NewYork-Presbyterian

2017 • Issue 1

ADVANCES IN CARDIOLOGY, INTERVENTIONAL CARDIOLOGY, AND CARDIOTHORACIC SURGERY

Weill Cornell Medicine

Columbia University Medical Center

Emile A. Bacha, MD
Chief, Division of Cardiac, Thoracic and Vascular Surgery
NewYork-Presbyterian/ Columbia University Medical Center
Director, Congenital and Pediatric Cardiac Surgery
NewYork-Presbyterian Hospital
eb2709@cumc.columbia.edu

Leonard N. Girardi, MD
Cardiothoracic Surgeon-in-Chief
NewYork-Presbyterian/ Weill Cornell Medical Center
lngirard@med.cornell.edu

Bruce B. Lerman, MD
Chief, Maurice R. and Corinne P. Greenberg Division of Cardiology
NewYork-Presbyterian/ Weill Cornell Medical Center
blerman@med.cornell.edu

Allan Schwartz, MD
Chief, Division of Cardiology
NewYork-Presbyterian/ Columbia University Medical Center
as20@cumc.columbia.edu

SAVE THE DATE

TCT 2017
Transcatheter Cardiovascular Therapeutics Annual Meeting
October 29 - November 2, 2017
Colorado Convention Center
Denver, Colorado

For More Information
info@tct2017.com
www.crf.org/tct

NewYork-Presbyterian Cardiology and Heart Surgery ranks #3 in the nation.

TAVR Branches Out: New Refinements, Broader Indications

Transcatheter aortic valve replacement (TAVR) – first performed in 2002 in France – clearly marked a sea change in offering a therapeutic treatment option for high-risk patients with severe symptomatic aortic stenosis. Since then TAVR has progressed dramatically in terms of device technologies and patient selection due, in large part, to the pioneering work of interventional cardiologists and cardiac surgeons at NewYork-Presbyterian/Columbia University Medical Center and NewYork-Presbyterian/Weill Cornell Medical Center.

Over the past decade, NewYork-Presbyterian cardiac surgeons and interventionalists have led a major series of clinical trials – the PARTNER Trials – with great success evaluating catheter-based treatment of aortic valve disease. This work has resulted in close to 200 publications, including several in *The New England Journal of Medicine* and *The Lancet,* detailing the significant outcomes of these clinical trials. This pioneering work established TAVR as the standard of care for inoperable patients, as an alternative to surgery in high-risk patients, and most recently as another treatment option for patients at intermediate risk.

Today TAVR accounts for 32 percent of all aortic valve replacements and is available in more than 65 countries with some 250,000 total implants to date. NewYork-Presbyterian's total case volume is over 4,000 procedures and we are currently performing more than 500 TAVR cases per year. Seventy percent of our patients are discharged in two days or less.

TAVR: Technology and Technique

Our physicians have had extraordinary success applying the TAVR technique to the sickest of sick. The TAVR technology has been a step forward for patient care, achieving equivalent results of surgery, but with a simpler and shorter recovery phase. Recovery has also been made easier for patients with a transition from the use of general anesthesia to conscious sedation or monitored anesthesia control. In fact, 75 percent of TAVR patients at NewYork-Presbyterian bypass the ICU and go from the Cath Lab directly to an observation unit for recovery.

TAVR is performed using either the transfemoral or transapical approach, allowing the physician to choose which one provides the best and safest way to access the valve. The preferred approach is to do the procedure transfemorally unless the artery is too small. Whether the sheath and delivery system is navigated through the groin depends on the patient's anatomy. If the patient has disease in the arteries of the legs then another entry site must be used. At NewYork-Presbyterian, TAVR is performed transfemorally in the overwhelming majority of patients.

NewYork-Presbyterian's total case volume is over 4,000 procedures and we are currently performing more than 500 TAVR cases per year.

With increasingly smaller TAVR delivery systems, the potential for trauma during the procedure has been lessened. The original system was a 26-Fr sheath in diameter. Today, with 14- to 16-Fr sheaths, there is less of a tendency to cause embolization, which can lead to procedural stroke when trying to navigate the system into the aorta, around the arch into the ascending aorta, and across the valve.

The miniaturization of the Edwards SAPIEN system allows expansion of the catheter as it crosses the aortic arch away from the wall. The result is less contact and a more gentle approach before crossing the aortic valve, and therefore less potential for traumatizing the wall. Enhanced technology mitigates any leaking of blood around the stent.

