The LOTUS *Edge* Aortic Valve System and SENTINEL Cerebral Protection System

Experts discuss the benefits and implications of these innovative technologies in an expanding patient population.

WITH VINOD H. THOURANI, MD, FACS, FACC, AND VIJAY IYER, MD, PHD, FACC, FSCAI

Vinod H. Thourani, MD, FACS, FACC
Professor of Surgery
Georgetown University School of Medicine
Chair, Department of Cardiac Surgery
MedStar Heart and Vascular Institute
Washington, DC
vinod.h.thourani@medstar.net
Disclosures: Research and consulting for Edwards Lifesciences, Cryolife, Gore Vascular, Boston Scientific Corporation, and Abbott Vascular.

What are the benefits and limitations of transcatheter aortic valve replacement (TAVR)?

With the advent of TAVR in the past decade, there has been a significant paradigm shift in the treatment of aortic stenosis (AS). Currently, patients who are considered to be at extreme, high, and intermediate risk most commonly undergo TAVR instead of surgical aortic valve replacement (SAVR). The benefits of TAVR in these patient risk categories lead to similar or improved early and midterm mortality. Moreover, morbidities including stroke, bleeding, the need for blood transfusion, and new postoperative atrial fibrillation are reduced in patients undergoing TAVR. Important additional benefits of TAVR include improved early quality of life and resource utilization, with decreased overall length of stay and, in some instances, no intensive care unit stay at all. TAVR allows for early mobilization, with an anticipated discharge 1 to 2 days after the procedure compared with approximately 4 days for SAVR. With the recent approval of TAVR for low-risk patients in the United States, the rapid growth of TAVR is sure to increase in the future.

With device iteration and technological advances, the number of complications associated with TAVR has decreased over the past decade. However, it is worth mentioning that some complications associated with TAVR do remain, including paravalvular leak (PVL), the need for postoperative permanent pacemakers, vascular injury, and stroke. Fortunately, with advances in technology and iterations of TAVR prostheses, we anticipate continued reductions of these complications.

What are the current needs of physicians, surgeons, and patients with regard to TAVR?

The current needs of physicians include providing state-of-the-art care in the management of AS. If this can be delivered with transcatheter options with minimal complications and mortality, then patients who are within the appropriate risk categories and who have been seen by a qualified heart team consisting of cardiologists, surgeons, and heart valve clinic coordinators, generally prefer this less invasive technique. The goal would be to relieve AS using a transfemoral route, with the anticipation that this would be performed with minimal to no PVL, with a lower rate of stroke than surgery, and with a pacemaker rate similar to that of SAVR.

Why is LOTUS *Edge* (Boston Scientific Corporation) needed by physicians and patients? What are the current unmet needs?

The LOTUS *Edge* provides excellent hemodynamics with almost no mild, moderate, or severe PVL. Currently, the LOTUS *Edge* is the only valve that can be fully deployed and interrogated using angiography and/or echocardiography for PVL, angles of deployment, and coronary patency before complete release. This allows physicians to

fully appreciate the outcomes before release. If any concerns remain, the valve can be repositioned. Furthermore, in patients with a heavily calcified annulus, the LOTUS *Edge* valve may provide excellent outcomes because the residual PVL rate is commonly very low and the risk of annular root rupture is extremely small.

What features of the LOTUS *Edge* are you most excited about?

A major advantage of the LOTUS *Edge* is the SAVR-like residual PVL rate. With the advent of these newer valves, like the LOTUS *Edge*, we are entering an era in which transcatheter technology will provide outcomes that are similar to SAVR.

Do you see the LOTUS *Edge* differently than the other TAVR valves available on the market?

Yes, the LOTUS *Edge* provides excellent outcomes in terms of PVL, positioning, and deployment, while minimizing chances for root rupture.

What are your thoughts about cerebral embolic protection?

Stroke remains one of the most dreaded complications associated with interventional cardiology and cardiac surgical procedures. Unfortunately, there remain very few predictors for the occurrence of a postoperative stroke. Although older patients with severe aortic calcification may have the highest risk for a neurologic event, we have also noted them in younger patients

