The Transapical Route for TAVR

Recent data regarding transapical access for transcatheter aortic valve replacement, as well as the devices used in this procedure.

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Since the first human transcatheter aortic valve replacement (TAVR) was performed by Alan Cribier, MD, through an antegrade transfemoral (TF) approach in 2002,[1] the procedure has developed rapidly as an alternative option for treating patients with aortic stenosis (AS). Recent results from the PARTNER trial showed that TAVR is superior compared to standard treatment in patients with severe symptomatic AS who are unfit for open surgery.[2] For patients facing high-risk surgery, the prospective randomized arm showed that TAVR is an alternative treatment with similar 1-year outcomes compared to surgical AVR.[3]

Nowadays, the procedure is most often performed through a retrograde TF approach[4] or through an antegrade transapical (TA) approach in which the device is inserted through the left ventricular apex.[5] However, alternative access routes using the subclavian artery or the ascending aorta are under clinical evaluation.[6,7]

In this article, we comment on the clinical and technical history of TA TAVR, current clinical results, and possible future options using this approach.

HISTORY

The number of patients with calcific AS is steadily increasing due to the demographic changes of our population, as it occurs primarily in elderly patients. Comorbidities and the general condition of this group of patients lead to underreferral and undertreatment of elderly patients with symptomatic severe AS, despite their very poor prognosis on medical therapy.[8] This combination of an unmet clinical need with a desire to find less-invasive interventional/surgical treatment options has driven the development of TAVR, which avoids not only the trauma of median sternotomy, but also does not need to be performed during cardioplegic arrest using cardiopulmonary bypass.

However, in its early development phase, it was recognized that appropriate vascular access is key for the success of the procedure. Given the size of currently used devices (smallest measured between 16–18 F and the largest 22–24 F) and the significant number of elderly patients with AS who also have peripheral vascular disease, severe aortic atherosclerosis, or other vascular comorbidities, it is not surprising that an alternative access for TAVR, possibly independent of vascular access, was searched for.

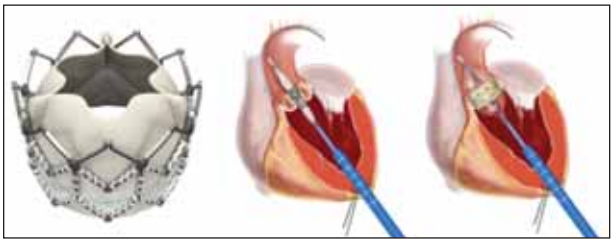

Figure 1. The Edwards Sapien XT and Ascendra II valve delivery system (Edwards Lifesciences, Irvine, CA) for TA TAVR.

TA access for heart valve treatment had been used in the early years of cardiac surgery to perform closed mitral valve commissurotomies and more recently for some left ventricular support devices. Based on this experience, the pioneers Michael Mack, MD, and Friedrich Mohr, MD, subsequently introduced TA TAVR in 2004 as a transcatheter heart valve technique that can be used independently of vascular access.[9,10]

Transcatheter heart valve treatment at that early phase clearly moved out of a single specialty and became an area in which cardiologists and surgeons work hand in hand during the diagnostic and therapeutic phases of patients' treatment. As a result, the PARTNER EU trial, the first European feasibility trial in which both the TF and TA approaches were used, was conducted in 2007. The route of access in this trial was determined by the joint decision of the heart team composed of interven-

tional cardiologists, cardiac surgeons, anesthesiologists, geriatricians, and cardiac imaging specialists.[11]

As a consequence, TA TAVR using the Edwards Sapien transcatheter heart valve (Edwards Lifesciences) received CE Mark approval in Europe in 2008 (Figure 1). Currently, 3 years later, the second-generation Edwards Sapien XT valve (Edwards Lifesciences) is still the only device with CE Mark approval for TA TAVR in Europe (Figure 2A). Modifications of the valve prosthesis included reduction of its profile, potentially making implantation more feasible and further development of pericardial leaflet shape and pretreatment to improve valve durability and performance. Using the Ascendra II delivery system (Edwards Lifesciences), the second generation of the Ascendra TA implantation system, delivery of 23- and 26-mm prostheses is now feasible through a 22-F sheath. In addition, a 29-mm Edwards Sapien XT for use in patients with large aortic annuli was approved in 2010, but still requires the original Ascendra delivery system using a 26-F introducer sheath.

POTENTIAL STRENGTHS AND WEAKNESSES

Access through the left ventricular apex rarely limits the size of the device advanced into the left ventricle, which is why the TA approach is currently the only option for implantation of the larger 29-mm Edwards Sapien XT bioprosthesis.

Antegrade passage of the device across the native aortic valve is, in general, technically easier than the retrograde approach that is currently used during TF TAVR. This plays a particular role in patients with degenerative bioprostheses, in whom trauma to the degenerated xenograft during retrograde insertion of the transcatheter heart valve can result in acute severe aortic regurgitation with catastrophic consequences. It also explains why there is usually a short interval between balloon valvuloplasty and valve deployment found in TA procedures, which is particularly helpful in patients with impaired left ventricular function who are at risk of hemodynamic instability during this period.

