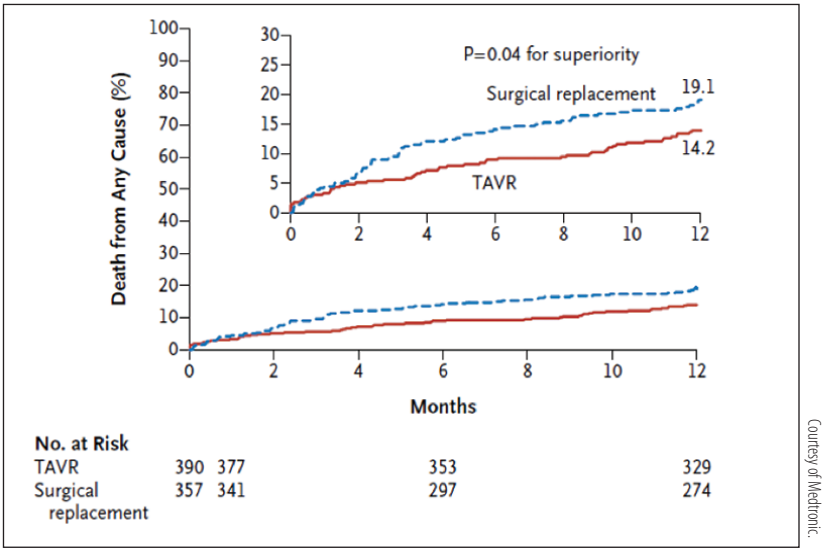
CoreValve Update

The current status and next generation of the CoreValve system.

BY RAJIV GOSWAMI, DO, AND NEAL S. KLEIMAN, MD

In November 2011, the US Food and Drug Administration approved the Sapien valve (Edwards Lifesciences) for treatment of inoperable aortic stenosis. Approval for use in patients at high risk for open cardiac surgery soon followed. The Centers for Medicare & Medicaid Services approved coverage of transcatheter aortic valve replacement (TAVR) for this indication on May 1, 2012. This approval resulted in a 96% increase in TAVR claims, from 5,400 claims in fiscal year 2012 to 10,599 claims in fiscal year 2013. The number of sites performing TAVR has increased from 228 to 336, and the median volume per site has increased from 10 to 23 cases per year during this same period.[1]



Courtesy of Medtronic.

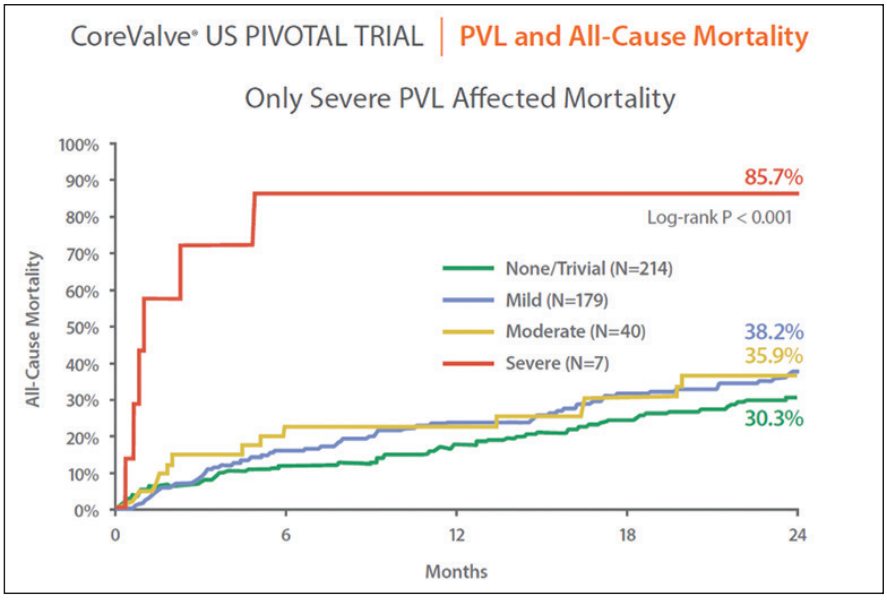
Figure 1. Cumulative frequency of all-cause mortality. The rate of all-cause mortality in the TAVR group was noninferior to that in the surgical group ($P < .001$). A subsequent test for superiority at 1 year showed that TAVR was superior to surgical replacement ($P = .04$). The inset shows the same data enlarged on the y-axis.

