Emerging valve systems and iterative technologies from around the world and how they could shape global practice going forward.

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Transcatheter aortic valve implantation (TAVI) has been adopted worldwide for the treatment of severe symptomatic aortic stenosis in patients at intermediate, high, or prohibitive surgical risk. Clinical outcomes from TAVI continue to improve regardless of patient risk categorization, thereby challenging the historical surgical gold standard. Several factors account for the enhanced patient outcomes with TAVI, including the introduction of preprocedural multislice CT for device sizing and selection and vascular access route, ever-increasing operator experience, and of course, newer transcatheter heart valve (THV) and delivery system iterations. Nevertheless, procedural complications leading to death and stroke continue to occur in up to 5.7% of patients. Important complications such as paravalvular leak (PVL), new permanent pacemaker placement, vascular complications, coronary occlusion, and annular rupture continue to occur. However, it is important to note that the impressive results associated with this novel technology have now enabled a focus on simplifying the procedure and expedient patient discharge, rather than the previously mentioned more traditional outcomes.

This article describes the key features of novel devices that have entered or are about to enter contemporary clinical practice and explains how these new concepts may shape the future of our field.

NOVEL WESTERN TAVI DEVICES

Sapien 3 Ultra
Sapien 3 (Edwards Lifesciences) is among the most frequently used THV systems worldwide. The current balloon-expandable valve is delivered using the 14- to 16-F Commander transfemoral expandable sheath and features an outer sealing skirt that has greatly reduced the incidence of PVL. Indeed, the impressive results of the PARTNER II trial, which included 1,077 intermediate-risk patients, reported an all-cause mortality rate of 1.1%, stroke rate of 2.7%, new pacemaker rate of 10.2%, and moderate or severe PVL rate of 2% at 30 days.

The most recent iteration of the system is due to be released in early 2018. Edwards’ Sapien 3 Ultra valve has an extended outer skirt to further reduce PVL, and the Ultra delivery system has a redesigned ergonomic handle with the valve preloaded on the deployment balloon to reduce procedural steps and improve cath lab efficiency. Furthermore, the 14-F Axela expandable sheath will accommodate all valve sizes, including the 29-mm THV, which previously required a 16-F expandable sheath (Figure 1A).

Centera
The novel self-expanding Centera valve (Edwards Lifesciences) just received CE Mark approval for European commercialization. The system consists of a nitinol...
self-expanding frame that is available in three sizes: 23, 26, and 29 mm (Figure 1B). The valve frame height is shorter than other commercially available self-expanding devices (18, 21, and 23 mm), and bovine pericardial leaflets sit at annular level inside a concave frame, which has minimal extension into the left ventricular outflow tract (2–4 mm). The self-expanding valve is premounted on a motorized steerable delivery catheter that is inserted via a 14-F expandable sheath for all sizes. The device can be repositioned, recaptured, and removed during deployment.

At EuroPCR 2017, the multicenter CENTERA-EU trial reported outcomes from 203 high-risk patients undergoing TAVI with the Centera device at 23 centers in Europe, Australia, and New Zealand. Clinical outcomes were impressive, including Valve Academic Research Consortium–defined device success in 96.4% and 30-day all-cause mortality in 1%. Stroke occurred in 4%, major vascular complications occurred in 6.4%, and new pacemaker implantation was required in 4.9%. Reported hemodynamics were excellent—the single-digit mean gradient was 7.2 mm Hg, large effective orifice area was 1.9 cm², and moderate PVL occurred in 0.5% (no severe PVL). Six-month data presented at PCR London Valves 2018 corroborate the short-term safety and efficacy.

**Acurate Neo 2**

On March 30, 2017, Boston Scientific Corporation announced the acquisition of Symetis SA for $435 million. The company’s Acurate neoprosthesis is a nitinol self-expanding THV available in three sizes (small, medium, and large), with supra-annular porcine pericardium leaflets and a pericardial sealing skirt on both the outer and inner surfaces of the valve frame (Figure 1C). The delivery system requires a 15- to 18-F access sheath, and the unique top-down delivery does not include recapture or reposition functionality. To date, nonrandomized clinical results are encouraging, primarily derived from the post–CE Mark SAVI-TF registry (N = 1,000). The rates of 30-day mortality, all-cause stroke, major vascular complications, and new pacemaker implantation were 1.4%, 1.9%, 3.2%, and 8.3%, respectively. The postimplantation mean gradient was 8.4 mm Hg, effective orifice area was 1.77 cm², and moderate/severe PVL occurred in 3.4%.

