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Transcatheter Aortic Valve Implantation – TAVI: so much done... yet so far to go

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The natural history of aortic stenosis (AS) was first described by Ross and Braunwald in 1968[1], and forty years later the prognosis of non operated symptomatic patients remains ominous[2]. Pharmacological therapies have not succeeded in improving AS outcomes and the only treatment at present with an impact on survival is surgical aortic valve replacement (AVR), which constitutes the gold standard of treatment for these patients[3]. Procedural global mortality for AVR is ≤ 4% for isolated aortic valve replacement[4] and long-term results are excellent.

Aortic stenosis is the most prevalent valvular heart disease in (western world) Europe[5], and its prevalence increases with advancing age (up to 4.6 % of individuals over 75 years have moderate or severe aortic stenosis[6]). Furthermore, with advanced age operative mortality increases[7,8]. Thus, 33% of patients with symptomatic aortic stenosis are either denied or not referred for surgery[9].

The development of lesser invasive – and potentially safer – percutaneous therapeutic techniques is a very attractive option for these patients that would otherwise be considered not candidates for surgery. Significant human efforts and great economical investments have been committed to the development of Transcatheter Aortic Valve Implant (TAVI) techniques. Nevertheless, procedural feasibility and safety and device effectiveness in the short and long term must be carefully evaluated and compared to the current gold standard, surgical valve replacement. Prior to the general acceptance of any such approach, these technologies will have to follow the path of scrutiny and prove their superiority. This can be a long and painful road, which can only be expedited by a strong collaborative effort among cardiovascular surgeons, interventional cardiologists, clinical cardiologists, imaging specialists, basic scientists and certainly industry.

In this issue of the journal Otten et al[10] report the two-year's one centre experience on outcomes of patients with severe aortic stenosis being referred for TAVI. It revealed that actually only 39% of the patients received the percutaneous valve and that 14% were indeed treated with conventional AVR. However, the logistic EuroSCORE for the patients treated with TAVI was near double of the logistic EuroSCORE of the patient that received AVR. What is remarkable is that survival at one year was 62% for the patients treated by AVR and 87% for those treated by TAVI.

Two percutaneous aortic valves have successfully completed necessary requisites in Europe to obtained CE-mark and have been commercially available since May 2007, the Edwards-SAPIEN valve (Edwards LifeSciences Inc., Irvine, CA, USA) and the CoreValve Revalving system (CoreValve Inc., Irvine, CA, USA). As of May 2008, there have been in excess of 2000 patients that have received a transcatheter aortic valve implantation and are currently under expanded evaluation. Several reports have been published regarding the initial experience with both the Edwards-SAPIEN valve[11-14] and the CoreValve Revalving system[15,16].

There is a steep procedural learning curve for these techniques, with a significant improvement in the procedural success rates (from approximately 75% to over 90%) and most important, with a clear decrease in mortality rates (30 days mortality of 16% vs. 8%) after a few cases[14]. The haemodynamic results, clinical functional improvement and valve functionality have been equally

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satisfactory up to a 2-years follow-up for both systems. Piazza et al[17] reports in this issue the 30-days outcome of 646 patients included in the CoreValve Multicenter Expanded Evaluation Registry, the largest report to date with a percutaneous aortic valve. Procedural success was 97% (balloon post-dilatation after the implant was necessary in 21.2% of the cases, with final aortic regurgitation grade ≤2 in 99% of the patients), and procedural death rate and the combined incidence of procedural death, myocardial infarction or stroke were 1.5% and 2.5%, respectively. The need for new permanent pacing at follow-up was 9.3%. All-cause mortality at 30 days was 8% and the incidence of the combined endpoint 9.3%. These competitive results compare favourably with the pre-procedural mean logistic EuroSCORE (23.1±13.8) and even to surgical reports of high-risk patients undergoing AVR[7,18,19].

