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EDITORIAL COMMENT

Midterm Sapien Transcatheter Valve Durability

Ready for Prime Time or Waiting to Fail?*

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Since the first in human transcatheter aortic valve replacement (TAVR) was performed nearly 15 years ago (1), it has been estimated that more than 250,000 procedures have been performed worldwide. The procedure has been refined, and there has been tremendous growth in the evidence supporting its application for intermediate and high-risk patients with symptomatic severe aortic stenosis. The study by Daubert et al. (2), in this issue of *iJACC* adds to the burgeoning evidence that TAVR is an attractive alternative to surgical valve replacement (SAVR) in high-risk patients.

In this study, investigators sought to evaluate long-term durability of the Sapien balloon-expandable TAVR bioprosthesis by using PARTNER I (Placement of Aortic Transcatheter Valves) trial echocardiographic data (3,4). Investigators compared echocardiographic parameters of prosthetic valve function at the time of the first post-implantation echocardiogram to the same parameters 5 years later. In 86 TAVR patients alive at 5 years, without repeat AVR and having follow-up echocardiography at that time, parameters of prosthetic valve function were stable, and echocardiographic evidence of valve degeneration or worsening paraprosthetic regurgitation was uncommon. Five (5.8%) of the 86 TAVR subjects had an increase in mean systolic gradient ≥10 mm Hg. None of the 86 patients developed new severe regurgitation during follow-up. Transvalvular and paravalvular aortic regurgitation, aortic valve area, mean gradient, stroke volume, and ejection fraction were also stable over time, and there was regression in left ventricular mass index.

This study has notable strengths and limitations. A clear strength of the data is the standardized core laboratory methodology for the evaluation of echocardiograms. The authors outlined their rigorous methodology to ensure consistency, reproducibility, and quality, which gives us confidence in the reported echocardiographic findings. However, a weakness of the study is the missing data. Among the 832 patients from PARTNER I cohorts A and B, including 519 patients who underwent TAVR and 313 who underwent SAVR, echocardiographic data at 5 years post-procedure were available in only 134 patients (16%; 86 TAVR, 48 SAVR). There was a high rate of mortality prior to 5 years (n = 522), echocardiographic data were missing in 171 patients, and 3 patients were excluded after AV reintervention for severe regurgitation and/or stenosis in 2 patients, and endocarditis in 1 patient. The low percentage of follow-up data is disappointing but not surprising, given the advanced age and multiple comorbidities of the PARTNER I cohort. Thus, the main findings of the paper, that the Sapien TAVR is durable up to 5 years post-implantation, is based primarily on results from just 134 of 832 (16%) of the original PARTNER I cohort. This could potentially introduce bias.

The authors attempted to mitigate this potential bias with a secondary analysis aimed at detecting sudden worsening of valve performance before death; this was observed in several patients. Of 207 TAVR patients who had at least 2 echocardiograms before death, 8 had an increase of >10 mm Hg, 6 had a Doppler velocity index decrease to <0.25, and 3 developed new severe aortic regurgitation.

Although the authors' definition of significant valve degeneration is based on consensus guidelines (5), these cutpoints lack formal validation and

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other studies have used different cutpoints to define prosthetic valve degeneration (6), making direct comparison challenging. Additionally, given the fact that even mild paravalvular regurgitation is associated with poor prognosis (7), it would be useful to know how many TAVR valves developed new mild or moderate paravalvular regurgitation during follow-up.

As we begin to consider TAVR in low-risk patients as part of the PARTNER III trial, it will be critical to understand the longer-term durability of these valves. Indeed, previous work has raised questions about the durability beyond 5 years. A series published by Toggweiler et al. (6) included 88 subjects who underwent balloon expandable TAVR. Prosthetic valve failure described as moderate stenosis or moderate regurgitation was not present in any patient at 4 years, but was present at 5 years in 3.4% or 9.7% of those surviving. In a recent series of 50 patients who required redo TAVR, the time interval between the index TAVR and redo procedure was 1,189 ± 706 days for the 25 who developed structural failure (8).

Many more data exist regarding long-term performance of SAVR. Two recent, large series reported average freedom from reoperation for bioprosthetic valve failure of ≤2% at 5 years and ≤4% at 10 years (9,10). However, rates of structural valve failure are known to vary with age. Younger age was a risk factor for accelerated degeneration in both of these series. Current data suggest very low rates of reoperation for structural valve failure (≤1%) at 10 years in patients older than 70 years of age (9). Previous SAVR series also indicate that short- and mid-term performance are not always indicative of long-term performance. More than 20 years ago, reports indicated that certain surgical bioprosthetic valves might perform relatively normally up to 5 years and then show accelerated degeneration between 5 and 10 years (11). This finding highlights the importance of long-term follow-up in large, diverse groups of patients to confirm safety.

Presently, great clinical effort is expended on determining the optimal time for AVR, taking into consideration the presence of symptoms, which may be difficult to discern, comorbidities, severity of stenosis, and other predictors of outcome, such as stroke volume index, ejection fraction, left ventricular hypertrophy, diastolic function, pulmonary artery pressure, and parameters of myocardial deformation. Meanwhile, in the patient with severe aortic stenosis, adverse cardiac remodeling progresses, paving the way for subsequent atrial fibrillation and heart failure. Growing evidence for TAVR offers hope for improved patient care in the future as earlier intervention will reduce the potential for adverse remodeling. Demonstrated safety and long-term efficacy of TAVR along with low rates of operative morbidity and mortality will be necessary to tip the balance toward earlier intervention.

In summary, Daubert et al. (2) have given us an important early glimpse into the durability of the Sapien balloon expandable TAVR valve in long-term follow-up. Overall their results are encouraging and indicate that structural degeneration is uncommon at 5 years in surviving patients. However, given the previously mentioned limitations, we must be cautious about inferring that these results would apply to all patients with TAVR or all types of TAVR valves or to extrapolate durability beyond 5 years. Importantly, there are no data for TAVR durability in younger patients, in whom the durability of surgically implanted bioprosthetic valves is known to be decreased (9). As we consider TAVR valve implantation in younger patients with fewer comorbidities and potentially increased longevity, it will be critically important that we agree on a definition of structural degeneration in TAVR valves and that we obtain longer-term follow-up in larger numbers of patients to ensure safety.

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