REVIEW: TRANSCATHETER AORTIC VALVE IMPLANTATION

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ABSTRACT

Transcatheter aortic valve implantation (TAVI) has evolved as a routine therapeutic option to treat elderly and high-risk patients with symptomatic aortic stenosis over recent years. Different prostheses with self-expandable nitinol frames or balloon expandable cobalt-chromium frames are available to be inserted by means of a retrograde transfemoral, retrograde transaortic, or an antegrade transapical approach. Current risks of TAVI include: malpositioning, particulate embolisation with subsequent stroke, vascular diseases, annular injury, or coronary obstruction, as well as the need for new onset pacemaker implantation; procedural complication rates for these remain at 5%. Second-generation valves, together with further technical developments, are expected to lead to easier and safer implantation techniques, translating into optimised outcomes for individual patients. The key to successful TAVI therapy is: joint pre-procedural indication, peri-procedural conduct, and post-procedural care of the patients by an experienced heart team.

Keywords: Transcatheter aortic valve implantation, aortic valve, high-risk, aortic stenosis, heart team.

INTRODUCTION

The aim of this review is to give an overview on transcatheter aortic valve implantation (TAVI), technical aspects, results, and perspectives. TAVI has evolved as a standardised and routine procedure to treat elderly and high-risk patients with aortic stenosis (AS) over the past years. Following initial implants using retrograde transfemoral (TF) access (2002 onwards) and antegrade transapical (TA) access (2004 onwards), different valve systems have received Conformité Européenne (CE) approval in 2007 and 2008. Since then, the numbers of TAVI procedures have seen a steep increase; in part due to referrals of elderly and high-risk patients who had not received treatment before. In Germany, the country with the largest number of implants in Europe, approximately 9,000 patients received TAVI in 2012, whereas a slightly larger and more stable number have received conventional aortic valve surgery (AVS) recently.[1] According to current guidelines there is an indication to perform TAVI in elderly and high-risk patients with relevant comorbidities as diagnosed by the heart team.[2,3]

TECHNICAL ASPECTS OF THE PROCEDURES

TAVI consists of two parts: 1) access to the cardiovascular system by means of a sheath or a sheathless application system; and 2) positioning and implantation of a prosthetic heart valve at the site of the native aortic valve. The usually calcified native aortic valve leaflets remain in place and are squeezed aside. The implanted prosthesis consists of a self-expandable or a balloon expandable stent with an integrated xenograft consisting of pericardial or porcine leaflets. Access for TAVI is gained using a retrograde TF, a retrograde transaortic (TAo), a retrograde trans-subclavian (TS) or an antegrade TA approach.

Access sheath size ranges from 14 F up to 24 F for the currently used TF devices and from 18 F to 26 F for TA devices, with some larger ones being sheathless. There are specific advantages and disadvantages of the antegrade versus retrograde approaches. Important factors influencing the approach include: the size and invasiveness of the respective incisions, the distances to the targeted aortic valve, potential manipulations on the aortic arch, coaxial versus oblique access with direct or remote control, and the feasibility of commissural alignment during valve implantation. Potential advantages and disadvantages of performing TAVI under conscious sedation versus fast track general anaesthesia must also be considered.

Optimal imaging is required to safely perform TAVI; this includes a fluoroscopic system with 3D visualisation, transoesophageal echocardiography with 3D visualisation, and a hybrid operative theatre if available. Additional software tools allow for specific evaluations of the dimensions as well as the morphology of the aortic root, including the amount of calcifications, etc.

Due to its inherent complexity and potential complications, TAVI has to be considered equivalent to an operative procedure. This is especially true when considering the specific challenges of some procedures as well as the complexities of underlying diseases of high-risk patients. Therefore it should be performed under circumstances quite comparable to conventional AVS. Utmost technical quality is paramount for procedural success. This includes: 1) an established heart team with a cardiologist and a cardiac surgeon, experienced experts in the field of TAVI, working together in the procedure; 2) standardised procedural workflows; and 3) a well-equipped hybrid operative theatre with optimal imaging modalities including 3D visualisation. All three aspects lead to high quality and, thus, maximum safety for the patients.

