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Transcatheter aortic valve implantation (TAVI): a European perspective in Spring 2011

Introduction

Transcatheter aortic valve implantation (TAVI) has now been performed in Europe for over 5 years. From 2006 onwards, a number of multicentre trials proved the feasibility of TAVI in high-risk patients with aortic stenosis (AS). Both the retrograde transfemoral (TF) approach and the antegrade transapical (TA) approach were shown to be feasible.¹⁻³ In Spring 2008, European approval was granted for the use of a retrograde TF approach (CoreValve™ and SAPIEN™) and an antegrade TA approach (SAPIEN™) in high-risk patients. Following this approval, training programmes on the new techniques were established, and proctored initial implants at each site performed. This led to a considerable increase in the number of clinical sites performing these approaches, leading to more than 20,000 implants by the end of 2010.

What impact has TAVI had on the clinical strategies used to treat AS in Europe? Overall numbers for Europe are not available. In Germany, however, prior to the availability of TAVI techniques, approximately 12,000 patients received conventional aortic valve replacement (AVR) every year. In 2010, this number decreased slightly, and further decreases can be expected in the future. In parallel, there has also been a

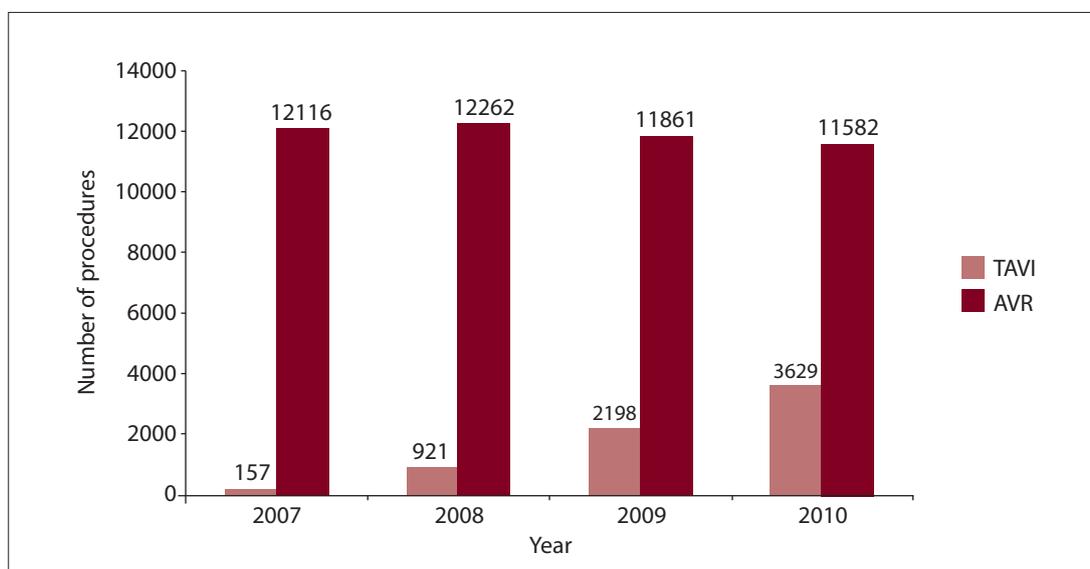
steady increase in the number of TAVI procedures performed (see Figure 1).⁴

It is worthwhile noting, however, that the overall number of patients treated for AS has also increased over this time period. Furthermore, it is likely that an increasing number of high-risk patients, who would not have been routinely referred for conventional surgery, are now being sent for TAVI, as awareness of minimally invasive therapeutic options is growing amongst physicians, patients and their families.