Newer second generation technologies with the capability of retrieving and repositioning the device are under feasibility and safety evaluation. The first-in-man (FIM) for some of them have already been reported[20-22] and in this issue of the journal Low et al[23] report the initial experience with the Direct Flow Medical valve which cannot be classified as balloon expandable or self-expandable device and is a completely new design that consists of two inflatable rings linked by a polyester fabric cuff to which three bovine pericardial leaflets are attached. This proof of concept was temporarily tested in nine patients prior to planned AVR. The attempt to implant was made in two under direct visualisation and in seven through a femoral approach. There was one partial premature dislodgement, one procedural failure secondary to inadequate sizing of the device, and seven successful implants, two of them after device exchange for a bigger size. Although permanent implantation was not achieved in this study (saline and contrast solution were not exchanged by the solidifying polymer), these results show the initial feasibility of this technology. Transvalvular gradients and area improved and there was no significant residual aortic regurgitation. Of note, there were two vascular perforations with the femoral approach, one of them resulting in the death of the patient, which highlights one more time the importance of adequate patient selection, and the need for the development of lower profile devices.

Despite the initial good results of the commercially available TAVI devices regarding safety in the high-risk patients and short-term durability, some concerns need to be overcome before broadening the indications of TAVI to lower risk patients:

1) Procedural mortality and morbidity have been considered acceptable when these technologies are applied to high-risk patients. But prior to its generalisation to lower-risk patients, TAVI procedural results must compare favourably with surgical results in this group of patients. This requires the design of specific non-inferiority trials for efficacy and safety, or even better, for superiority design trials for safety evaluation.

2) Vascular complications remain a major concern and emphasise the importance of a careful arterial evaluation and patient selection prior to the procedure, as well as the critical need for improving device's profile.

3) Defining the anatomical characteristics of the native aortic valve and surrounding structures prior to TAVI is of critical importance to ensure optimal positioning of the device, avoid complications (coronary obstruction, device migration, etc.) and achieve success. But the ideal imaging technique for pre-procedural patient evaluation or for the guidance of the procedure is still to be defined. None of the current imaging technologies individually, angiography, echo, CT or MR provides all the desirable information to ensure a correct and safe anatomical placement of the TAVI prosthesis. Thus, to obtain the most complete information, it is necessary a combination of imaging modalities, which also needs to be defined.

4) Long-term durability and the incidence of device-related long term complications need to be evaluated prior to their expanded use in younger and lower surgical risk patients. The impact of a previous TAVI on an eventual future AVR surgery will also need to be deciphered. The combined position statement of the European Association of Cardiothoracic Surgery (EACTS), the European Society of Cardiology (ESC) and the European Association of Percutaneous Cardiovascular Interventions (EAPCI)[24] briefly summarises the current status of TAVI techniques. This statement comes soon after the AHA scientific statement on percutaneous and minimally invasive valve procedures[25], which shows the great excitement that these new technologies arouse. This represents the initial approach to a novel technique from all the above scientific societies, and consequently shows the required prudence and restraint and defines the current limitations of the procedure, thus outlining the steps to follow for this technique to improve. In fact, both statements are a prudent call for caution against the uncontrolled widespread of TAVI at this stage, and emphasise the need for a refinement of these techniques prior to their expanded use. This said, safety and efficacy results of TAVI are promising and certainly TAVI techniques "are here to stay". What is still to be defined is just at what point we will be able to accept what results before moving towards their more extended use, and this will require a collective thought process. Furthermore, standardisation of the procedure and optimal location for doing them, such as hybrid suites, required skills and training for operators, and definition of the optimal imaging technique, among others, will be important.