The next iteration of this system, the Acurate Neo 2, has recently completed enrollment in a 120-patient CE Mark study. The new device has an improved delivery catheter and incorporates a modified skirt material to further reduce PVL. The device will be compatible with Boston Scientific’s 14-F iSleeve expandable sheath.

**Lotus Edge**

The Lotus valve system (Boston Scientific Corporation) has not been available for commercial use since October 2016 due to rare instances in which an early pin release impaired the ability to completely deploy and recapture the valve. In 2019, the valve is expected to return to the market, pending regulatory approval, and rather than reenter with the predicate Lotus valve, Boston Scientific plans to launch the Lotus Edge valve system (Figure 1D). Similar to the original Lotus device, Lotus Edge is a mechanically expandable valve with annular bovine pericardial leaflets and an adaptive seal. Lotus Edge is delivered via the 14/15-F iSleeve expandable sheath with a gentle preshaped delivery catheter. The valve will largely shorten from the top during the latter stages of deployment when contact with the left ventricular outflow tract risks conduction disturbance. This latter feature will be critical to the adoption of Lotus Edge technology, given the high rates of perma-
The hemodynamic advantages of supra-annular valve leaflets. At high or extreme surgical risk to receive either CoreValve (Medtronic) or the Lotus valve. The primary safety endpoint (30-day composite of all-cause mortality, stroke, life-threatening or major bleeding, stage 2/3 acute kidney injury, and major vascular complications) was noninferior between the groups. The primary effectiveness endpoint (1-year composite of all-cause mortality, disabling stroke, ≥ moderate PVL) occurred less frequently in the Lotus group, mainly driven by a significantly lower rate of moderate or greater PVL (0.9% vs 6.8%; \( P < .001 \)). The mechanically expanded valve had a considerably higher rate of new pacemaker implantation (35.5% vs 19.6%; \( P < .001 \)).

Preliminary data on the Lotus Edge system from a small study (\( N = 21 \)) suggest conservation of the first generation’s benefits but with a reduced pacemaker rate. Further study of this device is required.

Evolut PRO
Building on the success of its CoreValve Evolut R platform, Medtronic has added an external 12-mm pericardial wrap to its Evolut R valve (Figure 1E). The new wrap is expected to improve sealing and reduce the rate of PVL. The Evolut PRO system is CE Mark and US Food and Drug Administration approved and is available in 23-, 26-, and 29-mm valve sizes. The wrap has increased the profile of the current delivery system (14–16 F), but ongoing catheter development is expected to reduce the profile back to 14 F within 12 months. The current 34-mm Evolut R valve does not have the sealing wrap.

Evolut PRO was tested in a nonrandomized single-arm clinical study that enrolled 60 patients at high surgical risk. This small study demonstrated low rates of 30-day mortality (1.7%) and stroke (1.7%). Due to improved valve sealing with the new wrap, no patient had moderate or greater PVL. As expected, single-digit postimplantation gradients (6.4 mm Hg) and impressive effective orifice areas (2 cm²) were reported, while the requirement for permanent pacemaker occurred in 10% of cases.

Medtronic also has a next-generation THV development program known as Horizon. This project aims to develop a new self-expanding valve system characterized by concentric expansion, recapture and reposition function after complete deployment, and low frame height to allow unimpeded coronary artery access, all while maintaining the hemodynamic advantages of supra-annular valve leaflets.

Transfemoral JenaValve
The JenaValve transcatheter system (JenaValve Technology GmbH) consists of three porcine pericardial leaflets and a skirt, mounted on a self-expanding nitinol stent with three locators, and is the only TAVI device with CE Mark approval for treatment of native primary aortic regurgitation (Figure 1F). The system was withdrawn from the market due to the decline in the transapical procedures and to allow the company to focus on the development of a transfemoral device. Recently, the first-in-human implantation of this novel device was published in EuroIntervention. The 27-mm JenaValve was implanted in a patient with severe native aortic regurgitation via a 19-F vascular sheath and using the unique leaflet clipping mechanism of the predicate transcatheter device. Further study of this device is ongoing in the prospective CE Mark clinical study, with results expected in Q3 2018.