At present, it is not clear whether this shift – a decrease in conventional AVR and a steep increase in TAVI – will continue. In the meantime, it is important to perform a detailed analysis of the available outcome data for the different procedures, bearing in mind the excellent results seen with conventional AVR surgery. To this aim, a nationwide German aortic valve registry has been established to prospectively evaluate patients treated for aortic valve disease over five years (<http://www.aortenklappenregister.de>). The findings of this registry, taken together with information on the cost-effectiveness of the different procedures, will hopefully lead to a more defined approach when treating patients with severe symptomatic AS.

fig. 1

Change in the number of TAVI and conventional AVR procedures performed in Germany (2007–2010)



When is TAVI indicated?

For individual patients, a number of specific indications to perform TAVI have to be considered. Guidance can be found in the recent position statement by the European Society for Cardiology and the European Association for Cardio-Thoracic Surgery.⁵ This recommends that TAVI should be limited to patients with a high-risk profile (age plus comorbidities) and that choice of intervention in individual patients should be discussed by a heart team including cardiologists, surgeons, imaging specialists and anaesthesiologists. 'High-risk' is defined by both the clinical judgment of the team and the combination of quantitative measures, such as a logistic EuroScore >20% and/or a Society Thoracic Surgeons (STS) Score >10%. For more information on clinical indications for TAVI, please see Table 1 below.

These recommendations are still valid, despite being 2 years old, especially since the overall outcomes from TAVI have not really improved in recent years. Most interventional teams performing TAVI on a regular basis know that, despite being a straight-forward procedure for many patients, complications can happen at any time and occur in approximately 10% of patients. It is not possible to predict which patients are likely to suffer complications, and therefore, at present, the currently recommended indications for TAVI should still be respected.

Precise screening and correct risk scoring are important before performing TAVI; screening to guide the technical decisions that need to be made before choosing the optimal approach and correct risk scoring to understand whether the patient meets the specified indications for TAVI. Guidance is given with regard to when a

specific risk factor should be included in the scoring evaluation, and precise scoring will allow for meaningful comparison of data from different series. It is worthwhile noting, however, that risk scores, such as the EuroScore and the STS predicted risk of mortality score, do have inherent limitations. It is well accepted that they are both of less value when predicting risk in high-risk patients, particularly those with multiple comorbidities, and their predictive value for morbidity and long-term outcomes remains unknown. As a result, it is best to perform a more detailed assessment of risk that combines several risk scores, and to exercise clinical judgment, taking into account risk factors, such as previous coronary bypass or porcelain aorta, that are not captured by these risk scores. For a more specific and disease-oriented (higher risk patients with AS) risk assessment, a modified EuroScore or a new 'valve risk index' that takes into account factors, such as frailty in elderly patients, would be beneficial.

What outcomes are seen with TAVI?

The current outcomes associated with TAVI are somewhat ambivalent. Although there is currently considerable enthusiasm about TAVI, it is also important to remember that standard AVR leads to excellent short- and long-term outcomes. 30-day or in-hospital mortalities with elective AVR are as low as 1% in stable patients in many centres. In 2010, the overall mortality of conventional AVR surgery in Germany was 3%.⁴ Conventional AVR can also be performed using minimally invasive techniques (partial sternotomy) with excellent outcomes. As randomised data comparing TAVI and AVR are not available at present, there is a real need to perform prospective assessments of TAVI *versus* conventional surgery to better understand the respective roles of these two interventions. In the future, it may well be that interest and use of TAVI may plateau, the initial enthusiasm over the technique being dampened as a more realistic impression of its impact on outcomes is formed.

