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TCT 2016: Transcatheter heart valve highlights

The 2016 instalment of the annual Transcatheter Cardiovascular Therapeutics (TCT) meeting provided much excitement, as important scientific evidence in the field of transcatheter aortic valve implantations (TAVI) was presented. Herein, we present a summary of some of the most relevant information presented at the Convention Center in Washington DC, USA on October 29th – November 2nd.

The SENTINEL Study

Cerebrovascular events remain an Achilles' heel of TAVI technology, occurring in 2.7 to 5.5% of cases at 30 days after treatment.[1,2] Although adjudicated stroke rates have fallen with device iteration and improved operator technique, there remains much scope to further reduce the impact of debris from the aortic arch and liberated from the stenotic aortic valve during transcatheter valve positioning and deployment. Several investigators have demonstrated new cerebral lesions in up to 84% of post-TAVI magnetic resonance imaging (MRI).[3] Importantly, cerebral embolic protection has demonstrated the potential to reduce the number and volume of new cerebral lesions.[4]

The SENTINEL randomised, controlled trial tested the hypothesis that the Claret Medical Sentinel® transradial embolic protection system could reduce cerebral lesions and clinical stroke compared with usual practice among patients undergoing TAVI.[5] In total, 363 patients were randomised in a 1:1:1 fashion to a safety arm (N=123; TAVI + Sentinel), a test arm (N=121; TAVI + Sentinel), and a control arm (N=119; TAVI only). Clinical follow-up by a stroke neurologist was mandatory in all cases, and serial MRI imaging and neurocognitive function assessment were performed in the Sentinel and control arms at pre-specified time points. The primary safety endpoint was a composite of all-cause mortality, stroke, and acute kidney injury (Stage 3) compared to an historical performance goal (non inferiority). The primary efficacy endpoint was a reduction in median total new lesion volume in protected territories, assessed by diffusion-weighted MRI at Days 2 to 7 post-procedure.

Dr Susheel Kodali (New York, NY, USA) presented the trial results at TCT 2016. The mean age and Society of Thoracic Surgeon's (STS)-predicted risk of mortality score were 83.4 years (range: 70.0–88.2 years) and 6.0% (range: 4.2–8.1%), respectively. The Sentinel® device was successfully delivered in 94% of cases and the primary safety endpoint was achieved with ease; the rate of adverse cardiac and cerebral events was 7.3% compared to the 18.3% historical performance goal ($p_{\text{non inferior}}<0.001$). The authors noted debris in 99% of embolic filters post-TAVI and reported a numerically lower rate of stroke at 30 days in the test arm compared to controls (5.6 vs 9.1%; p=0.25); notably, this trial was not powered for stroke as a clinical endpoint. Crucially, the primary efficacy endpoint was not achieved, with a non-statistically significant 42% relative reduction in the volume of new cerebral lesions on MRI (102.8 vs 178.0 mm^3; p=0.33).

The interpretation of this important trial is somewhat difficult. Although the device is safe, a negative primary endpoint from a statistical point of view implies that one should disregard all subgroup or secondary analyses, and thus return a verdict that the Sentinal® device does not significantly reduce cerebral embolisation during TAVI. Despite not being statistically significant, the 42% relative reduction in new cerebral lesion volume is considerable, and the trend towards lower rates of clinical stroke should be considered hypothesis-generating and be sufficient enough to garner enthusiasm for conducting a larger trial powered for clinical endpoints. In the interim, the community will probably continue to use embolic protection selectively in those at highest risk of

cerebral embolisation; unfortunately, it remains difficult to identify those at high stroke risk. With available evidence, systematic cerebral protection in TAVI is not justified.

Transcaval TAVI

Dr Adam Greenbaum presented the results of an investigator-initiated, multicentre prospective trial designed to demonstrate the safety and efficacy of transcaval TAVI.[6] Greenbaum and Lederman first described this innovative technique in 2014.[7] The study enrolled 100 extreme-risk patients (STS predicted risk of mortality: 9.6 ± 6.3%) deemed not suitable for transfemoral or transthoracic TAVI. The results were impressive, with 98% device success and a 30-day mortality of 8%. Valve Academic Research Consortium adjudicated life-threatening bleeding occurred in 12 cases (6 due to transcaval access) and the median hospital stay was 4 days (range: 2–6 days). One third of patients had a persistent aortocaval shunt 1-month post TAVI despite closure with a nitinol cardiac occluder. Such shunts appear to be well tolerated, and the vascular access was not responsible for haemodynamic embarrassment in any case.

These data suggest that transcaval vascular access should be considered in patients not suited to more traditional vascular access routes. Although life-threatening bleeding (12%) was higher with transcaval TAVI than historical transfemoral cohorts, these rates are roughly similar to prior transthoracic TAVI experience.[8] The development of dedicated aortic occluder devices and ongoing procedural refinement will further reduce vascular complications. Whether this technique can surpass transthoracic or supra-aortic access routes is unclear, but the results achieved with operators and centres new to this procedure suggest that transcaval access will proliferate in the future.

