

ADVANCES IN ADULT AND PEDIATRIC CARDIOLOGY, INTERVENTIONAL CARDIOLOGY, AND CARDIOVASCULAR SURGERY

Affiliated with Columbia University College of Physicians and Surgeons and Weill Cornell Medical College

INSIDE FALL 2012

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Treatment for Aortic Valve Disease – Now and in the Future

On November 4, 2011, NewYork-Presbyterian Hospital/Columbia University Medical Center became the first hospital in the U.S. to implant the SAPIEN transcatheter aortic heart valve as an FDA-approved standard of care. This major advance in patient care followed the FDA's decision two days earlier to approve SAPIEN as a preferred treatment for patients too sick to undergo traditional aortic valve surgery. According to Martin B. Leon, MD, Director, Center for Interventional Vascular Therapy at NewYork-Presbyterian/Columbia, there is little doubt that transcatheter aortic valve replacement (TAVR) addresses an unmet clinical need for a common disease. The prevalence of aortic stenosis in people over the age of 75 years is approximately 5 percent and, with a rising aging population, the optimal treatment of calcific aortic stenosis has become an important global healthcare concern.

The FDA approval of TAVR nearly a year ago was based on results of the 26-center, rigorously designed PARTNER (Placement of AoRTic TraNscathetER Valve) clinical research trial with Dr. Leon and Craig R. Smith, MD, Chairman, Department of Surgery, NewYork-Presbyterian/Columbia, serving as national principal investigators.

The PARTNER Trial: A New Model for Research and Clinical Practice

It is estimated that some 200,000 people annually in the U.S. need a new heart valve. "When we looked at patients over the age of 75 with severe aortic stenosis, we found that a third of them, for whatever reason – poor ventricular function, failing kidneys, pulmonary hypertension, frailty, and other comorbidities – were considered too high risk to undergo surgery," says Arash Salemi, MD, a cardiothoracic surgeon and member of the PARTNER trial team at NewYork-Presbyterian Hospital/Weill Cornell Medical Center – the only other center in New York City participating in PARTNER. "Severe aortic stenosis is a disease entity that can lead to rapid, sudden death. If these patients are too sick for surgery, then what could we offer them?"

Only five years ago, the answer would have been nothing, and within two to three years of their diagnosis many of these patients would likely



"Approval of the SAPIEN transcatheter aortic heart valve was a monumental event on par with FDA approval of the bare metal stent in 1994."

– Martin B. Leon, MD

succumb. With the inauguration of the PARTNER trial, treatment options for this nonoperable patient population was about to change in a profound way; PARTNER would also introduce a new cardiovascular team approach – one in which the collaboration of cardiologists, echocardiographers, interventional cardiologists, and cardiothoracic surgeons is vital to the performance and outcomes of the procedure.

The PARTNER trial, which studied the Edwards SAPIEN transcatheter aortic valve, had two cohorts: high-risk surgical patients (cohort A) and inoperable patients (cohort B). Drs. Leon and Smith were the lead authors of an article in the October 21, 2010 *New England Journal of Medicine* presenting the results of cohort B of the PARTNER trial, which showed that TAVR can improve survival and quality of life of patients with severe aortic stenosis, compared with standard therapy. "For patients too sick for open-heart surgery, this new treatment means the difference between life and death," says Dr. Leon. In fact, TAVR was associated with a dramatic 20 percent improvement in one-year survival and reduced symptoms compared with standard medical intervention, including a combination of watchful waiting, medications, and balloon aortic valvuloplasty.

In the most recent edition of America's Best Hospitals published by the *U.S. News & World Report*, the cardiovascular programs of NewYork-Presbyterian Hospital were ranked #1 in the New York City metropolitan area and #4 in the nation.



Top Ranked Hospital in New York.
Twelve Years Running.

“This is a major shift in how we take care of aortic valve disease,” says Karl H. Krieger, MD, Vice Chairman, Cardiothoracic Surgery, NewYork-Presbyterian/Weill Cornell. “Open-heart surgery has done an amazing job of curing the problem for 50 years. But while we achieve these great results, the risk of operation and recovery is much higher for patients who have other medical problems.”

