Transcatheter Valve Replacement for Aortic Stenosis

Balancing Benefits, Risks, and Expectations

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TRANSCATHETER AORTIC VALVE REPLACEMENT (TAVR) represents a transformative technology with potential for the management of complex patients with aortic stenosis, including those who are not considered candidates for surgical aortic valve replacement because of age and medical comorbidities. Currently, more than 50 000 TAVR procedures have been performed worldwide,[1] with mounting enthusiasm for the "rational dispersion" of transcatheter therapies.[2] The US Food and Drug Administration recently approved TAVR as a reasonable alternative to surgical aortic valve replacement in high-risk patients with aortic stenosis. The increasing consumer expectations that this therapy might become available soon for even young, low-risk patients requiring valve replacement must be balanced against safety concerns that have arisen in both clinical trials and registries.

Stroke remains a major complication following TAVR, both short-term and long-term, likely due to embolism of atherothrombotic debris from the aorta or the native valve. In the Placement of Transcatheter Aortic Valves (PARTNER) trial,[3] the 30-day rates of major stroke among patients undergoing TAVR and surgery were 3.8% and 2.1%, respectively, and these differences persisted at 2 years (7.7% and 4.9%, respectively). The optimal stroke prevention strategy has yet to be determined. Patients assigned to TAVR in the PARTNER trial[3] received heparin during the procedure, followed by aspirin and clopidogrel for 6 months. Patients in the French Aortic National CoreValve and Edwards (FRANCE 2) Registry received dual antiplatelet therapy for 1 month followed by aspirin indefinitely.[1] These differences underscore the current variations in clinical practice and indicate that the most effective antiplatelet strategy remains uncertain. The question of whether anticoagulation with an oral vitamin K antagonist or direct thrombin inhibitor is more effective than dual antiplatelet therapy also remains unanswered. Embolic protection devices have the potential to mitigate the risk of stroke in patients undergoing TAVR,[4] but further research is needed to determine their efficacy.

An increasingly recognized complication following TAVR is the development of heart block necessitating permanent pacemaker implantation. There is a much higher risk of heart block (roughly 2-fold) with use of the Medtronic CoreValve compared with the Edwards Sapien valve. The self-expanding CoreValve device has a larger profile in the subvalvular outflow tract and is more likely to damage the conduction tissue than the lower profile Sapien valve. In the PARTNER trial[3] using the Sapien valve, permanent pacing was required in 6.4% of patients. However, in the FRANCE 2 Registry,[1] pacemaker therapy was needed in 24.2% of patients receiving the CoreValve compared with 11.5% with the Sapien valve. In a German TAVR registry,[5] heart block requiring pacemaker therapy occurred in 42.5% and 22.0% with the CoreValve and Sapien valves, respectively. It is the Sapien valve that has received Food and Drug Administration approval for high-risk patients in the United States; the CoreValve remains investigational in ongoing clinical trials.

The risks of stroke and heart block have been apparent since the inception of transcatheter aortic valve technology. More recently, paravalvular aortic regurgitation has also arisen as a major determinant of poor postprocedural outcome. Compared with surgical valve replacement, TAVR is associated with more frequent and more severe paravalvular regurgitation. It is anticipated that the sudden onset of a moderate or severe degree of volume overload would be poorly tolerated in a hypertrophied left ventricle that previously had adapted to severe pressure overload, and this has proved to be the case.[6,7] Moderate to severe regurgitation occurs in 12% of patients receiving TAVR compared with 0.9% undergoing surgical valve replacement.[8]

Registry data suggest that the incidence of moderate or severe paravalvular regurgitation may be even higher in clinical practice. In the FRANCE 2 Registry,[1] the 30-day incidence of grade 2 or higher paravalvular aortic regurgitation was 17.1%. More recent data indicate that even mild paravalvular regurgitation, which is far more common, is also associated with increased mortality. In the PARTNER A trial,[3] mild paravalvular regurgitation developed in 43% of patients and was associated with a 2-fold increased risk of all-cause mortality. Possible mechanisms for paravalvular

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regurgitation include malposition, undersizing, underexpansion, and malapposition of the prosthesis. In addition, aggressive dilatation of the valve during deployment and guidewire interference can produce regurgitation through the valve leaflets themselves, contributing to the total regurgitant volume burden. Further study is needed to determine whether improved preprocedure imaging to optimize prosthesis size, greater attention to advantageous prosthesis deployment, or new device design will be successful in minimizing the frequency and severity of aortic regurgitation after TAVR.

These complications of TAVR provide the opportunity for further investigation and device development to improve clinical outcomes. They also provide reason for pause in the rush to expand the patient population eligible for TAVR. Not only are complication rates likely to be higher in clinical practice compared with trials, the magnitude of benefit observed in many trials is often attenuated in practice. One of the most unique and remarkable aspects of the PARTNER trial was that all of the more than 3000 eligible patients were evaluated by local multidisciplinary teams of surgeons, cardiologists, and nurses, and then reviewed by an executive committee composed of specialists in cardiovascular interventions, imaging, and surgery. The results of this trial likely represent the best outcomes that can be achieved by such a team-based approach. This multidisciplinary collaboration may not occur in all real-world practices, where individual physician and patient preference may play an overly influential role in determining treatment recommendations. Collaboration between cardiologists and cardiac surgeons has the potential to reduce any bias attributed to physician preference and focus instead on patient characteristics that may be more amenable to percutaneous or surgical therapy. Due to the complexity of patients with severe aortic stenosis and of the procedure, a team-based approach involving physicians and nurses experienced in TAVR is necessary to achieve the magnitude of benefit observed in the PARTNER trial and also to minimize complications.

Faced with the need for valve replacement, patients and their families understandably will prefer a percutaneous treatment approach, if available, rather than open heart surgery. It is essential for clinicians to temper increasing consumer expectations for TAVR with a frank discussion emphasizing that the time has not yet come for TAVR in patients who fulfill criteria for aortic valve replacement and have low surgical risk. There is already evidence of "indication creep" in countries with a longer history of regulatory approval for TAVR. For instance, in the German registry,[5] patient preference was the indication for TAVR in 13% of patients, all of whom had a Logistic EuroScore of less than 20%. Furthermore, in a Netherlands cohort,[9] 67% of patients underwent TAVR for off-label indications. These examples are a cause for concern. Clinicians must emphasize the proven short-term and long-term benefits of surgical aortic valve replacement in patients with low surgical risk. As with all new technologies, it is essential that patient and physician expectations must be balanced with a realistic assessment of potential benefits, risks, and outcomes to provide the optimal therapy for severe aortic stenosis.

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