PATIENTS

Patients with relevant aortic valve disease, mostly AS, suffer relevant clinical symptoms such as dyspnoea on exertion, angina, or even syncope. Under these conditions, full physical functionality can only be regained by a new valve due to the fact that there is no effective medical treatment for AS. Conventional surgery, e.g. resection of the diseased native valve cusps and insertion of an artificial valve (mechanical, xenograft, or homograft) by means of standard suturing techniques, has been the only therapeutic option for decades. Conventional AVS has evolved as a standardised and low-risk procedure (risks of approximately 1% in experienced centres) with excellent long-term outcomes. Elderly and higher-risk patients, however, have frequently neither been referred for, nor accepted for, conventional surgery. Therefore, TAVI offers an appealing additional therapeutic option. According to the current guidelines, old age and increased risk profiles are factors required to select a patient for TAVI. Many patients who may not have been referred several years ago are now being treated. According to current guidelines, TAVI is indicated in high-risk elderly patients with AS according to the treating heart team's decision. In addition to high-risk elderly patients, some intermediate-risk patients may receive TAVI as well. In order to perform best practice, clear interdisciplinary heart team decisions should be performed taking individual patient-related factors into account.

Exact patient screening is important before performing TAVI. This includes specific imaging delineating the morphology of aortic valve disease and the respective dimensions of the aortic root. Due to the fact that TAVI is performed by means of valve implantation without resection of native calcified cusps and without direct measurement of the annular dimensions, annular sizing by transoesophageal echocardiography in a 2D and 3D view as well as computed tomography (CT) is important. For CT assessment there are specific software tools allowing for precise and automated measurement of the aortic root, including the effective aortic annulus based on its area and/or perimeter. Over the past years, these specific assessments have been an important contributing factor to the further improvement of the results of TAVI procedures throughout. The slightly decreasing incidence of severe paravalvular regurgitation after TAVI may be clearly related to improved preoperative patient assessment by improved imaging.

Regarding outcomes, there are several studies showing good outcomes with TAVI. Selected studies, however, may be at risk of reflecting a 'selected reality', whereas larger scale 'all-comers' registries may reflect the effective therapeutic outcomes in a better way. Therefore, the currently ongoing German Aortic Valve Registry (GARY), for example, is of utmost importance to build

further evidence of which therapeutic option is best for the respective patients.[4]

A prospectively randomised all-comers trial comparing TAVI to conventional surgery in intermediate-risk patients would be ideal; however, such a trial is neither available nor in view. The currently performed Placement of Aortic Transcatheter Valve (PARTNER) 2 and Surgical Replacement and Transcatheter Aortic Valve Implantation (SURTAVI) trials target an intermediate-risk population while having selective inclusion criteria, and thus, do not reflect everyday all-comers practice. The US PARTNER trial has been a prospectively randomised trial with quite selective patient inclusion, showing comparable outcomes of TAVI in comparison to conventional surgery in high-risk patients.[5] The initial results from the GARY registry indicate higher-risk profiles for TAVI patients in comparison to those receiving conventional surgery. Although this registry reflects all-comers clinical practice from Germany, the choice of procedure being performed was made by the physicians. Therefore, further comparison of outcomes may only, in part, be justified statistically.

Up to 1 year follow-up, conventional valve surgery led to the lowest mortality rates in patients with low and intermediate-risk profiles, as discriminated by the logistic EUROscore and the German Aortic Valve Score (AKL score). In very high-risk patients, however, TAVI was as good as conventional surgery in relation to 1-year outcomes.[4] The recently published randomised clinical trial on a self-expanding TF device led to superior results as compared to high-risk surgical patients; patients had a mean age of 83 years and mean Society Thoracic Surgeons (STS) score of 7.5%.[6] In the 'Transcatheter Valve Therapy' registry in the USA, 7,710 patients were included from November 2011 until May 2013. A total of 2.6% of cases were technically unsuccessful and 4.1% of patients had to be supported with cardiopulmonary bypass, while conversion to conventional surgery was required in 1.2%. Overall 30-day mortality was 7.6% and 30-day stroke was 2.8%, with data completeness at this time of 41%.[7]

TAVI DEVICES

Current devices to perform TAVI mostly are first or second-generation valves that have been used clinically for several years. Newer systems are being developed, aiming at offering additional solutions for improved patient outcomes and enhanced safety. This includes specific features to minimise paravalvular leakage, further reduction in crimped sheath diameter in order to allow for an easy insertion, options to retrieve the device in part or completely (if possible after it is already fully functional), possible commissural orientation with exact anatomical positioning, potential features to further ease perfect positioning, and eventually, automated functionality. Some of these features may be available for clinical practice soon whereas others warrant significant further developments.