These new avenues in the field of interventional cardiology are truly in their infancy and our understanding of these procedures is feeble at best. Nevertheless, they already have engendered strong passions amongst cardiologist and cardiac surgeons alike, but none of us should be intoxicated with foolish pride. The convergence of several multidisciplinary skills is mandatory for TAVI to evolve, and interventionalists, cardiac surgeons, clinicians, imaging cardiologists, anaesthesiologists and regulatory bodies must work together for the common aim of better patient outcomes and patient satisfaction. Interaction with basic researchers and engineers is an unreservedly positive for a more dedicated device design. But what we consider perhaps even more important, is to be able to learn from the very inception, and in our opinion we are at a time where TAVI is truly in its infancy with less than 3,000 implants worldwide; thus, before the number of implants becomes overwhelming we have a valuable opportunity to demand compulsory registries, to collect rigorous long-term durability and outcomes data. Finally, once in the market and prior to a widespread dissemination of these techniques, cost-effectiveness will need to be evaluated.

With the acceptance of TAVI and subsequent demand by patients and the medical community, the overall number of patients referred for an effective treatment of AS is expected to increase, as Otten et al report from a single centre experience[10]. At their centre, the overall number of referrals for the treatment of aortic stenosis increased by 30% during this two-year period. More than half of these patients, who would otherwise have continued on pharmacological treatment, received some type of aortic valve, and their study confirms the known ominous natural history of non operated symptomatic aortic stenosis[1,2]. Of concern is, on the other hand, the fact that 14% of these patients referred to a dedicated clinic for aortic stenosis therapies, evaluation did not fulfil the criteria for aortic valve interventions (11 of them without severe aortic stenosis), which reflects that correct indication for intervention is not always straightforward, and that careful re-evaluation of patients prior to any decision making is necessary. One cannot stop wondering if similar occurrences take place for those patients directly referred to surgical valve replacement. Therefore, we should encourage the development of valvular referral centres, where an integrated and multidisciplinary team can evaluate and advise as to the best therapeutic alternative.

Future directions

In this quest we cannot stand alone and a team spirit is essential, in which clinicians, interventionalists, imaging cardiologist, surgeons as well as basic scientists and the industry shall work together. There is a need for a true partnership, as feed-back between groups is fundamental for the progression of transcatheter techniques. Procedural failures and complications are an input for basic researchers to improve device design and for physicians to collaborate for a better patient selection. Technological improvements and procedural expertise will widen the spectrum of suitable patients and allow for a prudent testing of these technologies in a broader group of individuals. A careful follow-up of treated patients will uncover not only previously identified risks but update long-term risk estimates as well, which will ultimately have repercussions on technological evolution and patient selection. Finally, competent authorities and regulators must also be aware of the improvements (or failures) in these technologies in order to fulfil their commitment to better patient care.

Although some concerns regarding transcatheter aortic valve implant remain – i.e., vascular access injury, residual aortic regurgitation, long term efficacy – we strongly believe that close interdisciplinary collaboration will soon overcome actual limitations and that it is only a matter of time before TAVI stands as a competitive, first-line treatment strategy. Demonstrating that TAVI is a better alternative than medical therapy will offer those patients that traditionally have been denied surgery an option to improve their quality-of-life, which might even change their natural history. Lesser invasive procedure will always be preferred, with the proviso that efficacy and safety are equivalent to traditional treatment strategies. Thus, we believe that TAVI will eventually replace AVR as the preferred treatment strategy in a large majority of patients with severe degenerative aortic stenosis.

Ultimately, a better understanding of the physiopathology of degenerative aortic stenosis will determine newer treatment strategies. The ultimate goal should be in the direction of reversing, delaying or even preventing the onset and progression of aortic stenosis. We hope treatment options in the not too distant future are mostly pharmacological, so that interventional strategies (surgical and interventional) can be avoided. However, today it seems utopian to think that AVR will vanish any time soon, since most of the TAVI are aimed at patients with degenerative AS and there is more than just degenerative aortic stenosis. Major advances in the technology will be needed to address other indications for AVR, such as patients with primary aortic regurgitation, combined disease of the aorta, and paediatric patients with congenital aortic valve disease.

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