

Aortic Valves: What's Coming?

Devices in early clinical development, including devices with early human experience and those originating from China.

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Over the past 10 years, transcatheter aortic valve replacement (TAVR) has become a transformative technology for the treatment of severe aortic stenosis (AS). The role of TAVR as an alternative to surgical aortic valve replacement (SAVR) is well accepted in some patient subsets and is under investigation in others. Currently, TAVR has emerged as the standard of care for patients with severe symptomatic AS deemed to be either at excessive or high risk for SAVR and has proven to be equivalent to surgery in intermediate-risk patients.¹⁻³ However, a multidisciplinary team approach is recommended in patients with symptomatic AS. The choice between SAVR, TAVR, or medical therapy should be based upon estimated surgical risk and comorbidity factors.

In the last few months, strong data from prospective randomized trials have led to the expansion of TAVR indications worldwide, and these expanded indications have been incorporated into the guide-

lines for the management of valvular heart disease from both the European Society of Cardiology (will be reported next summer) and the American Heart Association/American College of Cardiology (recently updated at ACC 2017).⁴ Recently, PARTNER II and SURTAVI, two large randomized trials that used both balloon-expandable and self-expanding technologies, showed noninferiority of TAVR in intermediate-risk patients compared with SAVR.^{3,5}

DATA BACKGROUND

Both technical and technological progress can explain the remarkable reported safety and efficacy outcomes. With a better understanding of aortic root anatomy, patient selection for TAVR has improved.

The reported rate of paravalvular leak (PVL) has been shown to be very low in the latest literature data, with moderate-to-severe PVL approaching 0% with some devices.⁶ It is important to note that the etiology of

PVL is multifactorial; among the factors responsible for PVL are suboptimal positioning (the valve is placed too low or high), insufficient oversizing of the valve relative to the surrounding anatomy, and incomplete apposition to the contact surface (annulus and leaflets) due to recalcitrant calcific deposit. Progress in implantation technique and device technology iterations have helped reduce PVL rates; optimal sizing, a better understanding of the anatomy, and choice of device on a rou-

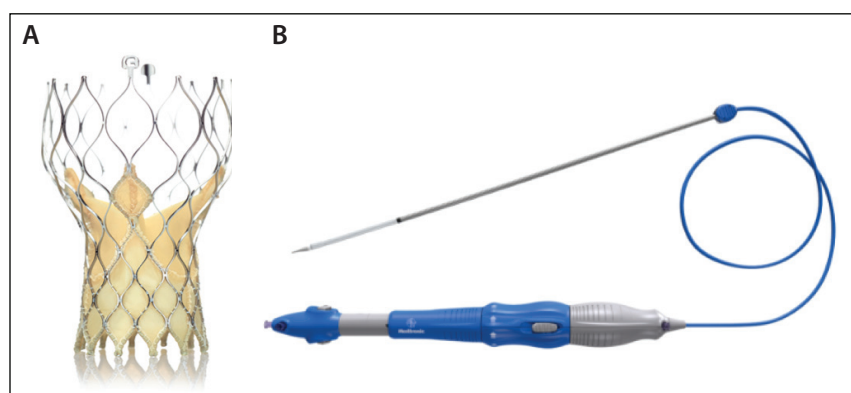


Figure 1. Evolut R valve (Medtronic) (A) and delivery system (B). The Evolut R is a supra-annular valve composed of porcine pericardial tissue, a conformable nitinol frame, and an extended skirt. The delivery system is fully resheathable, repositionable, and recapturable.

tine basis were responsible for PVL no longer being a real issue. The rate of permanent pacemaker implantation is also decreasing with accumulated experience. Importantly, the depth of TAVI implantation within the left ventricular outflow tract is a strong, independent predictor of disturbance. However, it remains the Achilles' heel of TAVR and has impeded the expansion of TAVR to younger and lower-risk patients. Up to 60% of patients with high-degree arteriovenous (AV) block in the early postimplantation period recover normal AV conduction within 6 months. Stroke pathophysiology is well understood now. There has been a decline in stroke risk after TAVR with improvements in valve technology, patient selection, and operator experience.⁷ Cerebroprotective strategies could be used; however, they do not fully protect the brain but rather reduce infarct size. Thanks to careful patient selection and procedure planning, other complications are minor and managed on a case-by-case basis.