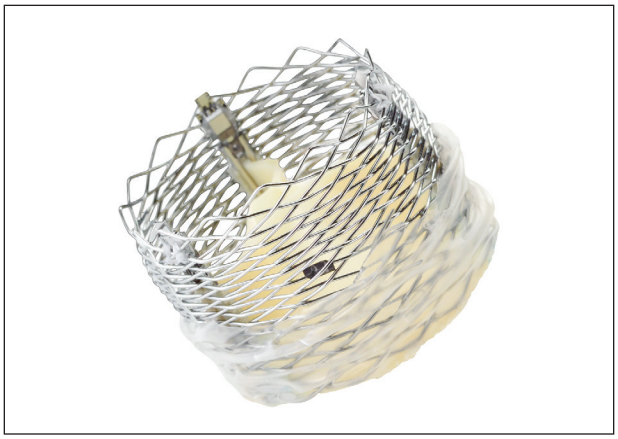

Figure 1. The LOTUS *Edge* aortic valve.

with little aortic calcification. In the United States, the only FDA-approved device for protection from stroke is the SENTINEL cerebral protection system (Boston Scientific Corporation). A major advantage of SENTINEL is that it selectively protects both the right and left carotid arteries and has a capture system that can capture and retrieve debris and aortic valve particulate matter. This remarkable device has shown significant decreases in debris on postoperative MRI analysis after TAVR.[1] Neuroprotection during TAVR may become even more important as this technology becomes more used in treating younger patients.

1. Kapadia SR, Kodali S, Makkar R, et al. Protection against cerebral embolism during transcatheter aortic valve replacement. J Am Coll Cardiol. 2017;69:367-377.

Vijay Iyer, MD, PhD, FACC, FSCAI
Chief, Division of Cardiovascular Medicine
Jacobs School of Medicine and Biomedical Sciences
Buffalo, New York
viyer@kaleidahealth.org
Disclosures: Proctor for Boston Scientific Corporation.

How would you describe the risk of stroke during a TAVR procedure?

The risk of stroke in current studies, especially debilitating stroke, is < 2%. These data are reinforced by the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy (STS/TVT) registry as well. However, the incidence of all strokes, including transient ischemic attacks, is higher and is variable depending upon the study. The rates have been reported to range from 4% to 9% (REPRISE III [NCT02202434], PARTNER 3 [NCT02675114], EVOLUT Low Risk [NCT02701283]).

How are you trying to avert the risk of stroke?

There are no guaranteed ways to avoid the risk of stroke other than cerebral embolic protection. Careful attention to the anatomy, especially the presence of plaque in the arch, and careful delivery of devices is an essential part of all TAVR procedures. However, this alone does not guarantee protection from stroke. The use of embolic protection devices further allows for stroke protection in all anatomies.

Why remove cerebral emboli rather than deflect it elsewhere?

It is probably better not to have any embolic material in any vascular bed. The risk of it in the cerebral vasculature is the most devastating. However, deflecting it to a different vascular bed or into the extremities also carries a risk. For example, the presence of atheroemboli in the kidneys can lead to progressive renal failure, and atheroemboli to the lower extremities can cause significant discomfort and even loss of limbs.

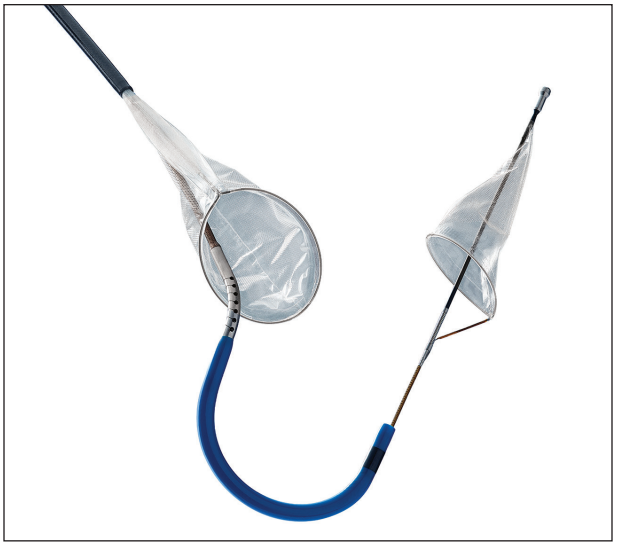

Figure 2. The SENTINEL cerebral protection system.

What does the term "protected TAVR" mean to you?

Protected TAVR refers to taking into account all factors that are possibly responsible for stroke during TAVR and using every possible method, including the use of cerebral embolic protection devices, to reduce the risk of stroke (both disabling as well as minor strokes).

What have you seen as a result of implementing cerebral embolic protection during TAVR?

At the Gates Vascular Institute, we have performed > 350 TAVR procedures every year. We have seen a stroke risk of < 1% over the last year and a half. We have had no disabling strokes since we have started using cerebral embolic protection, and we have only had two transient ischemic attack events; in both cases, we were unable to place a cerebral embolic protection device due to anatomic considerations.