Initial results with the technique were obtained in 'inoperable', high-risk patients. Studies performed between 2006 and 2008 revealed that the technique was associated with double digit mortalities, usually 10–15%, in patients with an estimated logistic EuroScore of between 15–30%. Furthermore, there are considerable stroke rates in these studies of about 5%. There are several series without strokes, however, and all of them are series using a TA approach. Despite the

Indication	RECOMMENDED	NOT RECOMMENDED
High-risk (age plus comorbidities)	✓	
Calcified pure or predominant AS	✓	
Pure aortic regurgitation		✓
Porcelain aorta or frailty	✓	
Prior coronary artery bypass graft	✓	
Presence of previous mediastinitis	✓	
Severe proximal coronary stenoses		✓
Contraindications for surgery	✓	
Refusal based on patient's personal preferences		✓
Life expectancy of <1 year		✓

Table 1
Indications for TAVI⁵

optimism prompted by these results, they are still not perfect, possibly as a result of the initial learning curve with the technique and the high-risk profiles of the patients treated. Between 2008 and 2010, TAVI was introduced at many more sites, usually with proctored initial cases, and this led to a steady increase in the number of patients treated during this time. More recently, however, published results show similar outcomes. 30-day mortalities still are double digit in many studies, and the recommended inclusion criteria⁵ are not commonly applied. For example, patients with a logistic EuroScore risk of <20% made up almost 50% of the patients enrolled in a recent multicentre study, and other potential inclusion criteria, such as frailty, were only present in 17% of patients.⁶ Results of the TA approach are very similar to those of the TF approach, especially when one considers the fact that patients undergoing the TA approach to TAVI (TA-AVI) usually have a higher risk profile. Randomised comparative studies are not available.

Despite proper risk assessment, outcomes from TAVI depend heavily on the patient selection process. At a specific site, an all-comers series will have more high-risk patients than a selected series of patients, in which some critically ill patients may have been excluded. Patients on a waiting list usually have better outcomes than patients presenting in an emergency to the hospital. A 'perfect result' is particularly important in younger patients, and improved outcomes need to be guaranteed before treating lower-risk patients.

PARTNER US: what is its impact on European practice?

The US PARTNER (Placement of AoRTic TraNscathetER Valve) trial is an important randomised trial comparing TAVI *versus* conventional surgery. The most important detail of the study design is the "TF-first" strategy, i.e. patients were screened for TF-AVI first and, if feasible, were randomised to receive TF-AVI or conventional surgery. Only patients that were not suitable for TF-AVI, usually patients with severe peripheral vascular disease and thus a higher risk profile, were considered for the TA approach (TA-AVI). This TF-first strategy is not supported by current literature, especially in the context of the results of a Canadian multicentre assessment, in which comparable outcomes were achieved at 2 years despite a higher risk patient profile in the TA cohort.⁷

Cohort A of the PARTNER trial comprised high-risk patients with AS that were considered operable. Cohort B consisted of patients who were considered 'inoperable'. From a European perspective, it remains relatively unclear whether patients with severe symptomatic AS are considered 'inoperable'. Interestingly, Cohort B was completed much earlier than Cohort A, and therefore those results were published first.⁸ A total of 358 inoperable patients were randomised to TF-AVI (n=179) or medical management including balloon valvuloplasty (n=179). Mortality at 1 year showed a significant advantage for TF-AVI (31%) *versus* medical management (51%). Interestingly, 12 out of the 179 patients randomised into the medical management group underwent conventional surgery. Their mortality at 1 year (33%) was very similar to that seen in the TF-AVI cohort. Thus whether these patients are in fact 'inoperable' remains questionable. Results from Cohort A were released at the recent American College of Cardiology (ACC) congress. 699 high-risk symptomatic patients were randomised to either TAVI (TF or TA approach) or surgical AVR. Mortality at 1 year was 24% *versus* 27% for TAVI and AVR, respectively, demonstrating that, in these patients, TAVI was non-inferior to AVR, and therefore TAVI is an acceptable alternative for conventional AVR in these high-risk, operable patients.⁹

All teams of cardiologists and cardiac surgeons involved in the PARTNER trial have to be congratulated for achieving excellent outcomes. The overall 30-day mortalities, which were as low as 6.4% in 'inoperable' patients and 3.4% in operable patients, are excellent. However, there was an incidence of stroke or TIA of 6.7% in 'inoperable' patients and 3.8% in 'operable' patients, and therefore when adding the incidence of mortality and stroke together in inoperable patients, again double digit numbers are reached. Furthermore, a number of questions remain unanswered. Firstly, can the excellent outcomes be repeated when starting TAVI on a broader basis? And secondly, how much does being on a waiting list impact on the outcomes seen? It is well known that study results will be good whenever patients with a high-risk profile have previously been on a waiting list, as they were for the US PARTNER trial: the sicker ones are likely to have died before reaching the study and while waiting for the procedure.