TAVI devices consist of a specifically designed valve and an application system, which is usually inserted over a guidewire by means of a sheath or in a sheathless manner. The valve consists of a thin stent, which is balloon expandable (stainless steel or cobalt-chromium) or self-expandable (usually nitinol). Valve leaflets consist of bovine pericardium, porcine pericardium, or of porcine leaflets. Some of these valves have an additional anticalcification treatment similar to conventional surgical xenografts in order to protect against tissue degeneration, and thus achieve optimal valve durability. Examples of common TAVI valves are shown in Figure 1. An overview on the sizes of the different devices and on treatable annulus diameters is given in Table 1. The different features of current and future TAVI valves are summarised in Table 2.

In the early years, the Edwards SAPIEN™ balloon expandable valve and the Medtronic COREVALVE™ self-expandable valve were available. These are the two devices with the largest clinical experience worldwide. Whereas the SAPIEN™ valve is available for retrograde (TF, TAo, TS) and antegrade (TA) insertion, the COREVALVE™ is available for retrograde implantation only. The SAPIEN™ is a rather short device (16-22 mm), designed for subcoronary implantation whereas the COREVALVE™ stent has a length of almost 50 mm, thus requiring an implantation that surpasses the coronary ostia while obtaining additional aortic stabilisation. After implantation, the leaflets are in a rather intra-annular position with the SAPIEN™, whereas, they are slightly supra-annular with the COREVALVE™. Available valve sizes are 23 mm, 26 mm, and 29 mm for both, and an additional 31 mm for the COREVALVE™.

