The Future for Transcatheter Aortic Valve Implantation

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Transcatheter aortic valve implantation (TAVI) is a minimally invasive transcutaneous procedure in which a collapsible valve is used to functionally repair the aortic valve via a catheter delivery system. Unlike surgical aortic valve replacement (SAVR), which requires a sternotomy, TAVI is performed in 90% of the cases through percutaneous arterial access site (leg artery) or in 10% of cases through a small opening in the chest. Since its commercialization in 2007, the number of TAVR procedures and centers has grown exponentially [Mylotte D et al. *J Am Coll Cardiol.* 2013], and its use is likely to continue to increase.

Julinda Mehilli, MD, Munich University Clinic, Ludwig-Maximilians University, Munich, Germany, reviewed the status of TAVI in Europe.

An increasing body of evidence shows that TAVI is similar to or better than SAVR regarding all-cause mortality in high-risk patients [Thyregod HG et al. *J Am Coll Cardiol.* 2015; Adams DH et al. *N Engl J Med.* 2014; Smith CR et al. *N Engl J Med.* 2011], and long-term (5-year) data show it to be associated with sustained clinical outcomes with low rates of prosthesis failure (< 2%) [Barbanti M et al. *JACC Cardiovasc Interv.* 2015].

TAVI can be performed exclusively under angiographic guidance without the need for adjunctive transesophageal echocardiography [Attizzani GF et al. *Am J Cardiol.* 2015]. It is as effective and safe when performed under local anesthesia plus mild sedation as it is when general anesthesia is used [Motloch LJ et al. *Clin Res Cardiol.* 2012]. Improvements in suture-mediated closure devices have significantly decreased vascular complications [Mehilli J et al. EuroPCR 2015 (http://sbhci.org.br/wp-content/uploads/2015/05/MehilliJulinda.pdf)]. Procedure, intervention, and labor costs have been reduced as the procedure has been refined and simplified.

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Improved and new prostheses such as balloon-expandable devices [Abdel-Wahab M et al. *JAMA*. 2014] have substantially reduced post-TAVI aortic regurgitation [Jochheim D et al. *EuroIntervention*. 2015] and 30-day moderate to severe paravalvular leakage [Kodali S et al. ACC 2015 (Kodali S. Early clinical and echocardiographic outcomes with the Sapien 3 transcatheter aortic valve replacement system in inoperable, high-risk, and intermediate-risk aortic stenosis patients. Presented at: American College of Cardiology/i2 Scientific Session; March 15, 2015; San Diego, CA), whereas increasing operator experience has led to more success and fewer complications. As a result of the reduction in complications and improved outcomes, the use of TAVI is being extended to intermediate-risk patients.

Peter Wenaweser, MD, University Hospital Bern, Klinik im Park, Zurich, Switzerland, discussed some of the progress that has contributed to TAVR's improved safety compared with SAVR. These include refinements in the prosthesis and delivery system that led to better deployment, positioning, retrievability, and durability, whereas the use of sealing skirts to reduce paravalvular leaks, better patient selection based on individual anatomic characteristics, and the use of the femoral artery access route have reduced procedural risks. Patient selection is being improved using scoring systems such as the STS score, but dedicated scores are still missing. Frailty index (based on assessment of cognition, mobility, nutrition, and instrumental and basic activities of daily living) has been developed, which can predict cognitive and mobility impairment [Schoenenberger AW et al. *Eur Heart J*. 2013].

Better patient selection has allowed the use of TAVR to be expanded to low- and intermediate-risk patients. When compared with high-risk patients or those judged to be inoperable, intermediate- and low-risk patients selected with a Society of Thoracic Surgeons score have favorable clinical outcomes [Wenaweser P et al. *Eur Heart J.* 2013].

