

The CoreValve Program

Cardiac Interventions Today interviews Carlos E. Ruiz, MD, PhD, who shares his expertise on the current status of the CoreValve device and trial data.

What is the current status of the CoreValve device?

Dr. Ruiz: Transcatheter aortic valve replacement (TAVR) offers a therapeutic option to patients with severe symptomatic aortic stenosis who are not considered good candidates for surgical valve replacement (SAVR). Until recently, these patients have been left untreated because of the belief that their operative mortality outweighed the benefits provided by traditional SAVR. These patients are typically elderly, frail, and have multiple comorbidities, making SAVR a challenge. CoreValve (Medtronic, Inc., Minneapolis, MN) is a porcine pericardial prosthesis mounted on a self-expanding nitinol frame that is placed across the left ventricular outflow tract and extends into the aortic root. The valve is self-centering and partially repositionable after deployment.

Optimal annular sizing and improved valve fit allow for difficult anatomic implantation, including nonround environments due to elliptical annulus shape or heavy annular or leaflet calcification. The CoreValve device can serve a broad range of patients with annular sizes ranging from 20 to 27 mm. The 26-mm valve with an 81-mm valve perimeter can be used in patients with an annulus of 21 to 23 mm, and a 29-mm valve with a 91-mm valve perimeter can be used for an annulus of 23 to 27 mm. CoreValve is designed and sized to provide appropriate radial force or interference between the frame and the native annulus. Future iterations of the CoreValve will broaden the range of treatment annulus down to 18 mm for the smallest valve and up to 29 mm for the largest valve. These valves will be introduced into the United States under an investigational device exemption (IDE) study this winter.

The CoreValve's flexible nitinol frame conforms to the native annulus, even in highly elliptical and heavily calcified anatomies. The device's supra-annular design retains a circular shape at the functioning valve level, allowing more optimal leaflet coaptation and performance.

The low-profile delivery system (18 F) and alternative

implant options allow broad patient access, which is important given the incidence of peripheral vascular disease and challenging vascular anatomy in this patient population. Vascular complications are a concern, and having a smaller-profile device can help avoid these complications. The anatomic criteria for placement requires a minimal luminal vessel diameter of ≥ 6 mm to facilitate valve delivery and placement. Due to its flexible platform, additional access routes, such as the subclavian artery and direct aortic implantation via a small sternal or right chest wall incision, offer opportunities to reduce vascular complications by providing alternatives for patients with poor iliofemoral access.¹⁻⁴ Outside of the United States, CoreValve has CE Mark approval for subclavian access. Subclavian and direct aortic access are being evaluated as part of the US Pivotal trial.

What is the current status of the CoreValve program?

Dr. Ruiz: CoreValve received CE Mark approval in Europe in the spring of 2007, and since approval, more than 20,000 patients have been treated in more than 50 countries worldwide. In the United States, CoreValve is being studied under an IDE, with enrollment actively underway at 41 sites.

What is the long-term performance of the CoreValve?

Dr. Ruiz: It is important that percutaneous valves achieve the same durability standards as traditional surgical valves. The CoreValve has been extensively bench tested to 600 million cycles or 15 years for frame testing and 200 million cycles or 5 years for tissue testing, which is consistent with surgical valves. There is no evidence of significant structural or tissue degradation. Four-year clinical experience with the CoreValve system was recently presented at the European Society of Cardiology meeting and showed sustained hemodynamic and clinical performance. Longer-term follow-up is necessary, particularly as this therapy is considered for more moderate- and intermediate-risk patients.

What is most relevant regarding some of the recent outcomes data?

Dr. Ruiz: More than 3,300 CoreValve patients have been enrolled in clinical studies. Large, multicenter national registries across Europe and Australia/New Zealand have provided insight into the clinical performance of the CoreValve system.⁵⁻¹¹ These registries show high rates of procedural success (nearly 98%), with immediate and significant improvements in hemodynamic and functional performance. They also provide a growing body of evidence regarding mid- and long-term benefits of TAVR therapy. A meta-analysis of these CoreValve registries was presented at EuroPCR this spring¹²: 2,156 patients from Australia, Belgium, France, Germany, New Zealand, Spain, and the United Kingdom were included in the analysis. The results of this meta-analysis revealed high procedural success with low vascular complications (4%), low stroke rates (3%), and positive 30-day and 1-year survival (93% and 83%). The rate for pacemaker implantation was 28.7%.

What is the most recent information regarding complications?

Dr. Ruiz: The CoreValve registries have shown relatively low complication rates. More recent single-center studies are helping to further inform and improve TAVR procedural practice. Standardized endpoint definitions proposed by the Valve Academic Research Consortium will provide more consistency and help to facilitate improved evaluation of transcatheter therapy.

With regard to stroke and the role of embolic protection, cerebrovascular events (likely secondary to debris dislodgement from the native valve and aortic arch) are a serious complication of TAVR. Rates of major cerebral ischemic attacks in TAVR can be as high as 10%, with CoreValve registry experience of approximately 3%.

Use of embolic protection devices during TAVR may have a role in reducing the risk of cerebral embolism and stroke. The Embrella device (Edwards Lifesciences, Irvine, CA) is a porous membrane system implanted via the right brachial or radial arteries that deflects debris away from the cerebral circulation. The Embrella received CE Mark approval last year but is not yet commercially available. Overall, procedural refinement, advancements in valve technology, attention to anticoagulation regimens, and embolic protection devices are all important to minimize the potential for stroke complications with TAVR.