Do you routinely use cerebral embolic protection in every TAVR case?

The heart team at the Gates Vascular Institute decided to begin using cerebral embolic protection in every case after the results of the SENTINEL investigational device exemption trial were published. The presence of debris in 95% to 98% of the filters and the number of MRI findings suggest that all patients have embolic debris being showered into the brain circulation and need to be protected. In the SENTINEL trial, we were unable to discern any specific patient groups that were at higher or lower risk for a stroke in the setting of TAVR. Therefore, we decided as a group that we would offer and try to place a cerebral embolic protection device in every patient undergoing a TAVR procedure irrespective of the risk status or the type of device being used.

How are you discussing the risk of stroke and the use of cerebral embolic protection with patients?

Every patient being evaluated for TAVR or SAVR in the heart valve clinic is presented with the data regarding the risk of stroke in both procedures. These data include data from the PARTNER II and PARTNER 3 trials, as well as the CoreValve trials. We discuss with the patients the risk of stroke and the potential mechanisms of minimizing the stroke risk, including the use of cerebral embolic protection. In the last year, we have had several patients who have specifically asked about the use of the SENTINEL device for stroke risk reduction.

As we look ahead, where do you see the future of cerebral embolic protection going?

We believe that as further data become available from both clinical trials and available registries, the case for the use of a cerebral embolic protection filter in TAVR will only be strengthened. I believe that the use of cerebral embolic protection devices will soon be the standard of care for all patients in all centers. ■

to severe patient compromise, additional procedures or death.

PRECAUTIONS
- Device implantation should only be performed by physicians who have completed training with the LOTUS Edge Valve System.
- Administer periprocedural antiplatelet and/or anticoagulant therapy at the discretion of the physician consistent with the local standard-of-care.
- Safety, effectiveness, and durability have not been established for valve-in-valve procedures.

The safety and efficacy of the LOTUS Edge Valve System has not been established in patients with the following characteristics/comorbidities:
  - Congenital unicuspid or congenital bicuspid aortic valve
  - Severe ventricular dysfunction with left ventricular ejection fraction <20%
  - Hypertrophic obstructive cardiomyopathy
  - Echocardiographic evidence of intracardiac mass, thrombus, or vegetation
  - Blood dyscrasias defined as: leukopenia (WBC<1000 cells/mm^3, acute anemia (Hgb<9g/dL), thrombocytopenia (platelet count <50,000 cells/mm^3), history of bleeding diathesis or coagulopathy
  - Pre-existing prosthetic heart valve or prosthetic ring in any position
  - Any considerations for coronary artery obstruction
  - End-stage renal disease or has GFR<20 (based on Cockcroft-Gault formula)
  - Severe (4+) aortic, tricuspid, or mitral regurgitation
  - Mixed aortic valve disease (aortic stenosis and aortic regurgitation with predominant aortic regurgitation >3+)
- Perform balloon aortic valvuloplasty (BAV) with an appropriately sized balloon prior to delivery of the valve to the aortic annulus at the discretion of the implanting physician.
- Partial resheathing (and subsequent unsheathing) can be performed an unlimited number of times during any phase of the procedure prior to valve release. Valve may be completely resheathed (past the post markers) once during the procedure at any phase prior to valve release. If a second full resheathing becomes necessary, exchange the device.

POTENTIAL ADVERSE EVENTS
Adverse events (in alphabetical order) potentially associated with transcatheter aortic valve implantation (including standard cardiac catheterization, BAV and the use of anesthesia) as well as additional risks related to the use of the LOTUS Edge Valve System are listed below.
- Abnormal lab values (including electrolyte imbalance)
- Access site complications (including arteriovenous (AV) fistula, hematoma or lymphatic problems)
- Allergic reaction (including to medications, anesthesia, contrast, or device materials, including nickel, titanium, tantalum, bovine-derived materials or polyurethanes)
- Anemia
- Angina
- Arrhythmia or new conduction system injury (including need for pacemaker insertion)
- Bleeding or hemorrhage (possibly requiring transfusion or additional procedure)
- Cardiac arrest
- Cardiac failure/low cardiac output
- Cerebrovascular accident, stroke, transient ischemic attack or cerebral infarction including asymptomatic neuroimaging findings
- Coronary obstruction
- Death
- Device misplacement, migration or embolization
- Emboli (including air, tissue, thrombus or device materials)
- Endocarditis
- Fever or inflammation
- Heart failure
- Hemodynamic instability or shock
- Hemolysis and/or hemolytic anemia
- Hypertension/hypotension
- Infection (local and/or systemic)
- Mitral valve insufficiency
- Myocardial infarction
- Myocardial or valvular injury (including perforation or rupture)
- Nerve injury or neurologic deficits (including encephalopathy)
- Pain
- Pericardial effusion or tamponade
- Peripheral ischemia or infarction
- Permanent disability
- Pleural effusion
- Pulmonary edema
- Renal insufficiency or failure
- Respiratory insufficiency or failure
- Restenosis (including pannus formation)
- Valve dysfunction, deterioration or failure
- Valve or device thrombosis
- Valvular stenosis or regurgitation (central or paravalvular)
- Vessel injury (including spasm, trauma, dissection, perforation, rupture, pseudoaneurysm or arteriovenous fistula).

