Editorial

Learning experience with transapical aortic valve implantation – the initial series from Leipzig

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Since the first successful transcatheter aortic valve implantation (TAVI) back in 2002 (1), the field of TAVI has seen a rapid development. Soon, two main options in regard to the access for valve delivery evolved. With the transfemoral route (TF) the common femoral artery is entered after surgical dissection or percutaneously using an endovascular closure device. The transcatheter valve is then delivered in a retrograde fashion. The antegrade option takes advantage of the close proximity between left ventricual apex and the aortic valve (TA). After an anterolateral minithoracotomy the apex is exposed, secured by purse-string sutures and valve implantation is performed in an antegrade manner. Recently other alternative access options have gained increasing interest. One is the trans-subclavian access (TS) the other uses the distal ascending aorta (TAo). However, the transapical approach remains the only antegrade one. The others can be subsumized as endovascular approaches being all retrograde in nature.

The manuscript by Holzhey *et al*. (2) reports the cumulative experience with the antegrade transapical TAVI technique to treat elderly high-risk patients suffering from severe symptomatic aortic valve stenosis. The center was one of the very first to implement the new TA-AVI technique from Leipzig, Germany. The series reported here represents today one of the largest single center experiences worldwide including the very early pioneering phase. Bearing this special nature of the dataset in mind the experience highlights several key issues related to the development of the still young TAVI technique.

The "TAVI explosion"

The authors provide insight into the development of the case load of isolated aortic valve replacement (AVR) procedures over time at their institution. During the initial pioneering phase the number of TAVI procedures can be interpreted as an "add-on" to the overall AVR case load (until 2008), obviously some of the patients were not referred previously. As stated by the authors, in the following two years, the reputation of the center gained with TAVI procedures even led to an increase in the total number of AVR cases performed conventionally. During the last two years however, a slight decrease of conventional AVR procedures in favour of TAVI can be noticed. This would most likely even be more obvious if combined cases (AVR + CABG) would be analysed as today an increasing number of TAVI procedures are performed after interventional treatment of coronary artery disease (PCI). In addition, one would expect a significant increase of conventional AVR cases over time due to the overall aging population in Germany. The development observed herein within a single center which was involved in TAVI very early may precede the overall development in Germany: a similar trend towards more TAVI while having stable numbers of conventional AVR procedures was observed in 2011 (3) and there may be a further development in 2012 (~40% TAVI of all AVR procedures).

In the past, the surgical community has seen the development of other minimally invasive new techniques. For example, the introduction of off-pump coronary surgery (OPCAB), minimally-invasive access (MIS) AVR and MIS mitral valve surgery. Although for all these techniques there is today clear evidence available proving either superiority or at least demonstrating a comparable safety profile with similar functional outcome compared

to conventional surgery, general adoption has been much slower. According to data of the German Cardiothoracic Society (2), in 2010 the rate of OPCAB was 14.2%, MIS mitral procedures 38.6% and MIS AVR 12.5%, only. So why took the adoption of TAVI place much faster despite the fact that there is a lack of evidence proving clear superiority of the technique and functional results are often not perfect (paravalvular leaks, requirement for pacemaker implantation)? It seems that TAVI in Germany fulfils all required key driving factors: (I) From a patient's perspective: offers a less invasive option; (II) From a physician's perspective: exiting new procedure, offering new research areas, avoids complex and tedious procedures (i.e. re-do AVR after previous CABG, patients with calcified aorta); (III) From an industry perspective: profitable market expectations; (IV) Almost unrestricted and sufficient reimbursement by insurance companies.

A similar "TAVI explosion" can be observed in other countries but only when reimbursement is liberal. Whether the indications for TAVI are justified in all cases has to be questioned given the exponential growth of implantation numbers. We clearly recommend to follow the well documented recommendations of the medical societies.

It has to be highlighted that within the series of TA procedures presented by the Leipzig group no "indication/risk creeping" is visible with a mean STS-Score of 11.4% and a mean age of the patients of 81.5 years. Thus, the authors have to be congratulated for achieving results that compare favourable to other series with lower risk profiles.

A word of caution: surgical AVR – still the gold standard

Although TAVI is a very attractive and viable alternative providing a clear benefit for selected high-risk patients (i. e. porcelain aorta, previous CABG, truly frail patients), surgical (minimally-invasive access) AVR is without doubt still the gold standard for younger lower risk patients as outcome is unmatched yet and functional results including known durability of valves and absence of paravalvular leaks is of utmost importance for younger patients. Even for octogenarians outcome after surgical AVR is probably better than often assumed (4). However, the surgical community most likely has to embrace minimally-invasive access (MIS) AVR more aggressively to "compete" with TAVI in the future. Several single center series report excellent outcomes in elderly selected patients using MIS AVR techniques. The MIS approach might even have a beneficial impact on survival in these elderly patients (5).

The future of the Heart Team concept

One positive side effect of TAVI, as mentioned by the authors, is the development of the Heart Team concept in many centers. In addition to future randomized trials required to assess the value of TAVI especially in regard to so called "moderate risk" patients, the Heart Team eventually together with insurance companies will be the only "gate keepers" in order to provide best care for each individual patient. In addition, the Heart Team concept ensures optimal patient safety combining the core skills of interventional cardiology (PCI, wire skills) and cardiac surgery (conversion to open surgery, cardiopulmonary bypass (CBP), broad experience with regard to valve pathologies and treatments). As mentioned by the authors severe complication cannot always anticipated and although rare in general (requirement for CBP 4%, conversion to open surgery 2.5%) clearly require the presence of a full Heart Team. Today, TAVI cannot be considered as a pure "cath lab procedure". The active involvement of surgeons especially in TF cases (joint treatment and surgeons implanting transfemoral) is critical to maintain surgical interest and thereby to ensure patient safety. Current European guidelines clearly indicate the "absence of a Heart Team and no cardiac surgery on the site" has to be considered as an absolute contraindication for TAVI (6).

