Challenges for Expanded Use of Transcatheter Aortic Valve Replacement

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Since its development >15 years ago, transcatheter aortic valve replacement (TAVR) has rapidly evolved and is now a well-established treatment option for patients with severe symptomatic aortic stenosis at increased risk for surgical aortic valve replacement (SAVR). In patients with a prohibitive risk for open-heart surgery, TAVR reduced the 1- and 2-year all-cause mortality by almost half compared with standard medical therapy.[1] TAVR with a balloon-expandable prosthesis in high-risk patients achieved similar 5-year rates of cardiovascular outcomes and mortality compared with SAVR.[2] At 3 years, TAVR with a self-expanding prosthesis reduced the incidence of stroke and provided similar survival outcomes compared with surgery in high-risk patients.[3] Most recently, TAVR achieved almost identical rates of the composite of all-cause death and disabling stroke compared with surgery for patients at intermediate surgical risk.[4,5] Consequently, guidelines now include TAVR as a treatment option for extreme-, high-, and intermediate-risk patients with severe symptomatic aortic stenosis.[6] The number of patients treated with commercial TAVR in the United States has nearly doubled from >26 000 in 2014[7] to >50 000 in 2016 and has already reached >300 000 treated patients worldwide. However, several challenges need to be resolved for TAVR to become the mainstream treatment for patients with aortic stenosis.

Low-Risk Patients and Valve Durability

TAVR is currently being examined as a therapeutic option for low-risk patients in 2 large multicenter randomized controlled trials (PARTNER [The Placement of Aortic Transcatheter Valve Trial] III and The CoreValve low-risk trial). Preliminary signals from the NOTION (Nordic Aortic Valve Intervention) trial are encouraging finding no significant difference in the 30-day and the 1-year rates of stroke and all-cause mortality in low-risk patients randomized to SAVR or TAVR with the CoreValve self-expanding prosthesis.[8] These reported outcomes are similar to those of low-risk patients who underwent SAVR in a contemporary analysis of the Society of Thoracic Surgeons registry.[9] In addition, TAVR is also currently being investigated for other patient populations, including patients with severe asymptomatic aortic stenosis and patients presenting with reduced left ventricular function and moderate aortic stenosis.

The question of valve durability is especially pertinent because we evaluate TAVR as a treatment option for lower risk, younger patients. Different definitions of bioprosthetic valve degeneration are available. These typically include a combination of clinical and echocardiographic end points. Such differences may account for the discrepancies in the reported rates of valve degeneration in the surgical and transcatheter literature. In addition, most of the surgical data on bioprosthetic valve durability comes from observational studies, some with incomplete echocardiographic and clinical follow-up, making comparisons challenging. Although no data is available for TAVR beyond 10 years, there are several reports demonstrating adequate TAVR prosthetic function after 5 to 10 years. The 5-year data from the NOTION trial reported that TAVR provides better prosthetic valve hemodynamics with no difference in all-cause mortality when compared with SAVR in low-risk patients.[10] Interestingly, the 5-year rate of structural valve deterioration was significantly higher with SAVR.[10] A large Italian registry including patients undergoing TAVR with the CoreValve or the Evolut R self-expanding prosthesis showed that the prosthesis-related clinical event rate was only 3.2% after 7 to 9 years, and the mean aortic valve gradients and areas remained unchanged.[11] The 5-year echocardiographic follow-up of patients undergoing TAVR with the balloon-expandable valve as part of the PARTNER trial showed no changes in prosthetic valve function and a low rate of structural valve degeneration.[12] Although the current evidence does not suggest significant valve deterioration over time, the need to demonstrate transcatheter bioprosthetic valve durability will continue to be an important challenge that must be met to support TAVR implementation for low-risk patients. The results of the final 10-year follow-up of the intermediate- and the low-risk randomized trials will provide important insights on this issue.

Bicuspid Aortic Valve Disease

The role of TAVR as a reasonable treatment option in patients presenting with bicuspid aortic valve disease remains undefined. More than half of patients of <80 years of age requiring SAVR in the United States have bicuspid aortic valves. Thus, as TAVR moves into the intermediate- and low-risk populations, bicuspid disease will inevitably be more frequently seen in these younger patients referred for transcatheter therapy. Several anatomic characteristics of bicuspid aortic disease render transcatheter treatment technically challenging, including

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severe leaflet calcification, fused raphe, annular asymmetry, and large annular and root dimensions, which may theoretically contribute to suboptimal TAVR results. Hence, patients with bicuspid aortic stenosis have been excluded from all pivotal trials and therefore TAVR for this population remains an off-label indication. However, TAVR for bicuspid aortic valve stenosis has been frequently performed with a reported frequency of up to 9%.[13] The initial experience with the use of early generation devices in this population was concerning given the high incidence of paravalvular regurgitation, valve malposition, and the need for new permanent pacemaker implantation.[14] Several features of the newer generation devices engineered to reduce valve malposition and paravalvular regurgitation have made TAVR for bicuspid aortic disease both feasible and safe. Patients with bicuspid aortic stenosis undergoing TAVR with the newer generation devices can achieve low rates of short-term adverse events, including paravalvular regurgitation, need for new permanent pacemaker implantation, stroke, and death, which are comparable to those of patients with trileaflet aortic valve stenosis.[15] However, randomized data are still needed if this technology is to be applied to the lower risk population with bicuspid aortic stenosis. Until then, TAVR for patients with bicuspid disease should probably be reserved for those at high or extreme surgical risk.