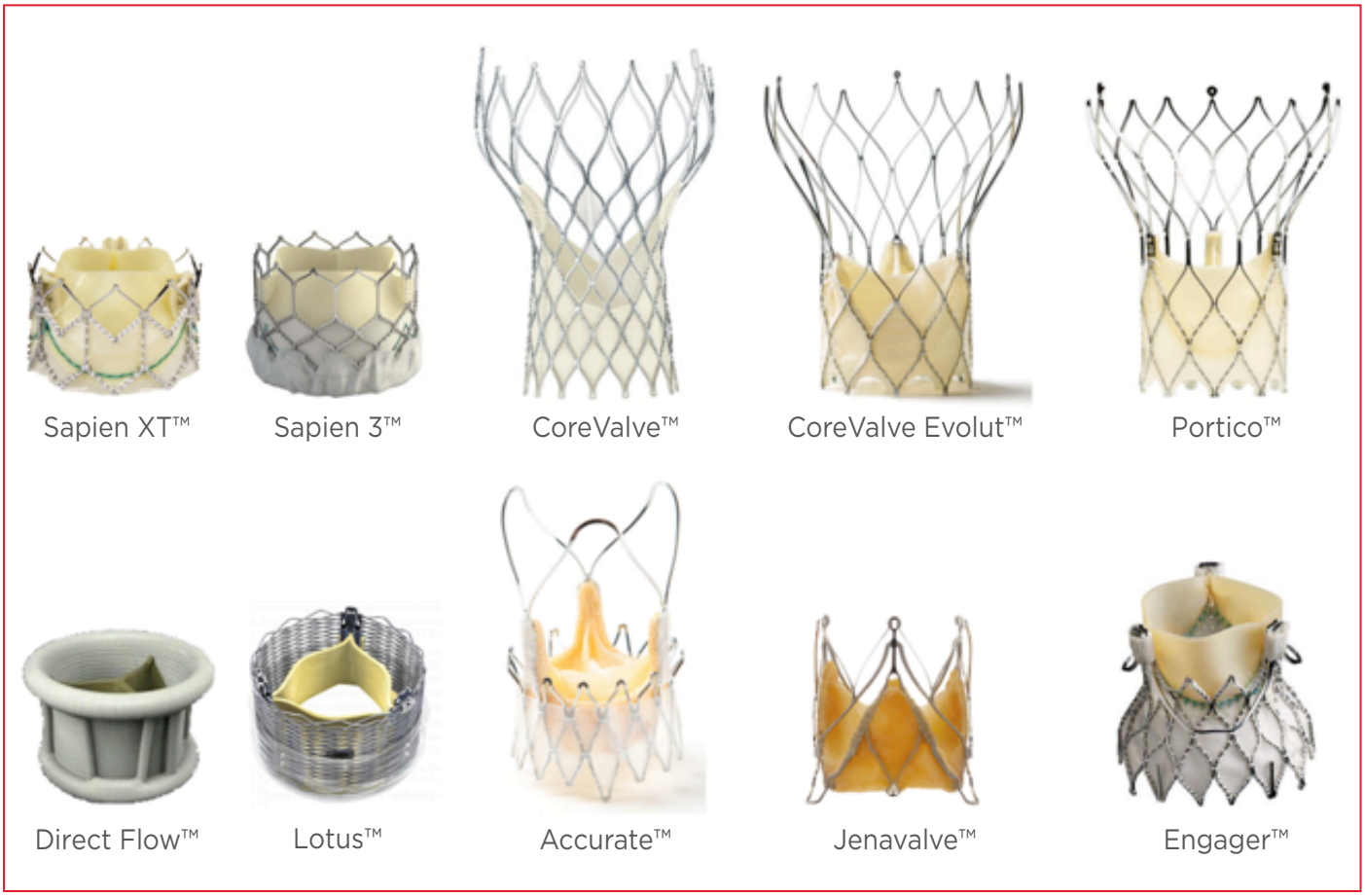

Figure 1: Common valves for transcatheter aortic valve implantation.

Table 1: Valve diameters and treatable annulus sizes of different currently available transcatheter heart valves.

Device	Sizes (mm)	Oversizing in relation to nominal size (mm)	Treatable annulus diameter (mm)
Sapien XT™	20, 23, 26, 29	1-3	18-27
Sapien 3™	20, 23, 26, 29	1-3	18-28
CoreValve™	23, 26, 29, 31	3	18–29
CoreValve Evolut™	23, 26, 29, 31	3	18-29
Portico™	23, 25, 27*, 29*	2-3	18-27
Direct Flow™	23, 25, 27, 29	2-3	19-27
Lotus™	23, 27	0-3	20-27
Accurate™	23, 25, 27	0-3	20-27
Jenavalve™	23, 25, 27	0-3	20-27
Engager™	23, 26, 29	1-3	20-27

** No CE approval yet, currently in clinical trial.*

Table 2: Current and new devices and their respective features.

Device	Access (TF, TA, TAo)	SE (self-expandable), BE (balloon expandable)	Re-positioning	Commissural alignment	Paravalvular leak prevention
Sapien XT™	TF, TA, TAo	BE	no	no	no
Sapien 3™	TF, TA, TAo	BE	no	no	yes
CoreValve™	TF, TAo	SE	no	no	no
CoreValve Evolut™	TF, TAo	SE	partially	no	no
Portico™	TF, TA*	SE	partially	no	no
Direct Flow™	TF	Inflatable	yes	no	no
Lotus™	TF	SE	yes	no	yes
Accurate™	TA, TF*	SE	partially	yes	no
Jenavalve™	TA, TF*	SE	partially	yes	no
Engager™	TA	SE	partially	yes	no

** Under development.*

The initial SAPIEN™ prosthesis was replaced by the SAPIEN XT™ prosthesis from 2009 onwards.

Recent developments of these two devices are the SAPIEN 3™ valve, which just received CE approval, and the COREVALVE EVOLUT™ prosthesis. The SAPIEN 3™ offers smaller sheath diameters (14-18 F) and an additional outer skirt to minimise the risk of post-implant paravalvular leakage.[8] The COREVALVE EVOLUT™ offers improved stability during positioning and some retrieval options.[9]

Besides these large players in the field, several other devices have been developed in the past years.

