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EDITORIAL COMMENT

Next-Generation Transcatheter Aortic Valve Replacement

Evolution of a Revolution*

Paul Sorajja, MD, Wesley Pedersen, MD

Transcatheter aortic valve replacement (TAVR) is a revolutionary therapy that has had a profound impact not only on the care of patients with aortic stenosis but also on the entire cardiovascular profession. To date, more than 100,000 patients worldwide have received this life-saving therapy. With continued population aging, the prevalence of candidates is expected to further increase (1). With its demonstrated efficacy in improving survival and quality of life, TAVR is now endorsed in U.S. and European practice guidelines for the treatment of symptomatic patients with severe aortic stenosis who are either inoperable or at high surgical risk (2,3). Now that the transformative benefits of TAVR are established, the remaining questions are focused on further improvements in the technology and its potential application in a broader population, including lower-risk patients.

Current TAVR therapy has its challenges. Even though procedural success rates for TAVR exceed 90%, the inability to retrieve and redeploy existing prostheses can lead to misplacement and complications such as aortic regurgitation, coronary occlusion, and device embolization, occasionally leading to emergency surgery. With high surgical risk or inoperable status established as an indication for TAVR, emergency surgery in these patients is considerably perilous and may be prohibitive. The irreversible nature of deployment with current TAVR prostheses therefore mandates an extraordinarily high level of training and expertise, usually facilitated by intense proctoring and a continued need for multiple physician operators to work cohesively to perform the procedure. Other concerns with TAVR include the need to demonstrate prosthesis durability and to further reduce the incidence of stroke, pacemaker dependency, vascular injury, and significant residual paravalvular regurgitation. Certainly, randomized trials and post-market registries have demonstrated that high levels of clinical efficacy can be achieved through systematic education and the use of dedicated, specialized healthcare teams (4). Nonetheless, these challenges remain and are relevant because complications of almost any degree in these procedures can lead to poorer survival given the high-risk aspects of these patients and their relative fragility.

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The report of the REPRISE II (REpositionable Percutaneous Replacement of Stenotic Aortic Valve Through Implantation of Lotus Valve System: Evaluation of Safety and Performance) registry by Meredith et al. (5) in this issue of the *Journal* highlights several innovations in TAVR therapy that help to address some present-day challenges. The Lotus valve (Boston Scientific Corp., Marlborough, Massachusetts) is a bovine pericardial, mechanically expanded, nitinol prosthesis with an adaptive seal to help prevent paravalvular regurgitation, deliverable with an 18-F (23-mm valve) or 20-F (27-mm valve) system. The valve leaflets are fully functional early during deployment (~50% of unsheathing), thereby allowing slow, deliberate placement without the need for rapid ventricular pacing. The most intriguing feature of the Lotus valve is its ability to be fully recaptured after deployment and before release. The Lotus valve can thus be repositioned in the event of device malposition or an untoward complication (e.g., coronary occlusion).

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From the Center for Valve and Structural Heart Disease, Minneapolis Heart Institute at Abbott Northwestern Hospital, Minneapolis, Minnesota. Both authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Indeed, in the current report of the REPRISE II registry of 120 patients treated with the Lotus valve, deployment occurred successfully in 100% of patients without a single case of device migration, embolization, need for valve-in-valve therapy, or emergency cardiac surgery. The lone procedural death was due to cardiac perforation. Partial or complete retrieval was used during deployment in 32 patients (26.7%), and this ability certainly was a major factor in the remarkable procedural success reported in this study.