NOVEL EASTERN TAVI DEVICES
Venus A-Valve
The Venus A-valve system (Venus Medtech Inc.) is composed of a multilevel self-expandable nitinol stent frame and three porcine pericardial leaflets in a supra-annular position (Figure 2A). The Venus A-valve is specifically designed with increased radial force at the initial 20 mm of the stent inflow segment to accommodate the heavily calcified and bicuspid valve morphology commonly seen among Chinese TAVI candidates. The valve also features three radiopaque markers at half a cell (of the open-cell frame) above the inflow to indicate the optimal landing position and is delivered via a 19-F vascular access sheath. Importantly, the current generation of the device is not repositionable nor recapturable, but the next-generation system will incorporate these features.

The safety and efficacy of the device were evaluated in high-risk and inoperable patients in the Venus-A study. This small, prospective, single-arm study included 101 patients with a mean age of 75.4 ± 6.4 years and had a median Society of Thoracic Surgeons predicted mortality risk score of 5.5% (interquartile range, 3.8%–9.2%). Bicuspid aortic valve anatomy constituted approximately 50% of the study population. Device success rate was similar in bicuspid and tricuspid patients (79.5% vs 86.8%; \( P = .06 \)). Similarly, 30-day mortality (6.8% vs 3.8%; \( P = .50 \)) and 2-year cumulative survival (90.9% vs 88.6%; \( P = .72 \)) were similar between patients with bicuspid and tricuspid valves, respectively. The China Food and Drug Administration (CFDA) granted approval of the Venus A-valve in April 2017, making it the first and currently only transfemoral TAVI device that is commercially available in China.
Venibri

The Venibri valve, a joint venture between Venus Medtech, Inc. and Colibri Heart Valve LLC, combines technology from the self-expandable Venus A-valve frame and “dry” tissue from the Colibri valve (Figure 2B). The dry tissue omits glutaraldehyde treatment of the bovine pericardium with the potential to reduce residual antigenicity, thereby improving biocompatibility, calcification resistance, and tolerance to chronic stresses and strains. The dry-tissue Venibri valve comes premounted and precrimped, allowing minimal on-site valve preparation and rapid deployment in cases of hemodynamic instability. The first-in-human implantation of the Venibri valve took place at the Institute of Cardiology of Corrientes in Argentina in October 2016. At the 2017 Transcatheter Cardiovascular Therapeutics conference, preliminary results from 17 patients treated with the device were presented. Outcomes were acceptable with regard to the technical success rate in all cases and a single 30-day death. Moderate paravalvular regurgitation occurred in one patient, and a new pacemaker was required in two cases (11.8%). The safety and efficacy of the Venibri valve will be evaluated in an upcoming international multicenter trial.

VitaFlow

The VitaFlow transcatheter aortic valve (MicroPort Medical) consists of a self-expandable nitinol stent frame mounted with supra-annular bovine pericardial leaflets (Figure 2C). The valve has inner and outer skirts to reduce PVL and increased inflow radial force for patients with severe calcification and bicuspid anatomy. The low-density cell design, particularly at the outflow, affords flexibility for alignment and deployment and facilitates coronary access. The delivery system features a motorized handle and is 16 F for the 21-mm valve and 18 F for the 24-, 27-, and 30-mm valves. A small, premarket, single-arm prospective study of the VitaFlow system in 110 high-risk patients completed enrollment in January 2017. Data were presented at EuroPCR 2017; mean patient age was 77.7 ± 4.8 years and 37.3% of patients had bicuspid aortic valves. Clinical results were competitive, with an all-cause mortality of 1.8% and 2.7% at 30 days and 6 months, respectively. Notably, the incidence of mild or greater PVL was only 1.9% at 30 days (n = 108) and 0% at 6 months (n = 102). Bicuspid and tricuspid morphology appeared to have similar outcomes. One-year follow-up was recently completed and will be submitted to the CFDA for review, with potential commercialization of the system in Q4 2018.

The next generation of the Vitaflow valve is in development and expected to commence clinical trials in China and Europe in 2018. This system features a lower-profile delivery system and the ability to recapture and reposition the system at up to three-quarter deployment.

CONCLUSION

Although great strides have been made in the TAVI realm over the last decade, new valve systems and iterative innovative technologies continue to emerge. These novel devices aim to overcome the limitations of early generation devices and will further improve clinical outcomes and extend TAVI technology to more patients globally.

Figure 2. Novel Eastern TAVI devices. The Venus A-valve (A), Venibri (B), and VitaFlow (C) transcatheter heart valves.

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7. Walters DL. First report of clinical outcomes with the next-generation Lotus Edge valve system: results from the LOTUS Edge feasibility trial. Presented at ACC.17; March 18, 2017; Washington DC.

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