The survivors are usually the healthier patients in whom less procedural complications and thus better outcomes are to be expected. In Europe, at present, there is no formalised waiting list for TAVI patients. Elderly high-risk patients come to the hospital for diagnosis and then receive their procedure immediately.

Conclusions

Whilst there has been considerable interest in the use of TAVI in patients with high-risk AS in recent years, there are still uncertainties over its benefits

relative to conventional AVR. The US PARTNER study represents an important first step towards better elucidating the respective roles of TAVI and conventional AVR in these patients; however, there are a number of important features of the study design, and unanswered questions, that mean that, although the results of the US PARTNER trial are interesting, it remains to be seen how applicable its findings are to the way in which high-risk patients with AS should be managed in Europe.

DISCLOSURES: The opinions and factual claims herein are solely those of the authors and do not necessarily reflect those of the publisher, editor-in-chief, editorial board and supporting company. TW and JK have no relevant disclosures to declare.

REFERENCES:

1. Webb JG, Pasupati S, Humphries K, et al. Percutaneous transarterial aortic valve replacement in selected high-risk patients with aortic stenosis. *Circulation* 2007;116:755–63
2. Grube E, Schuler G, Buellesfeld L, et al. Percutaneous aortic valve replacement for severe aortic stenosis in high-risk patients using the second- and current third-generation self-expanding CoreValve prosthesis: device success and 30-day clinical outcome. *J Am Coll Cardiol* 2007;50:69–76
3. Walther T, Simon P, Dewey T, et al. Transapical minimally invasive aortic valve implantation: multicenter experience. *Circulation* 2007;116 (Suppl-1):1240–5
4. Gummert JF, Funkat A, Beckmann A, et al. Cardiac surgery in Germany during 2008. A report on behalf of the German Society for Thoracic and Cardiovascular Surgery. *Thorac Cardiovasc Surg* 2011, in press
5. Vahanian A, Alferi OR, Al-Attar N, et al. Transcatheter valve implantation for patients with aortic stenosis: a position statement from the European Association of Cardio-Thoracic Surgery (EACTS) and the European Society of Cardiology (ESC), in collaboration with the European Association of Percutaneous Cardiovascular Interventions (EAPCI). *Eur J Cardiothorac Surg* 2008;34:1–8
6. Zahn R, Gerckens U, Grube E, et al, on behalf of the German Transcatheter Aortic Valve Interventions - Registry Investigators. Transcatheter aortic valve implantation: first results from a multi-centre real-world registry. *Eur Heart J* 2011;32:198–204
7. Rodés-Cabau J, Webb JG, Cheung A, et al. Transcatheter aortic valve implantation for the treatment of severe symptomatic aortic stenosis in patients at very high or prohibitive surgical risk: acute and late outcomes of the multicenter Canadian experience. *J Am Coll Cardiol* 2010;55:1080–90
8. Leon MB, Smith CR, Mack M, et al. PARTNER Trial Investigators: Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *NEJM* 2010;363:1597–607
9. Smith CR, on behalf of The PARTNER Trial Investigators. Transcatheter versus surgical aortic valve replacement in high-risk patients with severe aortic stenosis: results from the PARTNER trial. ACC 2011, New Orleans. Available online at: http://my.americanheart.org/professional/Sessions/AdditionalMeetings/AdditionalMeetingsResources/ACC-2011-PARTNER_UCM_425183_Article.jsp

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