The significant hurdles associated with first-generation transcatheter heart valves have been addressed and corrected, and relentless device iterations have yielded impressive reductions in delivery system size. For example, the CoreValve Evolut R in-line sheath (Figure 1) affords delivery of 23-, 26-, and 29-mm valves via a 14-F system. Such development has the potential to reduce the incidence of major vascular complications and decrease the number of patients who require alternative access for TAVR.⁸ Similarly, recaptur-

able, repositionable, and retrievable TAVR systems (eg, CoreValve Evolut R and Lotus [Boston Scientific Corporation; Figure 2] valves) are now routinely used. Such ameliorations allow operators to attempt more challenging cases, knowing that the system can be removed in the case of a suboptimal result. In addition, the recent introduction of sealing skirts/cuffs/membranes has further reduced the incidence of PVL in contemporary practice. Technologic iterations have helped address the requirements for a permanent pacemaker. Latest-generation devices, which have lower radial force and an additional skirt that covers the stent zone that comes into contact with conduction tissue, also helped decrease the need for permanent pacemakers.

Over the last several years, TAVR has been heavily studied, which has helped show favorable results in a short period of time, thus expanding use of the therapy. TAVR technology has also been successfully expanded to a variety of other clinical situations, including treatment of degenerative surgical aortic and mitral prostheses, bicuspid aortic valve stenosis, and pure aortic incompetence.⁹⁻¹¹

Three current randomized trials are comparing TAVR to SAVR in intermediate- and low-risk patients^{3,5} (SURTAVI: NCT01586910; PARTNER II: NCT01314313; Medtronic Transcatheter Aortic Valve Replacement in Low-Risk Patients: NCT02701283). Although there is currently a paucity of randomized data definitively confirming efficacy in these patients, there is an accumulating nonrandomized evidence base for this indication/expansion. However, a key issue influencing the choice of TAVR versus SAVR in intermediate- and low-risk patients is the lack of data on very long-term outcomes associated with TAVR. Thus, knowledge of the long-term durability (> 5 years after implantation) of TAVR is essential before unlimited expansion of indications in this patient category, as it is unknown if the bioprosthesis could deteriorate.¹²

Currently, clinical factors influencing the choice between TAVR and SAVR include the patient's preferences, age, estimated life expectancy with aortic valve replacement, as well as presence of comorbidities.

ACCESS SITE FOR TAVR

Vascular access selection and percutaneous closure device use has improved. Technical and technologic improvements have had a direct impact on access choice for TAVR. Currently, transfemoral access, the gold standard, is possible in nearly all cases (> 95%). Alternative (nontransfemoral) sites are predominantly subclavian, direct aortic, transapical, and, less