For retrograde TF access the PORTICO™ (St. Jude Medical), DIRECT FLOW™ (Direct Flow Medical Inc.), and SADRA™ Lotus valve (Boston Scientific Inc.) have received CE approval, with further devices being studied (ACCURATE TF™, Symetis Inc.) or being developed (JENAVALVE TF™). The PORTICO™ device consists of a nitinol stent of approximately 50 mm length, which looks slightly similar to the previously mentioned Corevalve™. It allows for retrieval after up to 80% of implantation, a position where valve functionality can already be assessed. At present, the 23 mm and the 25 mm PORTICO™ valves have received CE approval whereas the 27 mm and 29 mm versions will undergo further clinical evaluation.[10] A transapical version is being further developed in parallel.

The DIRECT FLOW™ valve is unique in design, as it avoids any metal and is made from two inflatable circular structures that are connected by cloth. It has a unique implantation and fixation technique, which leads to good outcomes with TF implantation in experienced hands.[11] The SADRA LOTUS™ valve consists of a nitinol mesh, which is quite long in the crimped position and foreshortens during TF implantation; it allows for complete retrieval of the device.[12]

The ACCURATE TF™ valve (Symetis Inc.) has recently entered clinical trials to reach CE approval.[13] For TA access, the ACCURATE™ system has gained relatively large clinical expertise with more than 1,000 implants at the end of 2013. The ACCURATE™ valve has a self-expanding nitinol stent that can be placed in an anatomically correct position, matching the commissures to the native ones quite easily. Furthermore, it allows for partial repositioning. The overall implantation procedure is strikingly easy. Future developments will include larger application system diameters down to 18 F and an active mechanism to seal against paravalvular leaks.

Clinical results with the first generation ACCURATE™ valve are promising.[13,14]

The JENAVALVE™ (Jenavalve Inc.) TA system received CE approval in parallel to the previously mentioned device and has seen several hundred implantations since. The JENAVALVE™ has a unique self-expandable stent with additional 'feelers' to guide positioning at the annular level together with commissural alignment and safe anchoring.[15] The ENGAGER™ (Medtronic Inc.) system has some comparable functionality as the previously mentioned JENAVALVE™ in terms of three 'arms' that are being placed at the three nadirs during implantation. The ENGAGER™ consists of a self-expanding frame, and has been implanted into several hundred patients.[16]

FUTURE DEVELOPMENTS

Over the past 10 years, TAVI has gained widespread acceptance in many countries for treating elderly and high-risk patients. At present, there are different ongoing discussions upon the future of TAVI; the assessment of risk profiles using currently available scoring systems versus the development of a TAVI-specific risk scoring system is of clinical interest. Morphological factors, especially the amount, extent, and eccentricity of aortic valve calcifications, together with specific aortic root anatomy, should be taken into account. In the future there may be specific patient-related factors that lead to a certain indication for one or another of the currently available TAVI valve systems. Imaging in general will further evolve towards an increasing use of 3D visualisation, coupled with online overlay of relevant structures. This will certainly lead to improved implantation procedures with better outcomes for patients.

The extension of indications for TAVI, extending from high-risk patients to intermediate-risk patients, is being frequently discussed. By means of all-comers clinical trials only, in the future we will be able to decide the best therapeutic option for these patients. Different access routes will be further discussed in the future. At present it remains clear that there is no clinical evidence to support a retrograde versus antegrade access route, or vice versa. For the patient, any access performed by an experienced heart team leading to a minimal complication rate is ideal.

TAVI is still associated with some severe complications, which may occur in up to 5% of procedures. Some of these complications have a significant and immediate, severe impact upon the patient, which could put their future at risk. Avoidance of complications, therefore, is of utmost interest for all physicians. Excellent quality of TAVI procedures, being performed by a heart team in a hybrid operative theatre, together with trained conduct of the procedures, is important. The goal of TAVI for the coming years - besides further standardisation - is the reduction of technical risks, including less malpositioning, the avoidance of post-implant renal failure, avoidance of other organ failures, and the minimisation of stroke. Further developments of TAVI devices, as outlined previously, will certainly contribute to an improved functionality during the procedures as well as even better patient outcomes for the future.

CONCLUSION

In summary, TAVI - after only 10 years of clinical practice - has already evolved towards a highly standardised and relatively safe procedure for minimally invasive treatment of severe symptomatic AS in elderly and high-risk patients. By means of a heart team approach, indications for selection of TAVI versus other therapeutic strategies will be set for the utmost benefit of our patients.

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