Archives of Cardiovascular Disease (2012) 105, 174—180

Available online at SciVerse ScienceDirect www.sciencedirect.com

Elsevier Masson France EM|consulte www.em-consulte.com/en

CLINICAL RESEARCH

Transcatheter aortic valve implantation: Surgical perspectives

Remplacement valvulaire aortique percutané : le point de vue du chirurgien

Thomas Walther[a,*], **Jörg Kempfert**[a], **Friedrich W. Mohr**[b]

[a] *Kerckhoff Heart Centre, Department of Cardiac Surgery, Benekestrasse 2—8, 61231 Bad Nauheim, Germany*
[b] *Heart Centre, Department of Cardiac Surgery, Leipzig University, Leipzig, Germany*

Received 6 February 2012; accepted 6 February 2012
Available online 22 March 2012

KEYWORDS
Aortic stenosis;
Aortic valve replacement;
TAVI;
Transapical

Summary Aortic valve replacement (AVR) is a routine procedure for decades to treat patients with symptomatic aortic stenosis. The introduction of transcatheter aortic valve implantation (TAVI) by Professor Alain Cribier has paved the way for minimally invasive therapeutic options for elderly and high-risk patients with aortic stenosis. Transfemoral and transapical aortic valve implantations have become routine procedures in many centres around Europe. TAVI is usually being performed together by experienced cardiologists and cardiac surgeons who build the interdisciplinary 'Heart Team'. In the future, improved devices together with advanced fusion imaging will lead to a further improvement in clinical outcomes for the sake of our patients.

MOTS CLÉS
Sténose aortique ;
Remplacement valvulaire aortique ;
Transapical

Résumé Le remplacement valvulaire aortique est depuis des décennies le traitement de référence du rétrécissement aortique symptomatique. Le développement des valves aortiques percutanées par Alain Cribier a ouvert la voie d'une approche moins invasive pour une population âgée et à risque chirurgical élevé. Les implantations aortiques percutanées par voie transfémorale ou transapicales sont maintenant réalisées en routine dans de nombreux centres en Europe. Cette procédure est d'habitude réalisée par une équipe médico-chirurgicale entraînée réalisant une équipe multidisciplinaire, la « Heart Team ». Dans le futur, les améliorations

Abbreviations: AVI, aortic valve implantation; AVR, aortic valve replacement; CE, *conformité européenne*; CPB, cardiopulmonary bypass; FDA, Food and Drug Administration; TA, transapical; TAVI, transcatheter aortic valve implantation; TF, transfemoral; TEE, transoesophageal echocardiography.

* Corresponding author. Fax: +49 6032 996 2567.
E-mail address: t.walther@kerckhoff-klinik.de (T. Walther).

1875-2136/$ — see front matter © 2012 Published by Elsevier Masson SAS.
doi:10.1016/j.acvd.2012.02.004

technologiques combinées aux progrès de l'imagerie vont permettre d'améliorer encore les résultats dans l'intérêt de nos patients.

Background

Transcatheter aortic valve implantation (TAVI) is a new method enabling off-pump and truly minimally invasive treatment of aortic stenosis by means of retrograde transfemoral, transsubclavian or transaortic aortic valve implantation (AVI) or antegrade transapical AVI. In industrialized communities, aortic stenosis is the most frequently acquired heart valve disease and if untreated is associated with high mortality. Medical therapy is scarce and symptomatic patients have a high attrition rate of up to 50% in the first year [1]. Thus, replacement of the degenerated valve is the only treatment option that improves symptoms and survival [2,3]. For decades, conventional surgical aortic valve replacement (AVR) via sternotomy, using cardiopulmonary bypass (CPB), was the only therapeutic option and thus evolved as the gold standard. The number of elderly patients presenting with aortic stenosis, however, is steadily increasing in parallel with improved life expectancy, and despite the fact that surgical AVR can be performed in octogenarians with good results [4–6], there are many patients with increased risk profiles for surgical AVR due to advanced age and several comorbidities. In the past, these high-risk patients were not even referred to the cardiac surgeon and adequate treatment was denied [7,8].