COREVALVE PERFORMANCE AND DESIGN

The second transcatheter heart valve that became commercially available in the United States is the CoreValve device (Medtronic). The CoreValve device consists of three bioprosthetic leaflets made of porcine pericardial tissue mounted on a self-expanding nitinol frame that is deployed by an unsheathing mechanism rather than by balloon expansion. The design provides the high radial force necessary to prevent recoil in the area of the annulus, but allows conformity to the natural elliptical shape of the aortic annulus. Hoop strength (the ability to resist deformation) is high at the distal-most portion of the valve that secures its position in the aorta. The inflow section of the valve contains a 12-mm-long sealing skirt that is also made of porcine pericardial tissue to minimize paravalvular regurgitation. The CoreValve device is available in sizes of 23, 26, 29, and 31 mm. These diameters are measured at the inflow (ventricular-most) portion of the valve. All sizes are delivered through an 18-F delivery catheter via transfemoral, subclavian, or direct aortic access.

The CoreValve device received CE Mark approval in 2007. It then received approval from the US Food and Drug Administration in January 2014 for the treatment of severe aortic stenosis in patients deemed to be at extreme risk for surgical valve replacement. This decision was based on the results of the Extreme-Risk study of the CoreValve US Pivotal trial, which showed a 25.5% rate of death or major stroke at 1 year. This outcome was 40.7% better than the objective performance goal determined based on the aggregate of previous series of balloon valvuloplasty.[2] An objective performance goal was used for the study because randomization to medical therapy in this group was judged to be unethical. The demographics of the CoreValve Extreme-Risk cohort were similar to the PARTNER B cohort with a mean age of 83 years and approximately 92% of patients in New York Heart Association class III or IV heart failure. CoreValve Extreme-Risk patients had a mean Society of Thoracic Surgeons predicted risk of mortality (STS-PROM) at

30 days of 10.3%, similar to the PARTNER B TAVR group, which had a mean STS-PROM of 11.2%. The US Food and Drug Administration issued approval for high-risk surgical patients in June 2014, based on the results of the High-Risk study of the CoreValve US Pivotal trial.[3] This trial demonstrated a superior rate of death or stroke compared with surgical valve replacement (85.8% vs 80.9% 1-year survival) (Figure 1). The TAVR patients in this study had a mean STS-PROM of 7.4%, making it a lower risk group than the TAVR patients in PARTNER A, with a mean STS-PROM of 11.8%. The rate of major vascular complications in the CoreValve High-Risk study at 1 year was 6.2%, and the pacemaker rate was 22.3%, both significantly higher than the surgical arm. A notable finding was the stroke rate at 1 year trended lower with TAVR at 8.8% versus 12.6% in the surgical arm. The recently presented 2-year results confirm a persistent lower all-cause mortality of 22.2% with TAVR versus 28.6% with surgical valve replacement.[4] The rate of all stroke at 2 years was lower with TAVR than surgery (10.9% vs 16.6%).



Courtesy of Medtronic.

Figure 2. Cumulative all-cause mortality stratified by degree of PAR. Only severe paravalvular leak had a significant impact.

UNRESOLVED CHALLENGES

There remain significant clinical unmet needs in transcatheter heart valve technology, such as limitations of design leading to paravalvular aortic regurgitation (PAR), lack of repositionability, and still relatively large delivery catheter size.

Moderate to severe PAR persisted in 6.1% of the patients in the CoreValve US High-Risk study, which is significantly more than with surgical valve replacement.[3] In the PARTNER trials of the Sapien valve, even mild aortic regurgitation had adverse prognostic significance,[5] whereas in the CoreValve trials, this association was not seen (Figure 2). The difference in findings between these studies remains unexplained. Although only severe PAR seemed to have an impact on 2-year mortality in the CoreValve US Extreme-Risk study (presented at TCT 2014),[6] perhaps further analysis of the 2-year results of the High-Risk study may elucidate the impact of PAR and other such factors on outcomes. The currently in-progress CoreValve Evolut R clinical study will assay the performance of a second-generation self-expanding device with enhancements in design to optimize annular fit and sealing. The study will enroll up to 250 patients at 25 clinical sites and report the primary endpoints of all-cause mortality or disabling stroke at 30 days in a high- or extreme-risk patient group.

The Evolut R valve is designed to address specific limitations of the current valve generation. The CoreValve design lends itself to a controlled and deliberate deployment process; however, it is subject to valve movement during deployment, which can result in suboptimal positioning. A low deployment would likely result in significant PAR and increase the chances of heart block. A possible solution for PAR after a low deployment is placement of another valve within the valve (valve-in-valve procedure) to create a better seal at the aortic annulus by application of more radial force. However, this technique would not improve the chances of avoiding heart block.

Another option would be to pull the valve out entirely. This maneuver may result in hemodynamic compromise because the patient will likely have acute severe aortic regurgitation due to disruption of the native valve. In this case, the valve can be collapsed by withdrawal into the access sheath, reloaded in the delivery catheter, and then will be ready for redeployment. If the valve had already been deployed, two tabs on the top of the frame can be grasped with a vascular snare. The valve can then be pulled back to

What will happen when we slide down the risk spectrum into the intermediate-risk population? Will the lower mortality with TAVR be replicated in this patient group?

the optimal position at the annulus, but it may also "pop out" and hopefully fixate in the ascending aorta; another attempt with a new valve can then be made. A high deployment can also result in significant PAR due to leak around the valve frame. The solution then is simple but expensive: performing a valve-in-valve procedure.