With regard to vascular access, vascular complications in TAVR are relatively frequent due to the large-caliber sheaths necessary for device deployment—they are especially common when a transfemoral approach is taken. The incidence of major vascular complications in TAVR ranges from 2% to 26%, with CoreValve registry experience of approximately

4%. Center or operator experience and a high sheath-to-artery ratio are predominant factors for vascular complications in our early experience with TAVR. In addition to lower-profile devices, alternative access routes offer opportunities to reduce vascular complications, specifically in patients with peripheral vascular disease and difficult vascular anatomy. Published results from both subclavian and direct aortic implantation techniques are encouraging.

Many patient-related and procedure-related factors are associated with conduction abnormalities and the need for permanent pacemaker implantation after TAVR. The degree of aortic valve calcification, aortic root angulation, septal wall thickness, preexisting conduction disease, and the location of the conduction system can all affect pacing rates. CoreValve registry permanent pacemaker experience is approximately 28%. Deep implantation into the left ventricular outflow tract is presumed to be the predominant mechanism, and proper device placement is important. An implantation depth of 4 to 6 mm below the aortic annulus is desired for CoreValve deployment. A recent study presented at EuroPCR that evaluated the AccuTrak CoreValve delivery system revealed that with this implantation depth, pacing rates were reduced from 35% to 14%.¹³

What is the role of multimodality imaging in device selection?

Dr. Ruiz: There are increasing data to support accurate imaging and sizing in selecting a TAVR device. The value of computed tomographic imaging in addition to angiography and echocardiography is increasingly being recognized. New algorithms are being developed to more accurately determine valve sizing, especially in elliptical or heavily calcified anatomies.

What is the role of antiplatelet therapy for the CoreValve prosthesis?

Dr. Ruiz: The CoreValve prosthesis is designed on a stent platform. Antiplatelet therapy with aspirin and clopidogrel is recommended for at least 3 months followed by aspirin (or clopidogrel) indefinitely after the procedure. In patients with atrial fibrillation and high CHADS2 score or with other indications for warfarin or dabigatran therapy, antiplatelet monotherapy in combination with warfarin should be continued indefinitely. There are, however, no studies addressing the duration of antiplatelet therapy after TAVR, especially in patients who also require chronic anticoagulation.

What new information is there regarding ongoing clinical trials?

Dr. Ruiz: Recent data were presented at the European Association for Cardio-Thoracic Surgery on

CoreValve implantation in failed surgical bioprostheses from six manufacturers.¹⁴ The data were encouraging. Eighteen patients implanted at three centers between 2007 and 2010 were evaluated in a prospective, single-arm, nonrandomized fashion. Patients were followed for 1 year and showed the following results: technical success of 94% with one conversion to surgery, 30-day mortality rate of 11%, pacemaker implantation rate of 6%, and no structural deterioration or valve migration reported at 1 year.

The CoreValve US Pivotal trial is actively underway. In the study, the CoreValve system is being investigated in two cohorts—patients at high and extreme risk for surgical valve replacement. Together, the two cohorts will enroll more than 1,400 patients.

Medtronic recently announced the start of the Engager Transapical System CE Pivotal trial. This 150-patient trial will be conducted at 11 centers in Germany, Israel, France, Belgium, and Switzerland and will evaluate the safety and clinical performance of their new valve and delivery system. The Engager valve is composed of bovine tissue leaflets and a self-expanding nitinol frame designed for transapical implantation.

The SURTAVI trial is a large, multicenter, randomized clinical trial comparing TAVR and SAVR in moderate-risk patients with severe aortic stenosis. The study will be conducted in Europe, Canada, and the United States under an IDE.

The ADVANCE trial is designed to evaluate the real-world application of the CoreValve system for the treatment of severe aortic stenosis. Data collected will further the understanding of TAVR safety, device performance, quality of life, and health economic impact. Enrollment of 1,000 patients is complete, and findings will be presented next spring.

ADVANCE-II is designed to characterize current CoreValve implantation best clinical practices to optimize implant procedures. ADVANCE-II is a small study conducted with experienced CoreValve implanters. Enrollment is expected to begin shortly.

When do you anticipate commercialization in the United States?

Dr. Ruiz: CoreValve US Pivotal trial enrollment is expected to be complete in 2012, with target commercial approval in 2014.

Will the CoreValve approval process be similar to that for the Edwards Sapien valve (Edwards Lifesciences)?

Dr. Ruiz: CoreValve is being investigated under a full premarket approval. The approval process is anticipated to be similar to that of the Edwards Sapien valve.

What is your opinion on the Centers for Medicare & Medicaid Services announcement about the national coverage decision (NCD) for TAVR?

Dr. Ruiz: It is important to develop a positive reimbursement environment for TAVR to help ensure ongoing access to treatment. The Centers for Medicare and Medicaid Services initiated an NCD for TAVR at the request of the American College of Cardiology and the Society of Thoracic Surgeons. The NCD is expected to reinforce the importance of specialized centers and multidisciplinary teams to ensure the availability of high-quality and appropriate TAVR treatment.

Prerequisites that have been recommended by the medical societies include that TAVR be performed by a well-trained multidisciplinary team that includes primary cardiologists, interventional cardiologists, and cardiac surgeons; that TAVR be performed at specialized centers of excellence that are able to maintain set standards of TAVR care; that national registries be established and mandated for postmarket surveillance and coverage; and that appropriate training and credentialing criteria be established and met. ■

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