With the introduction of TAVI by Professor Cribier in 2002 [9] and its further development [10–13], a truly minimally invasive alternative treatment option for high-risk patients with severe aortic stenosis has evolved. TAVI allows for AVI without cardioplegic arrest and without the use of CPB. Patients are treated on a beating heart and the new prosthesis is implanted within the calcified native valve leaflets that remain in place while being squeezed aside. Since Professor Cribier's pioneering initial clinical implantation in 2002, the fascinating technical achievements of transcatheter techniques that facilitate off-pump aortic valve implantations have developed further. Besides the mere technical factors that enable standardized transcatheter valve implantations, important additional developments have occurred. Most importantly, cardiologists and cardiac surgeons have come together within heart teams to decide jointly upon the best therapeutic options for each individual patient. Joint collaboration has probably been the most important improvement over the past decade and will lead to even further collaborative efforts for the sake of our patients in the future.

In this manuscript we will focus on some surgical aspects of these exciting, new and truly minimally invasive treatment options for patients with severe aortic stenosis.

Surgical aortic valve replacement (AVR) in 2012

Surgical AVR is a standardized procedure associated with low risks in most referred patients. Use of CPB allows for stable haemodynamics throughout the procedure; after aortic cross-clamping and cardioplegic cardiac arrest an aortotomy is performed and the calcified cusps are excised. Next, any modern xenograft or mechanical prosthesis is implanted using standardized suture techniques, which are associated with a very low risk of paravalvular leakage.

Besides conventional sternotomy, a minimally invasive approach can be routinely applied by means of partial upper sternotomy (J-cut in the third or fourth intercostal space) or parasternal right minithoracotomy in the third intercostal space. Access closure is performed with sternal wires and a standard suturing technique. Current results indicate low mortality rates of between 1% and 3% in an all-comers population.

Transcatheter aortic valve implantation (TAVI) from the beginnings to routine clinical practice

Since the first clinical patient was treated by Professor Cribier 10 years ago, TAVI has evolved as a standard therapy for high-risk elderly patients with aortic stenosis. Initially, TAVI was thought to be a transfemoral procedure, by means of a femoral venous and then a transseptal approach initially and via a retrograde transfemoral arterial approach subsequently. Both of these approaches were pioneered by Professor Cribier.

Cardiac surgeons were 'non-believers' in this new technique throughout the early years. Different thoughts, however, led to the initiation of unparalleled joint efforts between cardiac surgeons and cardiologists in order to further develop different therapeutic options for high-risk elderly patients: the awareness that a retrograde transfemoral approach may not be suitable in some patients, especially in presence of severe peripheral vascular disease; the thought that an antegrade approach from the left ventricular apex might be feasible; and the belief that due to their decades of experience of treatment of aortic valve disease, cardiac surgeons should be part of further technological developments. Mike Mack and Fred Mohr started an initiative at Edwards Lifesciences to work on a transapical antegrade access platform for TAVI. By means of the first generation of the Ascendra transapical delivery system (Edwards Lifesciences, Irvine, CA, USA), initial experimental experience was gathered in November and December 2004 at the laboratories in Irvine, USA and Leipzig, Germany. Cardiac surgeons from Dallas (Mike Mack and Todd Dewey), Frankfurt (Gerhard Wimmer-Greinecker and Mirko Doss) and Leipzig (Fred Mohr and Thomas Walther) formed a partnership to develop this procedure further. After ethical approval and based on experiences with transfemoral implantations, initial clinical implantations were done in two patients in Leipzig in December 2004, with the support of Professor Cribier (Fig. 1). Two more patients were treated in 2005 in

Figure 1. Professor Alain Cribier supporting the first transapical aortic valve implantations at the Heart Centre in Leipzig in December 2004, immediately after the procedure. This image shows him between Professors Mike Mack (Dallas, USA; left) and Friedrich W. Mohr (Leipzig, Germany; right).

Frankfurt and Leipzig. However, due to the lack of a 26 mm prosthesis, sufficient oversizing was not applied and patients therefore had severe paravalvular leakage. Further experimental evaluation led to the development of an additional cuff around the SAPIEN prosthesis, to provide a better seal against irregularities at the aortic annulus and thus avoid paravalvular leakage. Towards the end of 2005, a 26 mm SAPIEN prosthesis became available, together with a clear concept of using oversizing. The clinical use of TA AVI was restarted successfully in February 2006 in Leipzig, followed by Vienna and Frankfurt.

Current prostheses available for transcatheter aortic valve implantation (TAVI)

Over the years, different prostheses have become available for performing TAVI. Initially there were two prostheses, both of which received Conformité Européenne (CE) approval in 2008 and then became commercially available.