Results from a second arm of the PARTNER I trial – cohort A – were reported by Drs. Smith and Leon in the June 9, 2011 *New England Journal of Medicine* and were submitted separately to the FDA. “In high-risk patients with severe aortic stenosis, transcatheter and surgical procedures for aortic valve replacement were associated with similar rates of survival



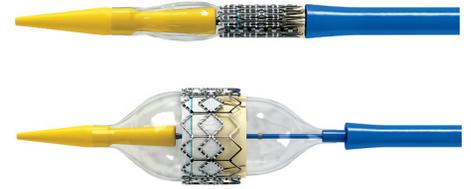
“Born of an unprecedented collaboration between surgery and interventional cardiology, the aptly named PARTNER trial has not only demonstrated the benefits of the transcatheter aortic valve, but it has also presented a new model for research and clinical practice.”
 – Craig R. Smith, MD

at one year,” says Dr. Smith. “Stroke and vascular complications are periprocedural risks associated with TAVR, although their incidence has decreased since the first report. Clinical experience and the development of smaller devices help to mitigate these risks.”

All patients were followed for at least two years, with assessment of clinical outcomes and echocardiographic evaluation. The two-year follow-up supported TAVR as an alternative to surgery in high-risk patients, confirming that the two treatments were similar with respect to mortality, reduction in symptoms, and improved valve hemodynamics.



The Edwards SAPIEN transcatheter heart valve with three tissue leaflets made from cow heart tissue in a stainless steel frame with a fabric skirt.



The Edwards SAPIEN transcatheter heart valve is placed on a delivery system and compressed on the balloon to make it small enough to fit through the sheath. The balloon is inflated with fluid, expanding the new valve within the diseased valve.

Performing TAVR: The Team Approach

“In an evaluation of the patient,” says Dr. Salemi, “we rely on input from interventional cardiology, cardiac surgery, general cardiology, echocardiography, and radiology. The procedural team includes the interventional cardiologist, the surgeon, percutaneous coronary intervention specialists, anesthesiologists, physician assistants, and nurses.”

“The heart team concept drives the whole process,” adds Shing-Chiu Wong, MD, Director, Cardiac Catheterization Laboratories at NewYork-Presbyterian/Weill Cornell. “Having surgeons and interventional cardiologists working together on the same patient is quite unique. As interventional cardiologists, we have a knowledge base in terms of catheter and guide wire techniques, but we are working in an anatomical space that is new for us. Surgeons, however, have been working on valves for decades, so this is a familiar space for them. Our work is image-driven, whereas our surgical colleagues open the chest and can look directly at the valve. It’s really a good complementary skill set, and at the end of

the day, it’s the patient who benefits from these combined experiences.”

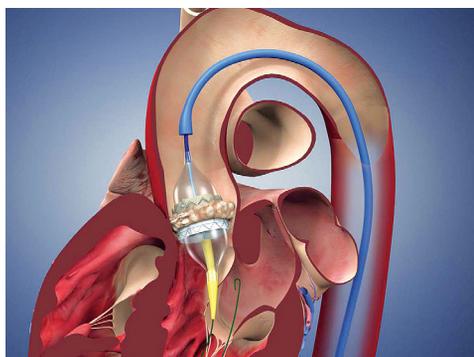
Mathew R. Williams, MD, and Susheel K. Kodali, MD, Co-Directors, Heart Valve Center at NewYork-Presbyterian/Columbia, serve as co-principal investigators for the PARTNER trial at Columbia. As the first U.S. physician to have joint training and appointments in interventional cardiology and cardiac surgery, Dr. Williams performs an increasing number of “hybrid” procedures using the best of both surgical and less-invasive methods to achieve optimal solutions.

“One of the exciting advantages in the treatment of aortic valve disease via the transcatheter approach is that several different platforms for access are being made available,” explains Dr. Salemi. “There is a transfemoral approach through the femoral artery and a transapical approach, which is through the apex of the heart, right through the heart muscle. We are now expanding into a transaortic approach, where we enter directly through the aorta and implant the valve without a breast bone incision and without need of the heart-lung machine.