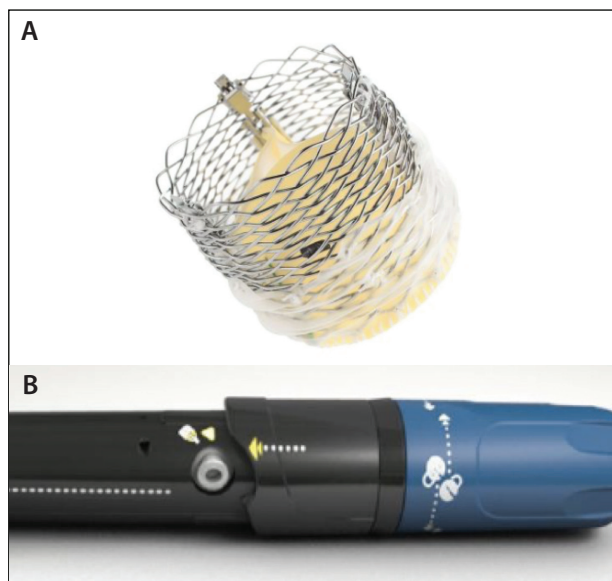


Figure 2. Lotus valve (A) and delivery system (B). The Lotus valve is composed of bovine pericardium with an adaptive seal to minimize PVL. It has a braided, nitinol, repositionable frame to enhance strength, flexibility, and retrievability.

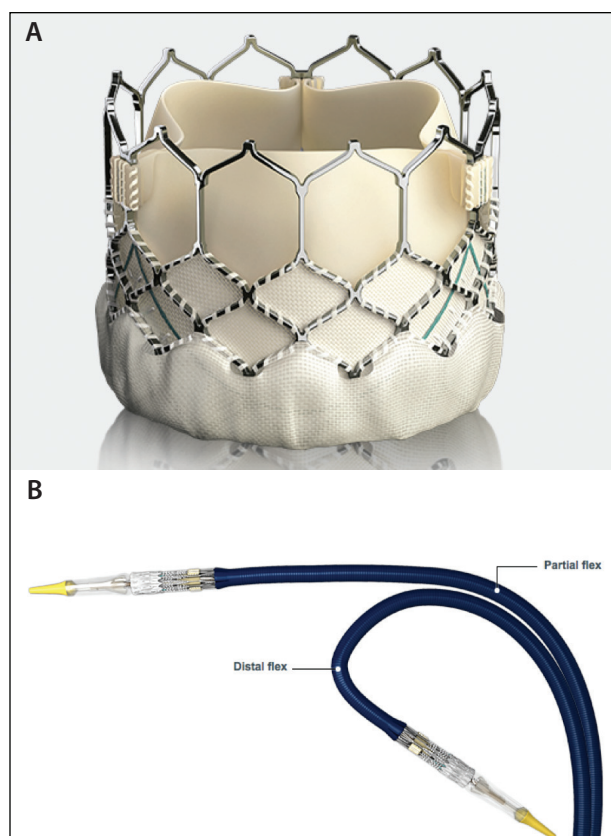


Figure 3. Sapien 3 valve (A) and delivery system (B). The Sapien 3 valve is composed of bovine pericardial tissue with a cobalt-chromium form for high-radial strength. The outer sealing skirt reduces PVL, and the low-profile 14-F eSheath (without valve) enhances the ease of coaxial positioning.

commonly, transcarotid and transcaval. The benefits of TAVR over SAVR in the PARTNER II trial and CoreValve US Pivotal Trial were greatest in transfemoral access cohorts.^{2,5} However, it is unclear if mortality in patients undergoing alternative access TAVR was caused by the alternative access procedure or if it was the result of the burden of peripheral vascular disease, which mandated the need for alternative access. Thus, a careful unbiased selection led by best practices within the confines of a heart team is recommended for access choice. Preprocedural assessment for TAVR includes assessment of the iliofemoral system and entire aorta (generally by CTA) to detect contraindications to vascular (transfemoral, subclavian, aortic, apical, carotid, or transcaval) access such as plaques with mobile thrombi in the ascending aorta or arch, inadequate vessel size, or extensive calcification or tortuosity.^{13,14} For the transapical approach, severe pulmonary disease, severe left ventricular disease, or other conditions may render the left ventricular apex inaccessible.