The short distance between the access point of the device and the native aortic valve, as well as the straight orientation of the device, improves direct digital control of its position. This is of particular importance in patients with a risk of prosthetic displacement due to asymmetrical septal hypertrophy or after mitral valve replacement.

Potential weaknesses of the TA route include the need for a limited left lateral minithoracotomy with its potential for associated postoperative pain and the need for general anesthesia. In addition, puncture of the left ventricular apex and introduction of the catheter device is not without risk and can lead to acute bleeding complications during implantation.[12] However, the incidence of severe left ventricular bleeding during implantation is low, and long-term complications such as left ventricular aneurysms[13] are rarely reported.

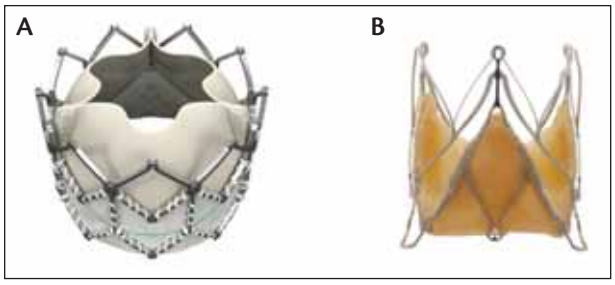

Figure 2. Edwards Sapien XT valve available for commercial use in Europe for TA TAVR (A). The JenaValve device (JenaValve Technology, Inc., Wilmington, DE) recently received CE Mark approval for commercial use in Europe for TA TAVR (B).

GUIDELINES AND REPORTED OUTCOMES

In 2008, European guidelines for TAVR were published by the European Society of Cardiology and the European Association for Cardio-Thoracic Surgery after CE Mark approval of the Edwards Sapien and CoreValve (Medtronic, Inc., Minneapolis, MN) systems.[14] Currently, TAVR is seen as an alternative treatment option for patients with AS facing high-risk surgical AVR based on a logistic EuroSCORE of > 20. Surgical AVR has remained the gold standard for treatment of AS in the low-risk population.

This view is currently supported by the results of the PARTNER trial, the world's first randomized, prospective controlled trial of TAVR versus standard medical therapy (cohort B)[2] and surgical AVR (cohort A).[3] In inoperable patients who were randomized to TAVR, a reduction in mortality of 20% (30.7% with TAVR vs 50.7% with standard therapy) at 1-year follow-up was found compared to medical treatment. For patients who are high risk for surgical AVR, no inferiority of TAVR was found in terms of mortality at 30 days and 1 year, with a 1-year survival rate of 75.8% (TAVR) and 73.2% (surgical AVR), respectively.

The PARTNER EU trial was the first feasibility trial in which both the TF and TA approach were used with the Edwards Sapien bioprosthesis.[11] The route of access was determined by the joint decision of the multidisciplinary heart team and according to best practice for TF or TA TAVR at that time. As expected, this resulted in a selection bias of the two groups and explains why the incidence of risk factors, such as coronary artery disease, peripheral vascular disease, prior coronary bypass grafting, and carotid artery disease, was significantly higher in the TA cohort, resulting in a higher logistic EuroSCORE of 33.8% com-

pared to 25.7% for TF. Despite this obvious selection bias, many have concluded that the lower mortality for the TF group of 8% at 30 days (TA 19%) and of 21% at 1 year (TA 49%), was a direct result of the route of access.

However, it is important to note that the PARTNER EU trial was not designed to compare TF with TA, but rather to prove the feasibility of the two implantation modes. In addition, it is important to mention that this trial took place in Europe during the second half of 2007, recruiting patients during a time when there was still very little experience with TAVR. Out of a total of nine participating centers, 78% had no initial experience with TA TAVR compared to 44% for TF TAVR.

Since then, the number of TA TAVR procedures has rapidly increased, and single-center experience with outstanding results has recently been published. Based on 299 patients, Kempfert et al from the Heart Center Leipzig in Leipzig, Germany demonstrated improvement in outcomes, with a decrease of 30-day mortality from 11.3% in their first 150 patients to 6% in their latest experience.[15]

In addition, the SOURCE registry began in 2008 after commercialization of the Edwards Sapien transcatheter heart valve in Europe. It is currently the largest dataset on experience with TAVR (N = 2,339), including the largest cohort of patients in which TA access was performed (n = 1,398).[16] In this registry, 55% of patients underwent TA TAVR compared to 45% who were treated using TF access. Patients who underwent TA TAVR presented with significantly higher comorbidities, which is not surprising keeping in mind that the route of access in the participating centers is usually a result of the heart team's discussions, with a "TF-first" approach. The mean logistic EuroSCORE in the TA group was 29% compared to 25.8% in the TF group.