PARTNER I Echocardiographic Data at 5 Years

Given the move towards treating intermediate- and lower-risk patients, the final 5-year echocardiographic data from the original PARTNER I (A and B) trials and the Continued Assess Registry were a welcome addition to the late-breaking trial session at TCT. These core laboratory-adjudicated data presented by Dr Pamela Douglas (Durham, NC, USA), demonstrate no significant increase in mean transvalvular gradient 5 years post-implantation of the first-generation Edwards transcatheter valve (Edwards Lifesciences, Irvine, USA): 12.1 mmHg (1 month) vs 9.2 mmHg (3 months) vs 10.3 mmHg (5 years); p=0.63.[9] Among 2,230 patients with serial post TAVI echocardiographic studies, only 10 patients had an interval increase of 20 mmHg. Such mid-term data are, of course, encouraging, though longer-term high-quality data are required to compare the durability of both transcatheter and surgical aortic valves.

PARTNER II Quality of Life

Dr David Cohen (Kansas City, MO, USA) presented the quality of life (QOL) data from the intermediate-risk PARTNER II trial.[10] QOL measures included the Kansas City Cardiomyopathy Questionnaire (KCCQ, primary endpoint), the SF-36 and the EQ-5D, and were measured at baseline, 1 month, 1 year and 2 years. Among the TAVI cohort vascular access route was a pre-specified sub-group analysis. Unsurprisingly, the authors observed significantly improved QOL following both TAVI and surgical aortic valve replacement (SAVR); the KCCQ summary score was 19.2 for Sapien XT (Edwards Lifesciences, Irvine, USA) and 18.3 for SAVR (p = not significant).

In transfemoral TAVI patients, there was a substantial QOL benefit compared with alternate access TAVI or SAVR at 1 month, though this benefit had waned by 1 year. These data support the "femoral first" mantra observed in high- and excessive-risk patients, and suggest that further work is necessary to improve the experience of patients undergoing non-transfemoral TAVI.

CoreValve® Evolut® R: US Investigational Device Exemption (IDE) Study

Dr Jeff Popma (Boston, MA, USA) presented important new data relating to the Evolut® R TAVI system (Medtronic Inc., Dublin, Ireland) at TCT 2016.[11] The US safety and efficacy study among high- and extreme-risk patients (N=241) demonstrated impressive 30-day and 1-year mortality rates of 2.5% and 8.6% (STS predicted risk of mortality: 7.4 ± 3.4%). Thirty-day rates of major vascular complications (7.5%), moderate paravalvular leaks (5.3%), and new permanent pacemakers (16.4%) were reported. Excellent haemodynamic results were achieved with a mean transvalvular gradient of 9 mmHg and valve area of 1.8 cm^2 at 1 year.

fig. 1

CoreValve® Evolut® R 34 mm Transcatheter Aortic Valve.

26	27	28	29	30
Treatable Annulus Range (mm)				

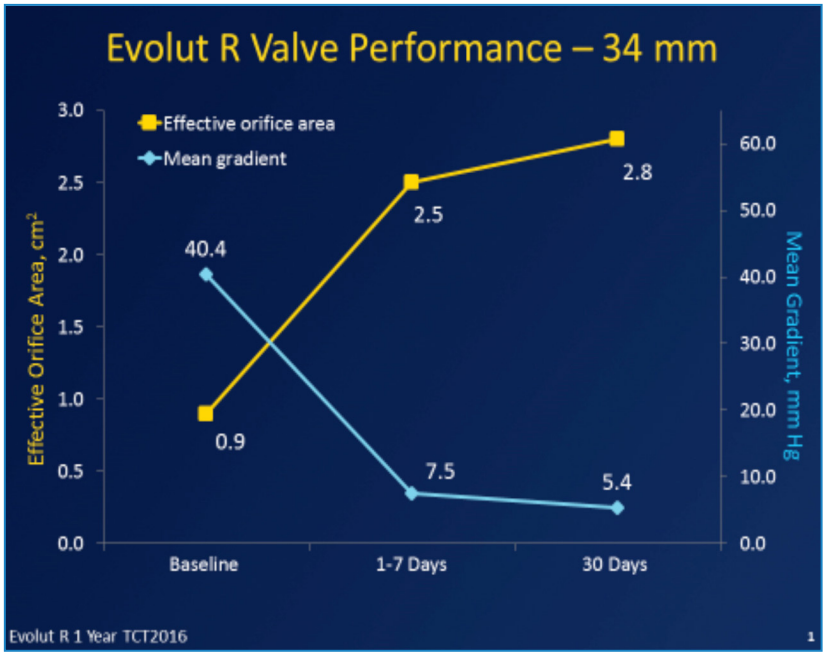
This presentation also included data from the first clinical experience of the 34 mm CoreValve® Evolut® R Transcatheter Aortic Valve (Figure 1). In this cohort (N=15), the mean age and STS-predicted risk of mortality were 80.8 ± 8.1 years and 4.8 ± 2.2%. In this small series, there were no deaths or strokes, one case of moderate paravalvular leak (7.7%), and two new pacemaker implants (13.3%) at 30 days. The post-implantation valve area was an impressive 2.8 mm^2 (Figure 2). Further experience with this device is eagerly awaited.

Conclusions

TCT 2016 provided important data in relation to the rapidly expanding field of TAVI. Although the role of embolic protection in TAVI remains unclear, clinical expertise and device iteration continues to deliver improved patient outcomes.

fig. 2

Haemodynamic data for the 34 mm CoreValve® Evolut® R platform demonstrates a mean gradient of 5.4 mmHg and an impressive effective orifice area of 2.8 mm^2.



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DISCLOSURES: Dr Mylotte is a proctor for Medtronic and Microport. Dr Neylon has no disclosures.