Cerebrovascular Events

Stroke continues to be one of the most feared complications of TAVR. Although the incidence of clinically evident cerebrovascular events was reduced with the use of the newer generation transcatheter prosthesis, further stroke prevention during TAVR will certainly play a role in the adoption of this technology for the lower risk population. Several embolic protection devices have been developed in an attempt to reduce the incidence of cerebrovascular events. Available data suggest that use of cerebral embolic protection may provide some reduction in postprocedural ischemic brain lesions detected by imaging. However, randomized trials evaluating the efficacy of these embolic protection devices have produced inconsistent findings.[16–18] In a recently published propensity-matched analysis, cerebral protection with the filter-based device reduced the short-term rate of adverse clinical events, mainly driven by a reduction in disabling strokes.[19] Increased use of these devices during TAVR demands for more consistent efficacy data and a better understanding of appropriate patient selection.

Procedural Aspects

Although transfemoral access is the preferred and most commonly used route for transcatheter valve delivery, a sizable number of patients undergoing TAVR will have peripheral vascular disease precluding femoral access. Therefore, alternative access sites have been used in 30% to 40% of patients during the early TAVR experience. With the improvements in technology leading to smaller delivery system sizes, the reported use of alternative access has decreased over time, and currently up to 90% of patients are treated transfemorally. The transapical and direct-aortic approaches have been associated with increased morbidity and mortality,[20] leading operators to explore other nonthoracic access routes. Subclavian access, obtained either percutaneously or via surgical cut down, is a frequently used alternative approach.[21] Transcarotid access via surgical cut down has been avoided because of the potential for an increased risk for cerebrovascular events.[22] Last, transcaval access has been gaining some popularity.[23] However, some safety concerns including risk of bleeding and development of aorto-caval fistula have limited its applicability. It is important to note that data on newer nonthoracic alternative access routes are derived from relatively small and nonrandomized studies. However, in our opinion, the small percentage of patients with no suitable transfemoral access can be approached via the left subclavian route.

Within the past few years, TAVR has evolved. Initially, it was an open-heart surgery–like procedure involving a surgical cut down for femoral access requiring general anesthesia in the operating room with standby cardiopulmonary bypass. Currently, many TAVR centers use a more percutaneous coronary intervention–like procedure, often called a minimalist approach. These procedures are performed in the cardiac catheterization laboratory or hybrid room under conscious sedation with a fully percutaneous approach. Smaller delivery sheath sizes, the development of large bore access and closure techniques, and increasing operator and center experience have made this evolution of TAVR possible. Some concerns arose in the early days of the minimalist approach, including the potential for suboptimal visualization during implantation given the absence of transesophageal echocardiography guidance. However, in experienced hands, this approach has proven to be safe facilitating shorter procedural times, faster room turn over, earlier hospital discharge, and lower costs, with no increase in safety concerns.[24] Conscious sedation is being increasingly used among US center as evidence by a recent report from the Society of Thoracic Surgeons (STS) Registry, which reported an increase from 11% in 2014 to 20% in 2015.[25] With the emerging data demonstrating reduced costs and favorable outcomes with TAVR under conscious sedation, practice patterns will likely continue to shift toward a minimalist approach for most patients.

Cost

The cost of TAVR has been a major concern for hospital administrators and healthcare stakeholders given that transcatheter valves cost up to 6× more than the surgical prostheses. However, with a reduction of adverse events and total hospital length of stay, transcatheter therapy has now become cost-effective as recently reported with the Sapien intermediate-risk cohort.[26] Furthermore, the cost of TAVR will likely decrease as other transcatheter prosthesis enter the United States market which is currently dominated by only 2 products. Both sustained clinical and fiscal benefit must be demonstrated to assure continued TAVR expansion.

In conclusion, the evolving technology and technical aspects of transcatheter aortic valve therapy, such as those discussed here, will continue to expand in the next few years and may allow more patients to be safely treated achieving excellent clinical outcomes. If the long-term valve durability, further reduction in the incidence of cerebrovascular events,

and appropriate outcomes in bicuspid valve disease are demonstrated, the use TAVR will likely be expanded into other patient populations, including those at low surgical risk. TAVR continues to be rapidly refined to the point it could become the mainstream therapy for most patients with aortic stenosis soon.

Disclosures

None.

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