(continued on page 2)

TAVR Branches Out: New Refinements, Broader Indications

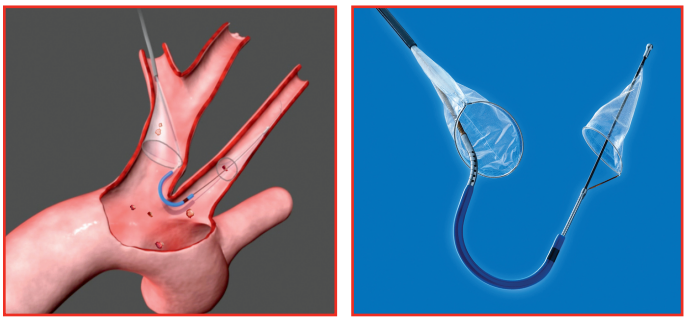
(continued from page 1)

These smaller caliber systems can be placed in a broader range of patients. There's less limitation related to the size of the artery being accessed. And the devices can enter and be withdrawn more easily. Recent results of TAVR have been excellent – 1 percent mortality in an intermediate-risk population with 1 percent major stroke. These results were less than what has been noted in a similarly matched surgical population.

With increasingly smaller TAVR delivery systems, the potential for trauma during the procedure is less. TAVR is now at a point where the stroke rate is less than with the surgical approach.

Stroke: Addressing a Formidable Complication

While the stroke rate for TAVR is now less than that of surgery, the potential for stroke continues to give physicians great pause. Three to 6 percent of TAVR patients experience a stroke caused by embolic debris that can dislodge during the valve replacement. With a goal of lessening the stroke rate, NewYork-Presbyterian physicians are leaders in the evaluation of cerebral embolic protection devices to reduce the potential for brain injury occurring during the procedure. They served as senior authors of the international Sentinel trial that evaluated a cerebral protection system with properties designed to work in concert with the TAVR procedure. The

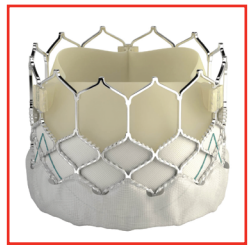


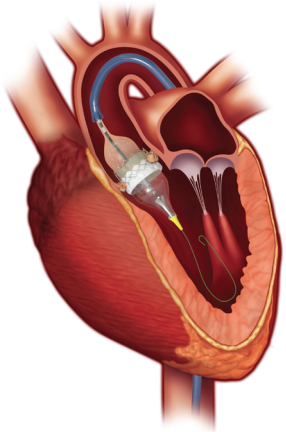
The Sentinel Cerebral Protection System is the only FDA-cleared device available in the United States to protect patients from the risk of stroke during TAVR.

system includes dual independent filters for capture and removal of embolic debris, right transradial 6F sheath access, and a deflectable sheath that facilitates cannulation of the left coronary cusp. The system maintains a low profile in the aortic arch to minimize any interaction with the TAVR delivery catheter.

The study, which was completed in 2016, enrolled 363 patients at 19 hospitals and is currently the largest randomized trial to date to examine the safety and efficacy of using neuroprotection during TAVR. The trial's clinical data showed a 63 percent reduction in neurology adjudicated strokes at 72 hours and maintained a substantial difference at 90 days. Additional studies indicated the device removed visible debris headed towards the brain in 99 percent of TAVR cases, regardless of the type of replacement valve used and with no added risk. Looking at the totality of this data from a risk-benefit standpoint, the critical need for an alternative accessory device to reduce ischemic brain injury in stroke, and demonstration

PARTNER 3:
TAVR for Low-Risk Patients





The Edwards SAPIEN 3 transcatheter heart valve offers several enhanced design features over previous versions. (Courtesy of Edwards Lifesciences)

that the device is safe, the authors concluded that the potential benefits outweigh the risks and should be made available to interventional cardiologists. On June 5, 2017, the FDA cleared the Sentinel TAVR stroke protection device for use in the United States.

