Straten AH, den Heijer P, Bentala M, van Ommen V, Kluin J, Stella PR, Prins MH, Maessen JG, Prinzen FW. Left bundle-branch block induced by transcatheter aortic valve implantation increases risk of death. *Circulation*. 2012;126:720-8.
30. Roy DA, Laborde JC, Sharma R, Jahangiri M, Brecker SJ. First-in-man assessment of a dedicated guidewire for transcatheter aortic valve implantation. *EuroIntervention*. 2013;8:1019-25.
31. Linke A, Woitek F, Merx MW, Schiefer C, Mobius-Winkler S, Holzhey D, Rastan A, Ender J, Walther T, Kelm M, Mohr FW, Schuler G. Valve-in-valve implantation of Medtronic CoreValve prosthesis in patients with failing bioprosthetic aortic valves. *Circ Cardiovasc Interv*. 2012;5:689-97.
32. Roy DA, Schaefer U, Guetta V, Hildick-Smith D, Mollmann H, Dumonteil N, Modine T, Bosmans J, Petronio AS, Moat N, Linke A, Moris C, Champagnac D, Parma R, Ochala A, Medvedofsky D, Patterson T, Woitek F, Jahangiri M, Laborde JC, Brecker SJ. Transcatheter aortic valve implantation for pure severe native aortic valve regurgitation. *J Am Coll Cardiol*. 2013;61:1577-84.
33. Himbert D, Pontnau F, Messika-Zeitoun D, Descoutures F, Detaint D, Cuffe C, Sordi M, Laissy JP, Alkholder S, Brochet E, Iung B, Depoix JP, Nataf P, Vahanian A. Feasibility and outcomes of transcatheter aortic valve implantation in high-risk patients with stenotic bicuspid aortic valves. *Am J Cardiol*. 2012;110:877-83.
34. Bourantas CV, van Mieghem NM, Farooq V, Soliman OI, Windecker S, Piazza N, Serruys PW. Future perspectives in transcatheter aortic valve implantation. *Int J Cardiol*. 2013 Apr 15. [Epub ahead of print].