The CoreValve® (Medtronic, Minneapolis, MN, USA) is a porcine pericardial valve mounted on a self-expandable nitinol stent, which is available in three sizes (26, 29 and 31 mm); the delivery system allows for retrograde implantation only. The CoreValve® prosthesis has not yet obtained Food and Drug Administration approval.

The SAPIEN XT™ (Edwards Lifesciences, Irvine, CA, USA) prosthesis consists of bovine pericardial leaflets mounted on a balloon-expandable cobalt-chromium stent. The prosthesis is available in three sizes (23, 26 and 29 mm) and can be implanted using either the retrograde transfemoral approach or the antegrade transapical approach; the 29 mm valve is for the transapical approach only. A large randomized trial for FDA approval was completed recently using the previous SAPIEN™ valve [14,15]. FDA approval has been granted for 'inoperable' patients according to the PARTNER cohort B study and will probably be granted for high-risk but 'operable' patients according to the PARTNER cohort A study in spring 2012.

In October 2011, two second-generation transcatheter valves for the transapical approach obtained CE approval: the JenaValve™ (JenaValve, Munich, Germany) and the ACURATE TA™ valve (Symetis, Ecublens, Switzerland). Both are porcine valves mounted on a self-expandable nitinol stent.

The main steps of transcatheter aortic valve implantation (TAVI)

The transfemoral and TA techniques allow for minimally invasive off-pump AVI. At the beginning of both procedures a 'safety net', including a venous back-up wire and an arterial sheath, should be placed in the femoral vessels to facilitate immediate conversion (femoral-femoral percutaneous cannulation) to CPB should any complications occur during the procedures [16].

For transfemoral AVI, puncture of both femoral arteries is necessary: one to deliver the device and one to insert the pigtail catheter. For balloon valvuloplasty, the native aortic valve is crossed retrogradely. Balloon valvuloplasty is performed under rapid pacing using a transvenous pacing wire. The prepared valve on its delivery system is introduced and positioned under fluoroscopic control after haemodynamic recovery from rapid pacing. The valve is deployed under a second brief episode of rapid ventricular pacing, once a good position is confirmed. After implantation, the valve function is assessed by either fluoroscopy and/or transoesophageal echocardiography (TEE). If any significant paravalvular leak is noticed, it is possible to reballoon the valve with a slightly larger balloon. For femoral artery closure after removing the delivery sheath, a closure device such as Prostar XL™ (Abbott Vascular Devices, Redwood City, CA, USA) can be used. Surgical closure of the femoral artery is an alternative option.

The transfemoral approach allows for a percutaneous procedure, which can be performed under local anaesthesia and then without TEE control. The drawbacks are the retrograde access with relatively long access wires and the necessity to cross the aortic arch retrogradely, thus risking stroke and leading to quite difficult valve positioning in some patients.

The transapical AVI approach is performed through a 5 cm short left anterolateral minithoracotomy at about the midclavicular line in the fifth or sixth intercostal space. After the pericardium is opened, the apex is secured with two teflon-pledgeted purse-string sutures. The apex can then be punctured, allowing for straightforward antegrade valve implantation. The native aortic valve is crossed antegradely with a soft guidewire, which is then changed to a super-stiff wire positioned down into the descending aorta. A pigtail catheter is positioned just above the aortic valve through the arterial sheath of the 'safety net'.

The apical guidewire is used for the valvuloplasty balloon and the valvuloplasty is performed under rapid ventricular pacing. After haemodynamic recovery, the prepared valve with its delivery system is inserted through the apex and deployed under fluoroscopic guidance. Valve function and position are again assessed by TEE and fluoroscopy. Also, for

TA-delivered valves, reballooning might be indicated in case of significant paravalvular leaks. After removal of the sheath and the guidewire, the apex is closed with the prepared purse-string sutures. Detailed step-by-step descriptions for both TAVI approaches have been published earlier [17,18].

The transapical approach offers some potential advantages, such as the short distance between the apex and the aortic valve, which allows for very precise implantation. As opposed to the transfemoral approach, where the sheath diameter is limited to the diameter of the femoral arteries, with the transapical approach there is no limitation to sheath diameter. The avoidance of the retrograde crossing of the aortic arch may be advantageous and may translate into a lower stroke rate with the transapical approach.