Mortality for the TA group at 30 days was 10.3%, and at 1 year, survival was reported to be 72%. With respect to the discussions about various access routes mentioned in the context of the PARTNER EU trial, it is worth pointing out that a direct comparison between the TA and TF cohorts is still hampered by the difference in patient characteristics, as mentioned earlier. However, 30-day mortality of 6.3% was slightly lower, and 1-year survival of 81% was slightly higher with TF compared to the TA group of patients. For certain risk groups, such as patients with a logistic EuroSCORE of < 20, 1-year survival of approximately 80% in each group was not significantly different between TF and TA. Not surprisingly, the largest difference in survival between the two groups was found during the first two postinterventional/postoperative months. Thereafter, the Kaplan-Meier survival curves for the two groups run almost parallel to each other.[16]

Postoperative complications in the TA cohort included vascular/access-related complications (2.4%), myocardial infarction (0.5%), and stroke (2.5%). Not surprisingly, the incidence of major vascular/access complications was quite low in the TA group. However, if they occurred, they were mainly attributed to complications with the left ventricular apex or trauma to the aortic root. These complications were highly predictive of a higher 30-day mortality rate.[17] Over time, the incidence of these serious complications declined, which may be a result of the learning curve experienced by participating centers.[16]

In this context, it may be interesting that recent data from the SOURCE registry have shown that in a subgroup of TA TAVR patients with previous coronary artery bypass grafts (n = 357), apical complications were nonexistent. This may explain why their 30-day mortality rate of 10% was similar compared to patients who underwent TF TAVR.[18]

Multivariable analysis from the SOURCE registry identified EuroSCORE > 30% and renal insufficiency as predictors of 30-day mortality after TA TAVR.[17] In contrast, analysis of TA TAVR data from the Leipzig Heart Center showed that poor respiratory function (defined as vital capacity < 70%) and concomitant mitral regurgitation (> mild) independently predict mortality. However, both of the classic risk-scoring algorithms (Society of Thoracic Surgeons score > 15%, logistic EuroSCORE > 30%) failed to predict outcomes.[15]

It is important to note that all of the patients in the PARTNER trials and the SOURCE registry had been treated using the first-generation Edwards Sapien valve prosthesis. Early results from the feasibility trial on the new generation of TA devices, the Edwards Sapien XT, have been presented recently. PREVAIL TA (Placement of Aortic Balloon Expandable Transcatheter Valves Trial) was a prospective, multicenter, nonrandomized clinical trial evaluating the Edwards Sapien XT transcatheter heart valve, including the next-generation Ascendra transapical delivery system. Thirty-day mortality was 8.7% for the total cohort and 3.5% for patients receiving the 29-mm valve—lower rates than ever previously reported for TA TAVR.[19]

One particular group of patients who may benefit even more from the development of transcatheter heart valve techniques are those who face repeat open heart surgery due to degeneration of a previously implanted bioprosthesis. In this group of patients, TAVR is used increasingly for valve-in-valve treatment. The TA approach is a very attractive option in this context because it guarantees antegrade access to bioprostheses in the aortic position, which may reduce the risk of intraprocedural acute prosthetic regurgitation. In addi-

tion, TA access has also been used for treatment of degenerated mitral bioprostheses with excellent outcomes.[20,21] In contrast to TAVR in the native aortic valve, the failing aortic bioprosthesis facilitates positioning, prevents the occurrence of conductance abnormalities, and protects coronary arteries.

FUTURE OPTIONS

TA TAVR has been described in great detail in previous reviews.[5] However, it is still under further development and will continue to undergo various modifications and improvements, which hopefully will improve patient outcomes. Recently, it has been shown that TA TAVR was even performed through endoscopic access.[22]

In addition, new devices with additional technical features to improve feasibility and safety during implantation have been developed, such as the JenaValve device (Figure 2B). This self-expandable, repositionable, and retrievable valve for TA TAVR has a unique anchoring and self-centering system. This design should reduce potential mitral valve distortion and conduction abnormalities. A multicenter study to evaluate TA delivery using the JenaValve was started in 2010,[23] and the device recently received CE Mark approval in Europe.

Reports on the early experience using the Symetis Acurate device (Symetis, Ecublens, Switzerland) were recently presented. This self-expanding transcatheter heart valve is designed for TA TAVR and is composed of a porcine biologic valve attached to a self-expandable nitinol stent. It allows for anatomical orientation and facilitates intuitive implantation, providing tactile feedback. The recently reported first experience in 40 patients was encouraging.[24]

CONCLUSION

The dynamic development of transcatheter heart valve techniques is a result of the excellent partnership between cardiologists and cardiac surgeons, which was supported by technical teams developing this technique. As a result, in less than a decade, TAVR has become a standard treatment for patients who are unsuitable or seen as high risk for surgical AVR.

Valve technology, delivery systems, and interventional/surgical technique will continue to undergo further development and improvements, and it remains to be seen how this will improve patient outcomes. Currently, there is no evidence to favor any particular access in general, and the heart team approach guarantees that the various approaches for TAVR are used in the patient's best interest to reduce the risks associated with the procedure and improve outcomes. In this context, it is most helpful to have TA TAVR available, as it is currently the approach that is least limited by vascular access. However, the key for future development of TAVR is the working partnership between the members of the multidisciplinary heart team. ■

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