Editorial

# Transcatheter aortic valve replacement: favorable clinical outcomes support role in intermediate risk surgical patients

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Transcatheter aortic valve replacement (TAVR) is now widely accepted as the preferred therapy for patients with severe aortic stenosis who are either inoperable or at high risk for complications following surgical aortic valve replacement (SAVR) (1-4). Outcomes of up to 5 years are now available that support the use of TAVR in this population (5,6). These clinical trials used first generation TAVR devices—balloon-expandable SAPIEN (Edwards Lifesciences) and self-expandable CoreValve (Medtronic). Both devices have since undergone design iterations with improvements in procedural success and clinical outcomes (7,8). In 2015, FDA approved the commercial use of SAPIEN 3, a third generation balloon-expandable transcatheter heart valve (THV) system.

Studies have demonstrated very low rates of adverse outcomes at 30 days with SAPIEN 3. In a prospective study of 150 high and intermediate risk patients, overall 30-day all-cause mortality was 5.3% and stroke was 2.7% following TAVR with SAPIEN 3. Moderate paravalvular leak (PVL) was noted in 3.5% of patients and no one had severe PVL (9). Despite a low profile delivery catheter with the SAPIEN 3 device, transfemoral (TF) approach was used only in 64% of patients in this study. Patients who underwent TAVR via TF approach had lower rates of mortality (2.1%) and stroke (1%) compared to patients who had TAVR via non-transfemoral (non-TF) alternate access (transaortic or transapical). In another study, 30 day outcomes of 583 high risk and inoperable patients undergoing TAVR with SAPIEN 3 revealed all-cause mortality of 2.2%. The incidence of stroke was 2.1%. Moderate PVL was noted in 2.9% of patients and no one had severe PVL (10). Despite the impressive short term data supporting use of SAPIEN 3, there has been a paucity of prospective long term data evaluating clinical outcomes.

One-year clinical outcomes of TAVR with SAPIEN 3 in high risk and inoperable patients with severe aortic stenosis were recently published by Herrmann *et al.* (11). The study involved 583 patients enrolled in a prospective, single-arm registry (PARTNER II SAPIEN 3 High Risk Cohort). Two-thirds of the patients were high risk and the rest were inoperable. TF access was used in 84.2% of patients. At 1 year, all-cause mortality was 14.4%. While there was no significant difference between HR and inoperable groups, 1-year all-cause mortality was significantly lower in patients who underwent TAVR via TF access (12.3%) compared to non-TF access (25.3%). The incidence of all stroke at 1 year was 4.3% and that of disabling stroke 2.4%. There was no significant difference in disabling stroke rates between HR and inoperable groups or TF and non-TF access groups. On echocardiography, the aortic valve area, peak, and mean aortic valve gradients were unchanged between 1 month and 1 year. PVL was also unchanged over time. Moderate PVL was observed in 2.7% of patients at 1 year and no patient had severe PVL. Moderate and not mild PVL was associated with reduced survival at 1 year. If patients with a permanent pacemaker (PPM) were excluded, the estimated rate for a new PPM was 20.1%. On multivariate analysis, independent predictors for all-cause mortality were major stroke, non-TF access and moderate PVL.

Overall, the most impressive finding in this study was the

low all-cause mortality of 14.4% at 1 year in high risk and inoperable patients with severe aortic stenosis undergoing TAVR with SAPIEN 3. It would be worth recalling that mortality at 1 year with the first generation SAPIEN THV was 24% in HR patients and 31% in inoperable patients. The benefit is even more impressive in the TF-TAVR group, where 1-year all-cause survival was 89.3% and cardiovascular survival was 93.3%. To understand the reasons for this striking benefit, one has to understand the technical advances and design changes of SAPIEN 3. While the first generation SAPIEN THV had a stainless steel frame and necessitated 22–24 F TF delivery sheath, SAPIEN 3 has a cobalt-chromium frame and altered leaflet design which allow for a smaller crimped profile and can be inserted through a 14–16 F expandable TF delivery sheath depending on valve size. This led to an increase in the use of TF access (84%) and a decrease in 30-day major vascular complications (5%). Though non-TF TAVR patients have significantly more co-morbidities, propensity matched comparisons have shown that TF-TAVR is associated with more favorable short-term and long-term outcomes compared to non TF-TAVR (12). Studies have also shown vascular complications to be an independent predictor of mortality post TAVR (13). Another significant change in design with SAPIEN 3 has been the addition of a polyethylene terephthalate skirt that covers the outer lower portion of the frame. This allows for effective annular sealing and hence a reduction in PVL, as attested by the very low rates of moderate PVL (2.7%) and absence of severe PVL at 1 year in this study. Moderate/severe PVL are known to be independent predictors of mortality post TAVR (14,15). The TF Commander delivery catheter provides a stable platform that allows for more precise and predictable positioning of the THV within the native valve. This contributes to the low incidence of PVL, valve embolization (0.2%) and implantation of multiple valves (0.9%). SAPIEN 3 is now available in four diameters—20, 23, 26 and 29 mm (SAPIEN THV was available only in two sizes—23 and 26 mm). This allows for more appropriate THV: native annulus size matching, which translates into lower risk of annular rupture (oversizing of THV) and PVL (under sizing of THV).