Transaortic [19] and transsubclavian [20] AVI have been introduced as two alternative approaches for implanting the CoreValve® prosthesis in patients where a transfemoral approach is not possible due to pronounced peripheral vascular disease. After performing either an upper partial sternotomy or a parasternal minithoracotomy, the ascending aorta is punctured for the transaortic approach, while for the transsubclavian approach the subclavian artery is exposed by surgical cut-down. For both approaches, the valve is implanted retrogradely in an analogous manner to the transfemoral approach.

Figure 2. The Symetis ACURATE TA™ prosthesis: nitinol stent including stabilization arches, 'upper-crown' and body of the valve stent covered by a skirt. Porcine aortic valve leaflets are used.

Focus on the newly approved devices

ACURATE TA™

The Symetis ACURATE TA™ valve obtained CE approval on 01 October 2011 and is designed for transapical use, with a transfemoral pivotal trial starting in 2012. It is a regular porcine valve on a proprietary diabolo-shaped nitinol stent (Fig. 2), is available in three sizes (S-23 mm, M-25 mm and L-27 mm) and can be implanted in patients with annulus diameters between 21 and 27 mm. The prosthesis is deployed in a two-step technique and has some unique features, which allow for easy positioning and implantation and might reduce the incidence of paravalvular leaks. The 'stabilization arches' (Fig. 2) form the upper part of the prosthesis; they are released in the ascending aorta and prevent tilting of the valve during deployment. The 'upper-crown' is located just above the valve prosthesis (Fig. 2); it allows for intuitive positioning and is pulled inside the aortic annulus. The stent body is coated by a polyethylene terephthalate skirt to minimize the risk of paravalvular leaks. The stent commissures are visible while the valve is crimped under fluoroscopy and can be anatomically aligned with the native commissures.

The device is inserted using a sheathless technique through the apex and advanced into supra-annular position controlled by two radiopaque markers at the level of the valve. Step one of the implantation is performed by first releasing the 'stabilization arches' and the 'upper-crown'. This step is reversible if any problems occur during this initial positioning period. For step two, the operator pulls slightly on the device to position the valve inside the annulus. The 'upper-crown' will be anchored in the calcified annulus, which gives the operator tactile feedback for positioning. Step two results in complete deployment of the valve and the delivery system can be removed. A detailed overview of the implantation technique has been published recently [21].

JenaValve™

The transapical JenaValve™ [22] system also obtained CE approval on 01 October 2011 and is a porcine root valve sewn on a nitinol self-expandable stent (Fig. 3). An outer pericardial patch mounts the stent as a so-called skirt.

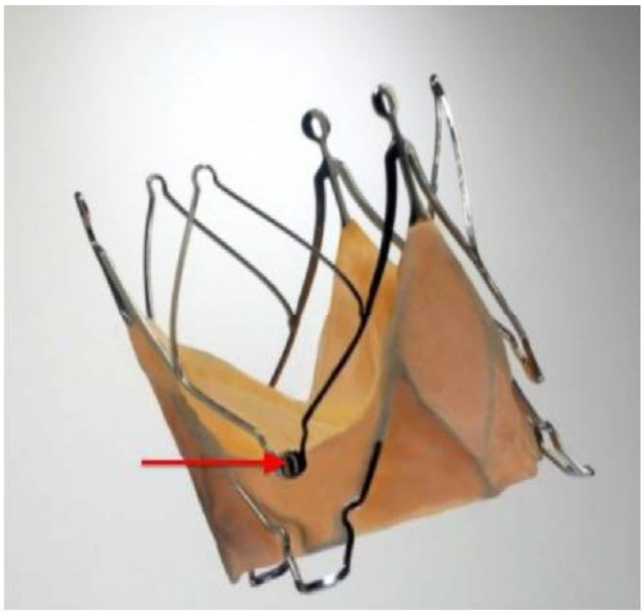

Figure 3. The JenaValve™, a nitinol frame with specific feelers (arrow), which allow for fixation at the three native calcified cusps.

A transfemoral system is under development. The valve is available in three sizes (23, 25 and 27 mm) allowing for implantation in patients with an aortic annulus diameter between 21 and 27 mm. The unique feature of the JenaValve™ is the release of three feelers of the stent in the first step of implantation (Fig. 3). These feelers are placed in the native sinuses and embrace them, which allows for anatomically correct positioning and provides active fixation of the valve. In a second step, the valve is partially released and valve function is achieved immediately. Steps one and two are completely reversible. Once step three is performed the valve is fully deployed.