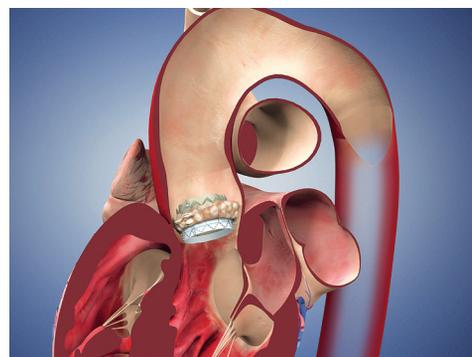
“For example,” continues Dr. Salemi,

“Our work is image-driven by ultrasound and by fluoroscopy, whereas our surgical colleagues open the chest and can look directly at the valve. So it’s really a good complementary skill set, and at the end of the day, it’s the patient who benefits from these combined experiences.”
 – Shing-Chiu Wong, MD





The delivery system carrying the new valve is placed through the sheath and pushed up to the aortic valve, guided by imaging. “To make room for the new valve, the patient’s non-working valve is simply pushed out of the way,” says Dr. Arash Salemi. “The new valve sits against the old valve so snugly that you don’t even need a suture to hold it in place.”



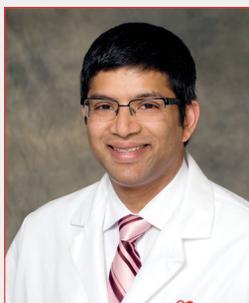
Images courtesy of Edwards Lifesciences

“you could have a patient whose femoral artery is too small and won’t accommodate the sheath. You then say, ‘How about going through the side?’ Well, you can’t go through the side because the patient has bad emphysema. If you go through the side, you might make the emphysema worse because you’re going to enter in the lung space. This is when we decide to go directly through the aorta. So having all these tools in the tool box is critical.”

and it requires catheter skills to replace the valve. The method avoids having to use the heart-lung machine.”

Since the completion of the PARTNER randomized trial, Drs. Leon and Smith, along with PARTNER trial investigators across the country, have had several manuscripts published in the *New England Journal of Medicine* and other peer-reviewed publications describing the results from nearly 1,100 patients in both cohorts of

PARTNER II trial will introduce the next generation technology, SAPIEN XT, which is 40 percent smaller in caliber, into the U.S. marketplace,” notes Dr. Leon. “But most importantly, this new randomized trial is studying the procedure in intermediate or moderate-risk patients. As we go down in the risk strata, we need to know if this technology is as good as surgery.” The 2,000-patient randomized trial involves 50 to 60 sites in the U.S. and Canada and, with 500 patients already enrolled, it is expected to complete enrollment by Spring 2013. Drs. Williams and Kodali serve as principal investigators at Columbia; Drs. Krieger and Wong are the principal investigators for Weill Cornell.



Since PARTNER began, Dr. Susheel Kodali (left), Dr. Mathew Williams (right), and colleagues at New York-Presbyterian/Columbia have performed more than 560 valve procedures – more than any other center in the country.

“Depending on the access that is decided upon, the team leader is either the interventional cardiologist or the surgeon,” notes Dr. Krieger. “This is based on the patient’s femoral or arterial anatomy. If we can put catheters up we generally go the femoral route and this is led by the interventionalist. If a patient has severe vascular disease, which is frequently the case with elderly patients, we use the transapical approach, in which case the procedure is led by the surgeon.”

“In the transapical approach, the surgeon makes a small incision in the chest, inserts a short catheter into the tip of the heart, and through this catheter replaces the aortic valve,” explains Dr. Williams. “This requires surgical skills to access the heart,

the PARTNER trial. An additional 2,000 patients have been enrolled through the FDA’s expanded access program.

“We continue to follow patients from the initial PARTNER trial looking at some of the late outcomes,” says Dr. Leon. “This is important in understanding the durability of this technology and how it compares to surgical valve replacement as we move further in time, and in improving our understanding of how this technology can be best applied.”

PARTNER II: Newer Technology and the Moderate-Risk Surgical Patient

For just over a year now, Drs. Leon and Smith have served as the national principal investigators of PARTNER II. “The

Beyond PARTNER: What’s New in the Pipeline

“Despite important improvements in current device technology and implantation techniques, specific complications still remain and warrant consideration,” says Dr. Kodali. “Emerging technologies and newer generations of devices seem promising in dealing with these matters.”