Caution is needed with balloon-expandable TAVR in patients with risk of aortic root rupture because this can lead to higher rates of mortality, disabling stroke, life-threatening bleeding, and

periprocedural myocardial infarction [Barbanti M et al. *Circulation*. 2013]. Symptomatic coronary obstruction following TAVR is a rare but life-threatening complication that occurs more frequently in women, in patients receiving a balloon-expandable valve, and in those with a previous surgical bioprosthesis [Ribeiro HB et al. *J Am Coll Cardiol*. 2013]. Moderate or severe paravalvular aortic regurgitation also leads to higher death rates. These problems are being addressed with improved TAVR prostheses, like the Lotus Valve System, the Sapien 3, and the Corevalve Evolut.

Looking forward, safety goals include reducing 30-day mortality to 1% to 2% by improved patient selection, using antithrombotics to reduce disabling stroke and life-threatening bleeding to < 1%, using a dedicated closure device to reduce major vascular complications to < 5%, reducing annulus rupture or malpositioning to < 0.5% with screening tools, and reducing the need for a permanent pacemaker to < 10%.

George D. Dangas, MD, Icahn School of Medicine at Mount Sinai, New York, New York, USA, discussed bleeding and vascular events following TAVR.

Calcified and thrombotic material can dislodge from the valve within 24 hours after TAVR, which increases the risk of cerebral vascular events, mainly stroke [Tay EL et al. *JACC Cardiovasc Interv*. 2011; Ghanem A et al. *J Am Coll Cardiol*. 2010]. Bivalirudin, an anticoagulant and direct thrombin inhibitor, could provide enhanced thrombotic protection and reduce stroke and bleeding risk. In one study, the use of bivalirudin during balloon aortic valvuloplasty resulted in significantly ($P = .003$) less bleeding vs heparin [Kini A et al. *EuroIntervention*. 2014], although a retrospective analysis of 461 patients found no difference in either bleeding or morality during and following TAVR [Lange P et al. *Can J Cardiol*. 2015].

Rivaroxaban targets hypercoagulability represented by factor X activation and thrombin formation, and may effectively prevent post-TAVR thrombotic complications through the inhibition of the pathways underlying thrombogenicity. The ongoing GALILEO study is a head-to-head comparison of rivaroxaban plus aspirin with clopidogrel plus aspirin in patients undergoing TAVR.

Nicolo Piazza, MD, PhD, McGill University Health Center, Montreal, Quebec, Canada, reviewed some of the limitations of TAVR and ways to overcome them.

Stroke remains a concern in high- and intermediate-risk patients because even devices with cerebral embolic capture appendages leave 25% of leaflet debris remains uncaptured [Van Mieghem NM et al. *Circulation*. 2013]. Major vascular complications can lead to significant increases in 1-year morality rates, and they remain a concern in up to 15.5% of patients depending on the device [Leon MB. ACC 2013].

Mild paravalvular aortic regurgitation (PAR) and moderate or severe PAR ranges both predict higher 1-year mortality rates [Kodali S et al. *Eur Heart J*. 2015; Moat NE et al. *J Am Coll Cardiol*. 2011]. Improved sealing skirts that make better tissue contact can reduce the incidence of PAR.

The need for a permanent pacemaker, which occurs in up to 28.9% of patients at 30 days after TAVR [Meredith I et al. PCR London Valves 2014], does not appear to impact mortality. Nor does left bundle branch block, which occurs in up to 38% of patients [Pereira E et al. *PACE*. 2013], although new and persistent bundle branch block acquired after TAVR is associated with an increased adverse event rate [El-Khally Z et al. *Am J Cardiol*. 2004].

Transcatheter valves are susceptible to structural failure but not as frequently as surgical bioprostheses [Mylotte D et al. *Eur Heart J*. 2015]. Other reasons for prosthesis dysfunction after TAVR include valve compression, thrombosis, delayed embolization, and endocarditis. Subclinical transcatheter heart valve thrombosis is the most recently identified complication associated with TAVR, and it appears more common than originally anticipated [Leetmaa T et al. *Circ Cardiovasc Interv*. 2015].

Improvements in operator experience, device engineering, and patient selection will overcome these and other limitations of TAVR and permit its expansion to other patient populations (ie, those with failed surgical bioprosthesis, bicuspid pathology, pure aortic regurgitation, and mitral stenosis).