Clinical results

TAVI is a standardized reproducible technique that can be performed safely in high-risk patients. Overall mortality rates published by experienced centres vary from 3% to 11% [14,15,23–26]. This wide range in mortality rates is best explained by patient selection; for example, most of the patients included in the PARTNER trial were on a waiting list and the sicker patients may have died before TAVI could be performed, whereas in Europe, TAVI is an 'all-comers' technique with even emergency TAVI procedures. Furthermore, strict selection criteria clearly lead to different outcomes.

More recent results have been presented from the PARTNER continued access registry. A total of 843 high-risk patients (Society of Thoracic Surgeons score risk for mortality, 12.3%) received transapical AVI between September 2009 and September 2011; their overall risk profile was similar to those patients who were included in the transapical arm of the PARTNER trial. Thirty-day mortality decreased from 8.7% to 8.2% and 1-year mortality decreased from 29.1% to 23.6% in this high-risk patient cohort. In parallel, the risk of stroke decreased from 7% (PARTNER) to 2% (continued access) at 30 days and from 10.8% to 3.7% at 1 year. These improvements clearly indicate that transapical AVI could be established as a reliable and valuable therapeutic option in high-risk patients in the USA, quite similar to the European experience.

None of the currently published data allows a preference to be had for either the transapical or the transfemoral approach, due to the fact that there is no clinical evidence in favour of transfemoral or TA. Many centres, however, treat their patients with a 'transfemoral-first' strategy and transapical is only performed in patients where transfemoral is not possible. This results in negative patient selection for transapical patients, reflected in the usually higher-risk profile and therefore certainly worse outcome of transapical patients [14,15,26–30]. Although the risk profile is usually higher in transapical patients, with more frequent peripheral vascular disease, there is a trend towards lower stroke rates for transapical [28,29,31], most likely due to the avoidance of the retrograde crossing of the aortic arch. Also disturbances of the conducting system seem to be more frequent after transfemoral AVI, resulting in a trend towards a higher incidence of postprocedural pacemaker implantations after transfemoral AVI, with this trend becoming statistically significant when using the CoreValve® [26,27,29,32–34]. The rates of postoperative aortic regurgitation more than 1+ vary between 4% and 18% [14,15,26,27,31,34–38] and the incidence of aortic regurgitation should always be kept in mind when talking about widening the indication for TAVI to include younger patients with lower-risk profiles. The very good results after conventional minimally invasive AVR in patients with low-to-moderate risk should also be considered when discussing TAVI procedures in lower-risk patients. A mortality rate between 0% and approximately 3% can be achieved with no relevant incidence of aortic regurgitation more than 1+ [39–42].

Perspectives

TAVI has evolved over recent years as a standard procedure to treat elderly high-risk patients with aortic stenosis using a retrograde transfemoral approach or an antegrade transapical approach. In parallel, interdisciplinary heart teams, led by cardiologists and cardiac surgeons, have been established at many sites to strive for optimized patient treatment. These joint efforts are one of the most beneficial 'side effects' of the initiation of TAVI. All medical disciplines involved in the treatment of sick patients work together to obtain the best individual solutions. In the future, cross training within these heart teams (e.g. a cardiologist performing transapical AVI and a cardiac surgeon performing transfemoral AVI, both with the support of the other colleague) should be further developed. Also, a joint training programme aimed at developing 'structural heart disease interventionalists' may be established by the different specialties.

We will see further technical developments in the coming years. Besides further miniaturization of the devices, it will be possible eventually to better avoid paravalvular leakage, by means of hydrophilic coatings around the stent of the valves. Retrievability of transcatheter prostheses will further enhance the safety margin during implantations. Advanced imaging with further integration of different modalities (angiography, computed tomography and TEE) by means of fusion imaging, will lead to optimized visibility of landmark structures during TAVI procedures.

Regarding the transapical approach, we will see devices that will allow for standardized apical access and closure. Further along, a percutaneous transapical approach may then become a reality.

All these developments, after thorough experimental testing and then careful clinical introduction, will benefit our patients.

Conclusions

From a surgical perspective, patients with symptomatic aortic stenosis require either conventional AVR or transcatheter AVI, both aimed at establishing haemodynamically good aortic valve function. In patients with a low-to-moderate risk profile, conventional AVR should be performed, preferably using a minimally invasive approach. For high-risk patients, TAVI has evolved as an alternative minimally invasive treatment option with good results using a retrograde transfemoral approach or an antegrade transapical approach. At present, there is no evidence that one approach is superior

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.