The Latest TAVR Trials

The PARTNER 1 and 2 trials paved the way for PARTNER 3. With our faculty serving as one of the two principal investigators, the multicenter study will compare TAVR using the SAPIEN 3 balloon-expandable platform with surgical valve replacement in patients with low operative risk. The SAPIEN 3 features new design elements including:

- a frame geometry for ultra-low delivery profile and high radial strength for circularity and optimal hemodynamics
- a low frame height that respects cardiac anatomy
- bovine pericardial tissue in a leaflet shape optimized for hemodynamics and durability and affixed with a process intended to reduce the risk of calcification
- an outer skirt design that minimizes paravalvular leak

The trial has begun to enroll approximately 1,200 patients across 50 sites. Subjects are age 65 or older with a Society of Thoracic Surgeons risk score of less than 4 percent. The noninferiority trial has a primary endpoint comprising a one-year composite of death, stroke, or rehospitalization.

PARTNER 3 randomly allocates participants to transcatheter or surgical valve replacement for symptomatic, severe aortic stenosis. The pivotal, groundbreaking trial has not been conducted anywhere else in the world. It could potentially show that transcatheter valve replacement is no worse – or perhaps even better – than open surgical procedures.

Columbia and Weill Cornell clinician researchers are also exploring TAVR as an option for patients with failing surgically implanted bioprosthetic valves who might have had an operation at age 70 and are now 80 to 90 years old and need a new valve. Rather than having a high-risk open chest procedure, selected patients may be candidates for having a new valve placed inside the older valve via TAVR.

The early experiences of using valve-in-valve TAVR for structural degeneration of bioprosthetic surgical aortic valves demonstrated

that TAVR is a reasonable therapeutic alternative. Updated data from the PARTNER 2 Valve-in-Valve Registry in patients with symptomatic aortic stenosis at high risk for complications during a reoperation substantiated this further. The study involved 365 patients across 34 sites enrolled over a two-year period. Their mean age was 78.9 plus/minus 10.2 years; the mean Society of Thoracic Surgeons score was 9.1 plus/minus 4.7 percent.

Outcomes at 30 days and one year showed low rates of mortality, stroke, rehospitalization, and new permanent pacemakers, improved hemodynamics, and significant improvements in functional status and quality of life. While the study had limitations in the careful selection of both patients and clinical study sites, the authors concluded that valve-in-valve TAVR presents a viable option for selected patients.

Valve-in-Valve TAVR

With TAVR now available for increasingly lower-risk operative patients and, therefore, young patients, the question arises on management of these patients in the long term. Columbia and Weill Cornell physicians are beginning to confront this in very specific ways, including valve-in-valve TAVR, which will need further investigation in larger, randomized trials.

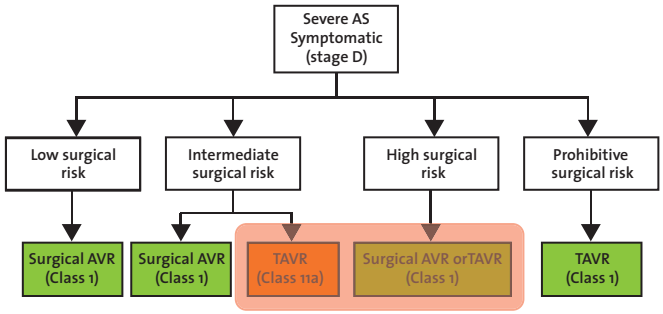
They are also looking at two new categories of patients – those with moderate aortic stenosis in heart failure and those with severe asymptomatic aortic stenosis – with a goal to identify patients who may benefit from early TAVR before they present with atrial fibrillation, severe heart failure, or with pulmonary hypertension. To this end, they are participating in two major multicenter clinical trials with potentially significant implications for the aortic stenosis population.

Early TAVR Trial Approved by the FDA in February 2017, this trial will compare the practice of active surveillance to early TAVR in patients diagnosed with severe aortic stenosis who have not yet developed symptoms.

TAVR UNLOAD Trial Begun in May 2016, this international study is comparing TAVR performed via a transfemoral approach in combination with optimal heart failure therapy (OHFT) to OHFT alone in patients diagnosed with heart failure with reduced ejection fraction and moderate aortic stenosis. The investigators hypothesize that unloading the left ventricle by reducing the transaortic gradient with TAVR may improve the clinical outcomes of these patients.

As indications for TAVR continue to accrue, guidelines for its use will also evolve; the most recent AHA/ACC clinical practice guidelines were released in July 2017. NewYork-Presbyterian clinicians expect that catheter-based approaches will be applied for the treatment of biscuspid aortic valve disease, aortic stenosis with concomitant disease, and high-risk aortic regurgitation and open up the potential for new transcatheter heart valve systems and ancillary devices.