The rate of all strokes at 1-year post TAVR with SAPIEN 3 in this study are almost halved compared to post TAVR with SAPIEN THV in high risk patients (4.3% *vs.* 8.3%). This is likely due to a combination of greater operator experience and a lower profile delivery system that allows atraumatic implantation. SAPIEN THV was available for study purposes since 2007 and commercial use since 2011. The learning curve with SAPIEN THV led to increased operator experience, more systematic and strategic case selection and planning with SAPIEN 3 and hence better clinical outcomes.

There are certain limitations and some questions remain unanswered with this study. Firstly, this is not a randomized trial and there was no comparative arm. Hence information from such a study should be hypothesis generating rather than deriving definitive conclusions. The incidence of mild PVL at 1 year was 29.1%. Though in this study, mild PVL was not associated with reduced survival at 1 year, long-term follow-up of such patients is paramount. Of note, even mild PVL was an independent predictor of mortality at 2 years with SAPIEN THV (16). The rate of all stroke at 30 days post SAPIEN 3 TAVR was 1.4% and increased to 4.3% at 1 year. Given the absence of comparator arm, it is not possible to be certain if this increase in stroke rates reflect the overall vascular risk of study population or the study device. The need for a new PPM at 1-year post SAPIEN 3 TAVR was 20%. This is much higher than the need for new PPM post TAVR with first generation SAPIEN (5.7%) and second generation SAPIEN XT (9.9%). It has been shown that implantation height is an independent predictor of need for PPM post SAPIEN 3 (17). The current recommendation is to aim for a high implantation resulting in an aortic extension of the stent >70%. It is yet to be seen if this change in implantation strategy is associated with reduction in PPM rates with SAPIEN 3. While the durability of first generation SAPIEN THV for 5 years is known, we cannot be certain of the same durability with the newer generation SAPIEN 3. Though these designs have undergone rigorous *in vitro* testing prior to approval, the potential for reduced durability exists. Finally, patients with left ventricular ejection fraction <20% and bicuspid aortic valve were excluded from this study and hence one cannot apply these results to such patients. The need for rapid pacing during deployment of balloon expandable SAPIEN 3 might be deleterious for patients with severely impaired left ventricular systolic function. More data is needed regarding the use of SAPIEN 3 in such patients.

Given the excellent outcomes with SAPIEN 3 TAVR in high risk and inoperable patients, it is only rational to raise the bar and look ahead to the next frontiers—low and intermediate risk patients with severe aortic stenosis. In a recent study of 1,077 intermediate-risk patients enrolled in PARTNER 2 SAPIEN 3 intermediate risk observational

 

study, who underwent TAVR with SAPIEN 3, all-cause mortality at 1 year was 7.4%. The incidence of disabling stroke was 2% and the incidence of moderate/severe PVL was 2%. Using propensity score analysis, these patients were compared with intermediate risk patients treated with SAVR from PARTNER 2A (randomized study of TAVR with second generation SAPIEN XT *vs*. SAVR in intermediate risk patients with severe aortic stenosis). This analysis indicated a significant superiority of TAVR over SAVR with regard to the primary composite outcome of all-cause death, all strokes and incidence of moderate/severe PVL (18). Though both PARTNER 2A and SAPIEN 3 intermediate risk observational study had identical inclusion, exclusion criteria, as well as same clinical event committee, this was not a randomized trial and hence has inherent limitations. Earlier this year, FDA approved the expanded indication study of SAPIEN 3 in low risk patients. In this randomized study (PARTNER 3), TAVR with SAPIEN 3 will be compared to SAVR in patients with symptomatic severe aortic stenosis, age at least 65 years and surgical risk score of less than 4% per the Society of Thoracic Surgeons (STS) adult cardiac surgery risk calculator. Medtronic is performing a similar low risk trial with the Evolut R system.