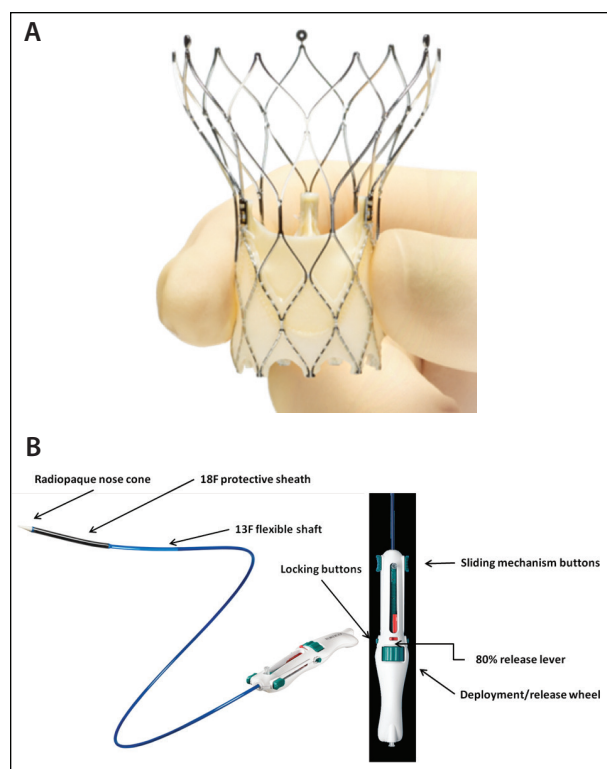


Figure 4. Portico valve (A) and delivery system (B). The Portico valve has a self-expanding nitinol stent, a nonflared annulus design with large open cells, and a bovine pericardial valve. A porcine pericardial sealing cuff at the annular level of the stent constitutes the sealing zone. It has a 24-F (outer diameter) sheathless system enabling resheathing, repositioning, or retrieval.

SELECTION OF VALVE TYPE

For the majority of patients undergoing TAVR, either a Sapien 3 (Edwards Lifesciences; Figure 3), CoreValve Evolut R, Lotus, Portico (St. Jude Medical; Figure 4), or one of the late-generation devices is suitable. However, there are certain patient-specific issues that might influence the choice of valve system type:

- Most valve types, but not all, cover the full range of annulus size.
- In a patient deemed to be at high risk for annulus rupture (eg, a patient with a small, highly calcified annulus), a self-expanding rather than a balloon-expandable valve may be chosen to reduce the risk of annular rupture (as one of several potential strategies to attempt to reduce the risk of rupture). Annular rupture has been observed almost exclusively after use of a balloon-expandable valve and very rarely after use of a self-expanding valve.
- If there are concerns about coronary obstruction, a valve system with recapturable technology may be favored.

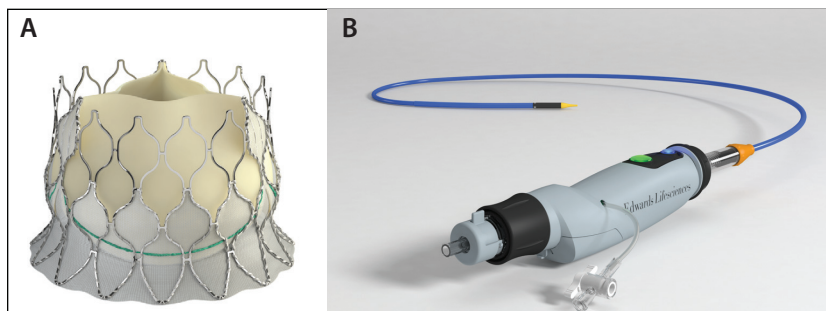


Figure 5. Centera valve (A) and delivery system (B). The Centera valve has a self-expanding nitinol frame composed of treated bovine pericardium with a repositionable, low-profile, 14-F eSheath. Deployment is achieved via a user-controlled motorized handle. It also has a flex mechanism for trackability and coaxial alignment.

