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EDITORIAL COMMENT

TAVR for Severe Aortic Regurgitation

Advancing the Frontier*

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People will visit Mars, they will settle Mars and we should because it's cool.

—Jeff Bezos (1)

Transcatheter aortic valve replacement (TAVR) has revolutionized the treatment of symptomatic patients with severe aortic stenosis. Since the first of these procedures was performed in 2002 and U.S. Food and Drug Administration approval was received in 2011, indications have expanded to include progressively younger and lower risk patients, and TAVR volume has been increasing exponentially. It is the tremendous friction force of the metallic stent frame against the calcification of the native valve, prevalent in patients with degenerative calcific aortic stenosis, which serves as the anchor for these suture-less balloon-expandable or self-expanding bioprostheses. Off-label applications of the procedure are now being expanded to patients without heavy calcification, including those with failed surgically implanted bioprostheses; bicuspid aortic valves; and, the subject of the paper in this issue of the *Journal*, pure aortic regurgitation (AR).

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Yoon et al. (2) describe the findings from an international 40-center registry that included 331 symptomatic patients undergoing TAVR for pure native severe AR. The study was approved by the institutional review board of each institution and all patients provided written informed consent. The mean age was 74.4 ± 12.2 years. All patients had comorbid conditions that were believed to preclude surgical aortic valve replacement (SAVR) and patients with aortic stenosis, defined as peak aortic velocity >2.5 m/s by Doppler, were excluded. Aortic valve calcification was mild or absent in 85.9% of patients. The registry was initiated in August 2016; data for eligible patients receiving TAVR before this time were included retrospectively and thereafter, prospectively.

Procedural complications were substantial. Procedure-related death occurred in 3%, conversion to open surgery in 3.6%, coronary obstruction in 1.2%, aortic root injury in 1.5%, reintervention in 4.2%, need for second valve implantation in 16.6%, and new pacemaker in 18.2%. Post-procedural AR was estimated to be at least moderate in 9.6%. At 30 days, all-cause mortality was 10.9%. At 1 year, the cumulative event rates for all-cause and cardiovascular death were 24.1% and 15.6%, respectively.

During the course of the study, with enrollment that spanned nearly 10 years, improvements in procedural success occurred. These included reduction in the frequency of significant AR, and decrease in the need for second valve implantation. The overall device success, 61.3% for the first 119 patients, improved to 81.1% for the last 212 patients. Although the authors were inclined to attribute these successes to the development of newer-generation prostheses, which very likely did play a role, other differences included increases in the use of pre-procedural computed tomography assessment, more frequent general anesthesia, smaller contrast volumes, and 3-fold increase in the nontransfemoral approach. Technical factors related to increased operator experience, such as sizing of the annulus, use of intraprocedural echocardiography, and refinements in patient selection, may also have contributed to these findings. One-year cardiovascular mortality

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also decreased from 23.6% to 9.6%, although all-cause mortality did not change significantly.

These findings correspond with those from another recently reported registry regarding trends and outcomes of off-label use of TAVR devices (3). Since November 2011, Centers for Medicare and Medicaid Services has required all commercial TAVR centers in the United States to participate in this registry to receive payment. Among 23,847 procedures involving the Edwards SAPIEN (Edwards Lifesciences, Irvine, California) or CoreValve (Medtronic, Dublin, Ireland), the off-label use was 9.5% and 75.7% of these were performed in patients with severe aortic or mitral regurgitation. In those with off-label indications, moderate or greater degrees of perivalvular AR were more common (12.4% vs. 7.6%) and 1-year mortality was also higher (25.6% vs. 22.1%).

SAVR is the current standard of care for most patients with symptomatic severe AR (4). Repair rather than SAVR can be accomplished by surgeons with special expertise in some patients with AR caused by dilated aortic root, cusp perforation, or prolapse if the valve is not heavily calcified or deformed (5). SAVR is also indicated in severe AR if the left ventricular ejection fraction is <50% and there is no other cause for this dysfunction, or there is severe left ventricular dilation, even if the patient is asymptomatic, or if cardiac surgery is indicated for another reason (4).

Yoon et al. (2) deserve congratulations for their successes and for sharing their results. However, a few limitations should be noted and remaining questions addressed. A core laboratory was not used for determining the severity of prosthetic and periprosthetic AR. Quantitation of such regurgitation is challenging, even for experts, despite publication of the Valve Academic Research Consortium criteria (6). Methods of assessment may involve transthoracic, transesophageal, and intracardiac echocardiography (7). Variability among readers at 40 sites would likely be substantial. Additionally, the mean Society of Thoracic Surgeons score in the patients studied was 6.7%, suggesting an intermediate-risk group. What other factors, not accounted for by this score made the patients ineligible for surgery? Patients were classified according to annulus diameter <25.2 mm versus ≥25.2 mm. Was there an upper limit for aortic annulus dimension? If all patients had pure AR without stenosis, why was balloon pre-dilation performed in 7.9%? Yoon et al. (2) provide a nice account of what they have accomplished over time but further study is needed before generalization of TAVR for pure native severe AR can be recommended.

Presently, the outcomes for patients undergoing TAVR for severe AR are worse compared with those with on-label indications. But with continued modifications in TAVR prostheses, including anchoring mechanisms, sealing cuffs, additional sizes, and capacity for retrievability and repositioning; refinements in best practices, such as optimal periprocedural imaging, patient sedation, and prosthesis sizing (perhaps using oversizing with decreasing levels of calcification but also avoiding cases with too little calcium); and patient selection, including refinements in risk assessment that incorporate frailty, outcomes will improve.

Percutaneous aortic valve replacement will eventually become a standard therapy for isolated severe regurgitation and will save lives. This will be easier than settling Mars; both achievements will be cool.

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