The TF-first selection reality

Holzhey *et al*. report excellent outcome using the antegrade TA approach. The results presented compare even favourable to current outcomes from real-world registries using a TF approach when taking into account risk profiles. The authors report a 30-day mortality of 9.6% in a truly high-risk patient subset (logES I 29.7%) including the very early pioneering phase. The French national registry (FRANCE) reported 30-day mortality rates using a TF access with different valve types ranging between 8.4% and 15.1% in presence of a risk score defined by a mean logES I of 24.7-25.6% (7). Similar results have been reported within a German multicentre registry where the vast majority of patients were treated by a retrograde TF approach (95.6% TF). 30-day mortality was 12.4% with a mean logES I of 20.5% only (8).

When comparing these results the conclusion should not be that TA leads to better results than TF. However,

it becomes obvious that a TF first selection strategy is not supported by any scientific evidence. In case of comparable risk profiles the TA approach will lead to as good results as the retrograde TF approach as it has been shown within the Canadian multicentre registry (9). Hence, we suggest a more balanced case distribution especially in regard to the evident advantages of the antegrade TA approach.

Due to the short distance over the wire the TA access offers unmatched device control and facilitates most precise valve positioning. As presented at the most recent TCT conference (2012, Miami FL, USA) a subgroup analysis of the FRANCE registry revealed that a non-TF approach is an independent protective factor leading to significantly lower rates of relevant (≥2+) paravalvular leaks most likely due to the fact of better axial alignment with a more direct approach. These data confirm the excellent results reported by the Leipzig group in regard to residual paravalvular leaks. They report a rate of 2+ leaks in 5.2% and >2+ in 0.5% only.

Major access site related complications associated to a TF approach have been reported quite frequently (15.3%) and have been identified as an independent predictor for mortality (10). New generation TF devices will require lower profile sheaths which hopefully will result in lower rates of major vascular complications – however only if this technical advancement will be used to improve safety and not to further push anatomical limits of the TF access.

Consistent to lessons learned from CABG surgery, the TA approach facilitates an almost "no-touch" technique in regard to the ascending aorta and the aortic arch. Hence, the theoretical risk of stroke should be very low even in case of significant calcifications. Recently, a large meta-analysis confirmed this theory with lowest stroke rate in the TA group despite higher risk profiles (11). Consistently, Holzhey *et al*. report a peri-procedural stroke rate of 2.1% only. However, they also describe the occurrence of "delayed strokes". The phenomenon of these delayed strokes is poorly understood yet and definitively require further research (12).

In summary, most centers follow a TF-first selection process potentially due to the idea that a TF approach might be less invasive and subsequently might lead to better outcomes. However, this assumption is not supported by any scientific evidence in the first place. This typically results in significantly higher risk profiles in the TA cohort ("calcified left overs"). Thus, TA outcome and mid-term survival will then look inferior in registries or randomized trials following such a TF first strategy due to higher risk profiles (comparison of "oranges and apples"). A well-known example is the PARTNER A trial (13) or the European SOURCE registry (14). Unfortunately, in a second step these outcome differences are then often used to "justify" the initial TF-first strategy. The TA Leipzig experience demonstrates clearly that the antegrade TA approach can lead to excellent outcomes despite a substantial risk profile of patients. In this context it is important to mention that this is not only true for one single German center but others [Berlin experience (15), Heidelberg experience (16)] also reporting similar promising results associated with the TA access.

The learning curve

One of the most interesting details reported in the manuscript by Holzhey *et al*. is the observed learning curve. The authors clearly demonstrate a survival benefit for those patients treated after the very first 120 procedures. The initial learning curve has been published in detail elsewhere (17). Several factors most likely contributed to the improved outcome: team building, patient selection, procedural refinements, device refinements and incorporation of advanced imaging [CT-based valve sizing, C-arm angulation based on the DynaCT (18)]. Especially the CUSUM analysis of the observed learning curve as provided by the authors will most likely stimulate further discussion. It seems that only after a total of 200 procedures the curve reaches a plateau followed by improved outcome. Although of utmost interest this observation has to be interpreted with caution and most likely cannot be generalized to centers who just recently initiated or are just about to build a TAVI program. The Leipzig learning experience summarizes the "individual" (center or operator specific) learning curve as well as the "global" learning experience that was pronounced in the early pioneering phase. As mentioned by the authors, today very well structured TAVI training programs are available including professional proctoring during the early cases. Thus, today's learning curve might be much steeper. On the other hand only centers with a substantial TAVI case load will be able to provide most optimal results. Hence, thoughts treatment of TAVI at higher-volume heart centers might be justified.

Perspective

The field of TAVI has seen an exponential development over the last few years. The Leipzig TA experience published in

this issue provides insights into a unique dataset as it covers the early pioneering phase as well as latest developments. The outcomes reported herein are very well comparable to results from registries using a TF approach. Several topics today are still under discussion including the issue which access to choose when and the impact of learning curves.

Several new TAVI devices will become commercially available soon in addition to technical refinements of the systems that were established for some longer time. Overall, several issues associated with the still young TAVI technology has to be solved prior to further liberalization of indications. This includes the problem of relevant paravalvular leaks known to negatively impact survival, the requirement of pacemaker implantations, unknown durability of the valves and the rate of major vascular complications associated mainly with the TF approach as well as a better understanding of strokes after TAVI. In this context it is critical to note that despite the on-going "TAVI explosion" surgical (minimally-invasive) AVR still leads to unmatched outcome in younger lower risk patients.

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