2017 TAVR Guidelines: The New AHA/ACC Focused Update



Source: 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guidelines for the Management of Patients with Valvular Heart Disease. Report of the American College of Cardiology/ American Heart Association Task Force on Clinical Practice Guidelines.

Reference Articles

Baron SJ, Arnold SV, Wang K, Magnuson EA, Chinnakondepali K, Makkar R, Herrmann HC, Kodali S, Thourani VH, Kapadia S, Svensson L, Brown DL, Mack MJ, Smith CR, Leon MB, Cohen DJ; PARTNER 2 Investigators. Health status benefits of transcatheter vs surgical aortic valve replacement in patients with severe aortic stenosis at intermediate surgical risk: Results from the PARTNER 2 randomized clinical trial. *JAMA Cardiology*. 2017 Jun 28. [Epub ahead of print]

Webb JG, Mack MJ, White JM, Dvir D, Blanke P, Herrmann HC, Leipsic J, Kodali SK, Makkar R, Miller DC, Pibarot P, Pichard A, Satler LF, Svensson L, Alu MC, Suri RM, Leon MB. Transcatheter aortic valve implantation within degenerated aortic surgical bioprostheses: PARTNER 2 Valve-in-Valve Registry. *Journal of the American College of Cardiology*. 2017 May 9;69(18):2253-62.

de Biasi AR, Wong SC, Minutello RM, Voudris K, Worku B, Girardi LN, Salemi A. Short- and mid-term results after transapical transcatheter aortic valve replacement in nonagenarians. *Journal of Cardiovascular Surgery* (Torino). 2017 Feb;58(1):99-104.

Kapadia SR, Kodali S, Makkar R, Mehran R, Lazar RM, Zivadinov R, Dwyer MG, Jilaihawi H, Virmani R, Anwaruddin S, Thourani VH, Nazif T, Mangner N, Woitek F, Krishnaswamy A, Mick S, Chakravarty T, Nakamura M, McCabe JM, Satler L, Zajarias A, Szeto WY, Svensson L, Alu MC, White RM, Kraemer C, Parhizgar A, Leon MB, Linke A; SENTINEL Trial Investigators. Protection against cerebral embolism during transcatheter aortic valve replacement. *Journal of the American College of Cardiology*. 2017 Jan 31; 69(4):367-77.

Voudris KV, Wong SC, Kaple R, Kampaktsis PN, de Biasi AR, Weiss JS, Devereux R, Krieger K, Kim L, Swaminathan RV, Feldman DN, Singh H, Skubas NJ, Minutello RM, Bergman G, Salemi A. Transapical transcatheter aortic valve replacement in patients with or without prior coronary artery bypass graft operation. *Journal of Cardiothoracic Surgery*. 2016 Nov 29; 11(1):158.

Kampaktsis PN, Ullal AV, Minutello RM, Feldman DN, Swaminathan RV, Voudris K, Baduashvili A, Pastella K, Pawar S, Kaple RK, Vavuranakis M, Bergman GS, Skubas NJ, Lin F, Salemi A, Devereux RB, Chiu Wong S. Impact of paravalvular aortic insufficiency on left ventricular remodeling and mortality after transcatheter aortic valve replacement. *Journal of Heart Valve Disease*. 2016 May;25(3):301-08.

Leon MB, Smith CR, Mack MJ, Makkar RR, Svensson LG, Kodali SK, et al; PARTNER 2 Investigators. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients *The New England Journal of Medicine*. 2016 Apr 28;374(17):1609-20.

NewYork-Presbyterian

AMAZING THINGS ARE HAPPENING HERE

BEST HOSPITALS U.S.News HONOR ROLL 2017-18

New York's #1 Hospital
17 Years in a Row

ADVANCES IN CARDIOLOGY, INTERVENTIONAL CARDIOLOGY, AND CARDIOTHORACIC SURGERY

NewYork-Presbyterian Hospital
525 East 68th Street
New York, NY 10065
www.nyp.org

NON-PROFIT ORG.
US POSTAGE
PAID
STATEN ISLAND, NY
PERMIT NO. 169

Weill Cornell Medicine

Columbia University Medical Center