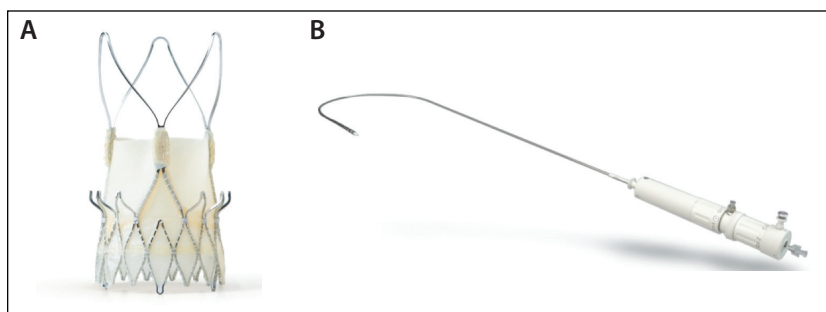


Figure 6. Acurate neo valve (A) and delivery system (B). The Acurate neo is a repositionable, self-aligning, porcine tissue valve with a PET skirt to seal PVL. It has an easy, two-step, sheathless delivery (similar to the 28-F sheath system). The first turn is a partial release (arches and upper crown), and the second turn is a full release (stent body).

- When performing a valve-in-valve procedure to treat a small surgical bioprosthetic valve, a supra-annular TAVR valve might offer greater effective orifice area.
- If there is a spur of asymmetric calcification protruding into the outflow tract, choosing of a valve with an external sealing skirt may be preferable.

WHAT'S COMING

Ultimately, the expansion of TAVR technology to lower-risk patients is inevitable. The latest device iterations of the Lotus, Portico, Centera (Edwards Lifesciences; Figure 5), and Acurate neo valve (Symetis; Figure 6) are all based on self-expanding technology and are being developed and spread worldwide. Colibri (Colibri Heart Valve; Figure 7), which has a smaller catheter, is balloon-expandable. The previous devices are self-expandable; few iterations are balloon-expandable, except the J valve (JieCheng Medical Technology Co., Ltd.; Figure 8), Myval (Meril; Figure 9), and Colibri. Additionally, there are several Asian

companies that are trying to venture into this high-potential market with lower prices. The Asian continent is a fertile field, and devices from Indian companies are showing potential (eg, Myval).

China has a huge TAVR market. According to the China National Bureau of Statistics, more than 140 million people were aged older than 65 years at the end of 2015. No large-scale statistics are available, but 300,000 patients were deemed to be potential TAVR candidates, according to estimates. At present, TAVR is still in the initial stages in China and faces multiple challenges. The technology has not moved as quickly as expected and is likely years behind the technology in the United States and Europe. The anatomic characteristics of Chinese patients with AS are different compared to patients in the United States and Europe; a higher percentage of Chinese patients have a bicuspid aortic valve, there is severe valve calcification, and a higher population of horizocardia (technically challenging horizontal heart with horizontal ascending aorta). Other factors should be

considered in the Chinese population, including poor body habitus, high frailty index, and low acceptability of new technologies.



Figure 7. The Colibri valve is a prepackaged, premounted, and precrimped porcine pericardium valve with a 14-F sheath and a balloon-expandable delivery system.

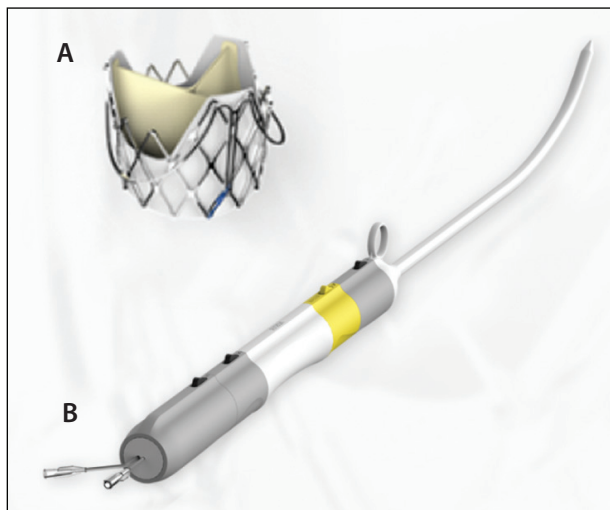


Figure 8. J valve (A) and delivery system (B). The J valve is composed of a porcine root prosthesis with no transfemoral system. Locators capture native valve leaflets that coapt with THV to enhance seal.