The primary device performance endpoint of the study was mean aortic valve gradient at the 30-day follow-up, assessed by an independent echocardiographic core laboratory. The REPRISE II registry demonstrates the efficacy of Lotus valve implantation for the relief of aortic stenosis: the mean aortic gradient was reduced from 46 ± 15 mm Hg to 11 ± 5 mm Hg ($p < 0.001$), in association with an increase in the effective orifice area from 0.67 ± 0.21 cm^2 to 1.67 ± 0.43 cm^2 ($p < 0.001$). Post-implant paravalvular regurgitation also was much lower than reported in previous TAVR studies. There were no incidences of severe regurgitation; only 1 patient had moderate regurgitation, and 84% had no or trace regurgitation. This improvement could have been due, in part, to protocol-mandated use of computed tomographic imaging for annular sizing but is also likely attributable to the adaptive seal technology of the prosthesis, hoop strength, and its ability to be repositioned. The data on the Lotus valve meet or exceed the hemodynamic performance of other currently available TAVR prostheses, although it is important to note that echocardiograms were not evaluable for the aortic gradient in 19.2% of patients, nor for the valve area in 35% of the cohort. Incomplete echocardiographic data are hardly unique to this study; for example, 8% of the patients in the U.S. CoreValve High-Risk Study and 13% of those in the PARTNER (Placement of AoRtic TraNscathetER Valves) A study did not have 30-day data on mean gradient or aortic valve area (6,7). However, a higher rate of follow-up for such data might have been expected for REPRISE II, because hemodynamic assessment of the valve prosthesis was the primary endpoint of the study. Certainly, clinical outcomes and comparative data on safety and efficacy are of paramount concern in these studies, and the upcoming pivotal, randomized REPRISE III trial will enable analyses on the performance of the Lotus valve compared with other commercially available prostheses.

The REPRISE II data suggest that TAVR can be performed with a high rate of implantation success using a therapy that, absent certain potential complications (e.g., vascular injury, stroke), is reversible if not believed to be effective. A small-profile reversible prosthesis for TAVR therapy, with a seal for prevention of paravalvular regurgitation, is the emerging hallmark of next-generation devices, with other examples such as Portico (St. Jude Medical, St. Paul, Minnesota) and Direct Flow Medical (Direct Flow Medical Inc., Santa Rosa, California). These innovations and their association with favorable outcomes can engender discussion regarding the expansion of TAVR indications to a broader, lower-risk patient population. Although the precision of the Society of Thoracic Surgeons risk calculator does have limitations, recent data suggest that TAVR already is being used in patients who are at less surgical risk than those who were enrolled in the trials used for commercial approval (4,6–9). Of note, the mean Society of Thoracic Surgeons risk score for the patients in the recent report of the post-market TVT Registry was ~7% (similar to both REPRISE II and U.S. CoreValve High-risk studies), but it was ~11% in the PARTNER I studies. The PARTNER 2, SAPIEN 3, and SURTAVI (Surgical Replacement and Transcatheter Aortic Valve Implantation) studies are all evaluating TAVR in intermediate-risk patients. The emerging availability of completely retrievable prostheses, such as the Lotus valve, will only serve to embolden discussion for expanded indications, even in patients at lower risk of open surgery.

Nonetheless, deployment success does not equate to clinical success, and the availability of a therapeutic option, by itself, is not justification for its expanded use. Concerns regarding stroke have plagued TAVR, and stroke occurred in 5.9% of patients in REPRISE II (disabling stroke in 1.7%). This observation could be attributable to the small sample size, although theoretically, an increased risk of stroke could arise from excessive manipulation of the aortic valve during device retrieval, and this should be addressed with further study. Although there was a significant gradient reduction in REPRISE II, the investigators also reported that the post-procedural indexed effective orifice area was >0.85 cm^2/m^2 (or >0.70 cm^2/m^2 if body mass index was ≥30 kg/m^2) in only 60.7% of patients. Because of the flow-dependent nature of gradients and the relation between orifice area and long-term outcomes after aortic valve replacement, an integrated approach is recommended for the assessment of prosthetic valve stenosis, with the Valve Academic Research Consortium (VARC)-2 criteria for successful relief being a peak velocity <3 m/s or mean gradient <20 mm Hg and an effective orifice area >1.1 cm^2 or indexed orifice area >0.85 cm^2/m^2 for patients with body mass index <30 kg/m^2 (10).