The Evolut R valve has a redesigned R delivery system (EnVeo) that offers several advantages. The delivery catheter itself is more flexible in one plane than that of the previous generation, while "shaft spines" reinforce the delivery catheter and allow transmission of longitudinal forces without stretching the catheter. Rotations of the deployment knob are thus transmitted to the unsheathing mechanism with minimal temporal lag, allowing the operator more precise control over the rate of valve deployment. Importantly, the CoreValve Evolut R can be recaptured and repositioned if the deployment location is judged to be unsatisfactory, obviating the need for some of the repositioning maneuvers at which we have become so adept.

Notwithstanding the progress made from the 22- or 24-F sheath sizes needed for the first-to-market Sapien valve, sheath size at the present time is still an important limitation. The first-generation CoreValve also requires an 18-F sheath, so the minimum recommended vessel size for the current generation of valves is 6 mm. CoreValve Evolut R is delivered through the 14-F (outer diameter) Inline sheath, thus permitting access via iliofemoral vessels as small as 5 mm. The Evolut R is already available in Europe; currently, the United States investigational device exemption clinical trial is estimated to be completed by May 2015. This will certainly broaden the application of TAVR to patients with smaller vessel sizes or peripheral vascular disease.

SUMMARY

TAVR is currently offered to patients at high surgical risk with an STS-PROM ≥ 8% or with two or more indicators of frailty by measures such as a Katz Activities of Daily Living score ≤ 2, a 5-meter walk time > 6 seconds, or hand grip strength ≤ 18 kg.[7] The CoreValve High-Risk study had a lower-risk patient profile than PARTNER A, but rather than equality in outcomes, as seen in PARTNER A, it showed lower all-cause mortality at 1 year with TAVR over surgical valve replacement without the trade-off of a higher stroke rate seen in the PARTNER A study. What will happen when we slide down the risk spectrum into the intermediate-risk population? Will the lower mortality with TAVR be replicated in this patient group? The SURTAVI clinical trial is currently enrolling intermediate surgical risk patients with severe aortic stenosis who are older than 75 years with an STS-PROM between 2% and 10% for a randomized comparison between TAVR and surgical AVR. The primary endpoint is all-cause mortality or disabling stroke at 2 years, and the estimated date of completion is August 2016. A favorable trial result could mean that surgical aortic valve replacement may be rendered obsolete, at least for the majority of patients with this disease. ■

Rajiv Goswami, DO, is a fellow in structural heart intervention with the Houston Methodist DeBakey Heart and Vascular Center in Houston, Texas. He has stated that he has no financial interests related to this article. Dr. Goswami may be reached at rajivgoswami@hotmail.com.

Neal S. Kleiman, MD, is with the Houston Methodist DeBakey Heart and Vascular Center in Houston, Texas; and Weill Cornell Medical College in New York, New York. He has stated that he has no financial interests related to this article. Dr. Kleiman may be reached at nkleiman@houstonmethodist.org.

1. Contos T, Tooley M. What can you learn from the FY 2013 TAVR data? The Advisory Board Company website. http://www.advisory.com/research/cardiovascular-roundtable/cardiovascular-rounds/2014/07/what-can-you-learn-from-fy-2013-tavr-data. Published July 24, 2014. Accessed March 29, 2015.
2. Popma JJ, Adams DH, Reardon MJ. Transcatheter aortic valve replacement using a self-expanding bioprosthesis in patients with severe aortic stenosis at extreme risk for surgery. J Am Coll Cardiol. 2014;63:1972-1981.
3. Adams DH, Popma JJ, Reardon MJ, et al. Transcatheter aortic-valve replacement with a self-expanding prosthesis. N Engl J Med. 2014;370:1790-1798.
4. Reardon, M, et al. A randomized comparison of self-expanding transcatheter and surgical aortic valve replacement in patients with severe aortic stenosis deemed at increased risk for surgery: 2-year outcomes. Presented at the ACC annual meeting; March 2015; San Diego, California.
5. Kodali SK, Williams MR, Smith CR, et al. Two-year outcomes after transcatheter or surgical aortic-valve replacement. N Engl J Med. 2012;366:1686-1695.
6. Yakubov SJ, et al. Long-term outcomes using a self-expanding bioprosthesis in patients with severe aortic stenosis deemed extreme risk for surgery: two-year results from the CoreValve US Pivotal Trial. Presented at the TCT annual meeting; September 2014; Washington DC.
7. Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease. J Am Coll Cardiol. 2014;63;22:e57-185.