Figure 9. The Myval valve is composed of a single bovine pericardial patch (origami design) to reduce stress. It is balloon-expandable and mounted on a nickel cobalt alloy frame. The pericardial tissue and PET skirt reduce PVL.

Independent valve research by Chinese companies will usher in new technology and development in the next few years. Many new TAVR devices have been tested, but only Venus-A (Venus, MedTech; Figure 10), VitaFlow (MicroPort Medical; Figure 11), and J-Valve have completed or started clinical study. J-Valve has the particularity of being a transapical balloon-expandable TAVR device, which targets AS, as well as aortic insufficiency.

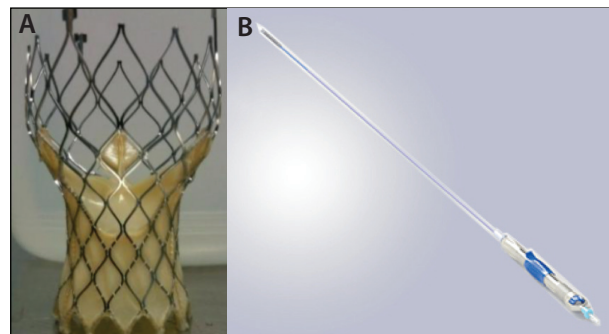


Figure 10. Venus-A valve (A) and delivery system (B). The Venus-A valve is a partially retrievable, porcine pericardial, supra-annular valve with a self-expanding frame.

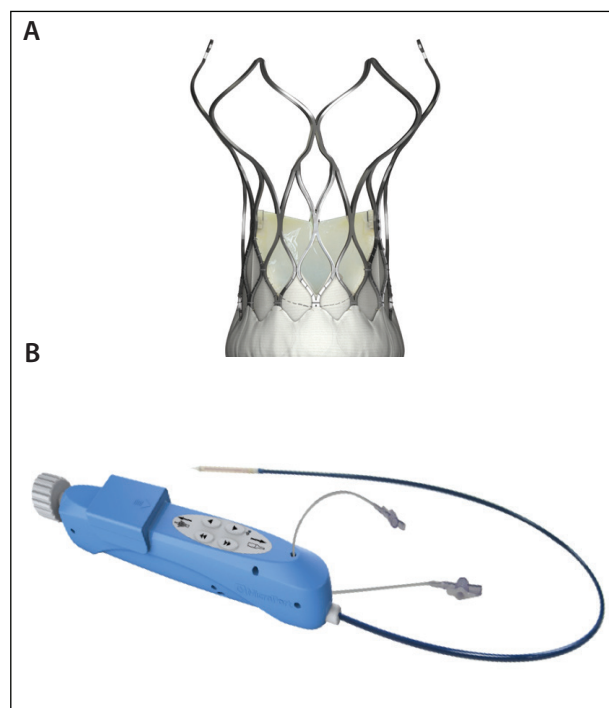


Figure 11. Vitaflow valve (A) and delivery system (B). The Vitaflow valve is composed of bovine pericardium and has a self-expanding nitinol frame and extended inner and outer skirt to reduce PVL and heart block to treat large cells with low density. The delivery system uses a hybrid-driven handle.

CONCLUSION

There have been huge improvements in the era of the treatment of valve disease using transcatheter techniques, and research is ongoing. The clinical successes of TAVR are increasingly well described by both randomized trials and observational research, and technical and technologic progress are making the therapy safer and more efficient. Valve choice might be adapted to clinical situations, with

(Continued on page 67)

(Continued from page 63)

the latest generations of prostheses offering additional security features. Expansion of the indications for TAVR will require more data on durability over the long term. ■

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