Finally, a new permanent pacemaker was required in 28.6% of patients. Implant depth has been shown

to be a predictor of pacemaker dependency in TAVR patients, and the rate in REPRISE II occurred despite the ability to reposition the valve higher in the left ventricular outflow tract, if necessary (11). Approximately half of the pacemaker-dependent patients (56%) were those with left ventricular outflow tracts that were overstretched ≥10%, and thus, this problem may be addressed with the availability of more prosthesis sizes (i.e., only the 23- and 27-mm sizes were available in REPRISE II). Although studies thus far have not suggested that pacemaker dependency after TAVR affects survival, the effect of pacemaker dependency may vary according to ventricular function. In a recent study of 1,552 patients undergoing TAVR, new pacemaker dependency was associated with worse left ventricular ejection fraction at 6 to 12 months follow-up (12). These data in TAVR patients are consistent with well-studied effects of dyssynchrony on ventricular function in patients with other forms of systolic heart failure and could become more relevant if data continue to demonstrate different rates of pacemaker dependency for the available TAVR prostheses.

The Lotus valve is emblematic of the ongoing technological innovation in TAVR and is a harbinger of next-generation therapy in this field. The high deployment success and the low rate of complications (except for pacemaker dependency) in the REPRISE II study are indeed remarkable. Of note, the outcomes of TAVR with next-generation devices should be considered in the context of outcomes with open surgery, which represents the gold standard and the results of which are benefiting from the heart team approach in TAVR centers and continuing to improve. Currently, there are ~400 centers focused on delivering TAVR to high-risk patients. Could an easy-to-use, reversible technology such as that demonstrated in REPRISE II lead to more centers and relatively less experienced operators performing TAVR, even for patients who are not at high surgical risk? It certainly could, but only if the clinical outcomes from expanded studies justify the indications to do so.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Paul Sorajja, Center for Valve and Structural Heart Disease, Minneapolis Heart Institute, Abbott Northwestern Hospital, 920 East 28th Street, Suite 300, Minneapolis, Minnesota 55407. E-mail: paul.sorajja@allina.com.

REFERENCES

1. Nkomo VT, Gardin JM, Skelton TN, Gottdiener JS, Scott CG, Enriquez-Sarano M. Burden of valvular heart diseases: a population-based study. Lancet 2006;368:1005–11.

2. Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014;63:2438–88.

3. Vahanian A, Alfieri O, Andreotti F, et al. Guidelines on the management of valvular heart disease (version 2012): the Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J 2012;33:2451–96.

4. Mack MJ, Brennan JM, Brindis R, et al., for the STS/ACC TVT Registry. Outcomes following transcatheter aortic valve replacement in the United States. JAMA 2013;310:2069–77.

5. Meredith IT, Walters DL, Dumonteil N, et al. Transcatheter aortic valve replacement for severe symptomatic aortic stenosis using a repositionable valve system: 30-day primary endpoint results from the REPRISE II study. J Am Coll Cardiol 2014;64:1339–48.

6. Adams DH, Popma JJ, Reardon MJ, et al., for the U.S. CoreValve Clinical Investigators. Transcatheter aortic-valve replacement with a self-expanding prosthesis. N Engl J Med 2014;370:1790–8.

7. Smith CR, Leon MB, Mack MJ, et al., for the PARTNER Trial Investigators. Transcatheter versus surgical aortic-valve replacement in high-risk patients. N Engl J Med 2011;364:2187–98.

8. Leon MB, Smith CR, Mack M, et al., for the PARTNER Trial Investigators. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. N Engl J Med 2010;363:1597–607.

9. Lange R, Bleiziffer S, Mazzitelli D, et al. Improvements in transcatheter aortic valve implantation outcomes in lower surgical risk patients: a glimpse into the future. J Am Coll Cardiol 2012;59:280–7.

10. Kappetein AP, Head SJ, Généreux P, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. J Am Coll Cardiol 2012;60:1438–54.

11. Muñoz-Garcia AJ, Hernández-García JM, Jiménez-Navarro MF, et al. Factors predicting and having an impact on the need for a permanent pacemaker after CoreValve prosthesis implantation using the new Accutrak delivery catheter system. J Am Coll Cardiol Intv 2012;5:533–9.

12. Urena M, Webb JG, Tamburino C, et al. Permanent pacemaker implantation after transcatheter aortic valve implantation: impact on late clinical outcomes and left ventricular function. Circulation 2014;129:1233–43.

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