In conclusion, we continue to see the evolution of the revolution created by TAVR in the management of high risk and inoperable patients with severe aortic stenosis. The 1-year clinical outcomes with SAPIEN 3 in this population have been very impressive, but it would be prudent to be aware of the need for long-term follow up with this device. However, the stage has been set for the next phase of the evolution already underway with studies in low risk patients.

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## References

1. Leon MB, Smith CR, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. N Engl J Med 2010;363:1597-607.
2. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. N Engl J Med 2011;364:2187-98.
3. Adams DH, Popma JJ, Reardon MJ, et al. Transcatheter aortic-valve replacement with a self-expanding prosthesis. N Engl J Med 2014;370:1790-8.
4. Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014;63:e57-185.
5. Toggweiler S, Humphries KH, Lee M, et al. 5-year outcome after transcatheter aortic valve implantation. J Am Coll Cardiol 2013;61:413-9.
6. Barbanti M, Petronio AS, Ettori F, et al. 5-Year Outcomes After Transcatheter Aortic Valve Implantation With CoreValve Prosthesis. JACC Cardiovasc Interv 2015;8:1084-91.
7. Binder RK, Rodés-Cabau J, Wood DA, et al. Transcatheter aortic valve replacement with the SAPIEN 3: a new balloon-expandable transcatheter heart valve. JACC Cardiovasc Interv 2013;6:293-300.
8. Manoharan G, Walton AS, Brecker SJ, et al. Treatment of Symptomatic Severe Aortic Stenosis With a Novel Resheathable Supra-Annular Self-Expanding Transcatheter Aortic Valve System. JACC Cardiovasc Interv 2015;8:1359-67.
9. Webb J, Gerosa G, Lefèvre T, et al. Multicenter evaluation of a next-generation balloon-expandable transcatheter aortic valve. J Am Coll Cardiol 2014;64:2235-43.
10. Kodali S, Thourani VH, White J, et al. Early clinical and echocardiographic outcomes after SAPIEN 3 transcatheter aortic valve replacement in inoperable, high-risk and intermediate-risk patients with aortic stenosis. Eur Heart J 2016;37:2252-62.
11. Herrmann HC, Thourani VH, Kodali SK, et al. One-Year Clinical Outcomes With SAPIEN 3 Transcatheter Aortic Valve Replacement in High-Risk and Inoperable Patients With Severe Aortic Stenosis. Circulation 2016;134:130-40.
12. Blackstone EH, Suri RM, Rajeswaran J, et al. Propensity-

 

matched comparisons of clinical outcomes after transapical or transfemoral transcatheter aortic valve replacement: a placement of aortic transcatheter valves (PARTNER)-I trial substudy. Circulation 2015;131:1989-2000.
13. Généreux P, Webb JG, Svensson LG, et al. Vascular complications after transcatheter aortic valve replacement: insights from the PARTNER (Placement of AoRTic TraNscathetER Valve) trial. J Am Coll Cardiol 2012;60:1043-52.
14. Généreux P, Head SJ, Hahn R, et al. Paravalvular leak after transcatheter aortic valve replacement: the new Achilles' heel? A comprehensive review of the literature. J Am Coll Cardiol 2013;61:1125-36.
15. Athappan G, Patvardhan E, Tuzcu EM, et al. Incidence, predictors, and outcomes of aortic regurgitation after transcatheter aortic valve replacement: meta-analysis and systematic review of literature. J Am Coll Cardiol 2013;61:1585-95.
16. Kodali SK, Williams MR, Smith CR, et al. Two-year outcomes after transcatheter or surgical aortic-valve replacement. N Engl J Med 2012;366:1686-95.
17. De Torres-Alba F, Kaleschke G, Diller GP, et al. Changes in the Pacemaker Rate After Transition From Edwards SAPIEN XT to SAPIEN 3 Transcatheter Aortic Valve Implantation: The Critical Role of Valve Implantation Height. JACC Cardiovasc Interv 2016;9:805-13.
18. Thourani VH, Kodali S, Makkar RR, et al. Transcatheter aortic valve replacement versus surgical valve replacement in intermediate-risk patients: a propensity score analysis. Lancet 2016;387:2218-25.

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