As a result of these adverse events, the subject may require medical, percutaneous or surgical intervention, including re-operation and replacement of the valve. These events may lead to fatal outcomes.

Sentinel Cerebral Protection System – Claret PL-11435-01_E

CAUTION: *Federal law (USA) restricts this device to sale by or on the order of a physician. Rx only. Prior to use, please see the complete "Directions for Use" for more information on Indications, Contraindications, Warnings, Precautions, Adverse Events, and Operator's Instructions.*

INTENDED USE/INDICATIONS FOR USE
The Sentinel Cerebral Protection System is indicated for use as an embolic protection device to capture and remove thrombus/debris while performing transcatheter aortic valve replacement procedures. The diameters of the arteries at the site of filter placement should be between 9 – 15 mm for the brachiocephalic and 6.5 – 10 mm in the left common carotid.

CONTRAINDICATIONS
- Do not use in patients for whom anticoagulant and antiplatelet therapy is contraindicated.
- Do not use in patients with a known hypersensitivity to nickel-titanium.
- Do not use in vessels with excessive tortuosity.
- Do not use in patients with uncorrected bleeding disorders.
- Do not use in patients with compromised blood flow to the right upper extremity.
- Do not use in patients who have arterial stenosis >70% in either the left common carotid artery or the brachiocephalic artery.
- Do not use in patients whose brachiocephalic or left carotid artery reveals significant stenosis, ectasia, dissection, or aneurysm at the aortic ostium or within 3 cm of the aortic ostium.

WARNINGS
- The appropriate antiplatelet/anticoagulation therapy should be administered pre- and post-procedure in accordance with standard medical practice.
- It is recommended that the patency of the right radial or brachial artery be assessed prior to the introduction of the Sentinel System.
- It is recommended that the patient be tested for occlusion of the radial or brachial artery prior to device introduction.
- Do not use the device in left radial or left brachial access.
- Do not use the Sentinel System to deliver any type of fluid to the patient e.g. contrast media, heparinized saline, etc. due to risk of air embolization and comprise to device performance.
- Excessive movement of filters may lead to embolization of debris, vessel and/or device damage.
- Do not deploy the filters within a previously repaired artery, an artery that has been used for dialysis purposes, or an AV fistula.
- Indwell time of the Sentinel System is not to exceed 90 minutes as occlusion could occur, resulting in slow or no flow.
- Do not undersize or oversize the filters in relation to the selected vessel diameter. This may result in inadequate vessel wall apposition or incomplete deployment of the filters. (Refer to Sizing Guide, Table 1 in the DFU).

PRECAUTIONS
- Do not forcefully bend or reshape the Articulating Sheath of the Sentinel System.
- Use of TAVR delivery systems other than those designed to cross the aortic arch with a valve frame in a sheathed or crimped configuration may result in device interference or entanglement.

ADVERSE EVENTS
Possible adverse events associated with Sentinel System use and application procedure include, but are not limited to, the following:
- Access site complications
- Angina
- Aortic dissection
- Arrhythmia
- Arteriovenous fistula
- Atelectasis
- Bleeding, operative or post-operative
- Cardiac Tamponade
- Cardiogenic Shock
- Conduction system injury
- Congestive Heart Failure (CHF)
- Death
- Endocarditis
- Embolism, including air
- Gastrointestinal (GI) bleed
- Hematoma
- Ischemia (coronary, limb, carotid)
- Infection (local or systemic)
- Myocardial Infarction (MI)
- Nerve injury
- Pericardial effusion
- Pneumonia
- Pulmonary edema
- Pulmonary embolism
- Respiratory failure
- Respiratory insufficiency
- Stroke
- Vessel injury (e.g., dissection, rupture, perforation, pseudoaneurysm)