Transaortic valve replacement continues to evolve and undergo examination and, in just the past year, several new systems, technology, and devices have entered the field for testing. “Now, and especially in the future, all major and minor components of a TAVR system will be fully customized and designed for specific functional tasks,” notes Dr. Leon. “Moreover, adjunctive technology is being developed to enhance TAVR outcomes and reduce complications. We are continuing to try to reduce the size of the device so that it is easier to use in patients who have smaller vessels, but also to be able to have a capacity to retrieve



“The most important thing is that TAVR provides lifesaving technology for a group of patients, particularly the elderly, who have significant comorbidities – patients too sick for traditional surgery.”

– Karl H. Krieger, MD

and reposition the device if we don't like the initial position. Right now with the SAPIEN device, once you position it and expand the balloon, that's it. There are no redos. With many of these newer devices, we can actually position it while it's still attached to the catheter. If we don't like the position, we can recapture the device and then reposition it.”

Smaller devices are also expected to reduce the incidence of stroke in patients undergoing TAVR. “The stiffness found in aortic valve stenosis is caused by an accumulation of calcium deposits on the valve leaflets,” says Dr. Salemi. “When a new valve is inserted, these deposits can break off, causing a stroke. Many of these devices also traverse the major arteries of the head. As you come up through the artery in patients who have atherosclerotic disease of their aorta, a portion of plaque can be released and cause an embolic stroke.”

“The newest devices – the sheath plus the delivery device with the valve – are only five millimeters, almost half the size of the current devices, making it much easier to navigate the vessels,” says Geoffrey W. Bergman, MB, BS, Associate Director, Cardiac Catheterization Laboratory, NewYork-Presbyterian/Weill Cornell. “This potentially causes less trauma and irritation to the vessels as it crosses the arteries. Smaller devices can

(continued on page 5)

NewYork-Presbyterian Hospital Valve Centers: Leaders in Innovative Approaches and Interdisciplinary Care

Combining the expertise of cardiologists, cardiothoracic surgeons, and cardiac imaging specialists, NewYork-Presbyterian Hospital has established leading centers in cardiac valve procedures at each of its main campuses.

NewYork-Presbyterian/Columbia Heart Valve Center

177 Fort Washington Avenue, Room 5C-501 • New York, NY 10032 • (212) 342-0444

In Fall 2011, NewYork-Presbyterian/Columbia, in partnership with the Center for Interventional Vascular Therapy, launched the NewYork-Presbyterian/Columbia Heart Valve Center, a multidisciplinary program for valve patients, providing surgical, interventional, and hybrid options for a variety of valvular conditions. The heart valve team at Columbia has years of clinical and academic leadership in transcatheter aortic valve replacement (TAVR) and serve as the principal investigators of the national PARTNER trials that established the effectiveness of this minimally invasive procedure. “On average, we perform six to eight procedures per week on some of the most complex and difficult-to-treat patients,” says Mathew R. Williams, MD, Co-Director, Columbia Heart Valve Center. “In addition to treating aortic stenosis patients, we have a number of mitral valve disease patients enrolled in clinical trials.”

According to Susheel K. Kodali, MD, Co-Director, Columbia Heart Valve Center, the Center has also established a formal training and education program in valvular disease. “The Center approaches valvular heart disease in its totality, including outreach to referring doctors, patient screening, patient evaluations, and all forms of patient therapy.”

William Acquavella Heart Valve Center at NewYork-Presbyterian/ Weill Cornell

525 East 68th Street • F 439 • New York, NY 10065 • (646) NYP-VALV/(646) 697-8258

Specialists at the William Acquavella Heart Valve Center at NewYork-Presbyterian/Weill Cornell develop and evaluate novel, less-invasive techniques for repairing and replacing damaged mitral, aortic, and pulmonary valves. The Center's team has played a leading role in clinical trials assessing the latest percutaneous valve replacement approaches, giving it greater experience than most centers in these emerging new techniques.

“The Acquavella Heart Valve Center is dedicated to finding new therapy modalities in the treatment of valvular heart disease,” notes Karl H. Krieger, MD, Vice Chairman, Department of Cardiothoracic Surgery. “From a cardiovascular point of view, most of the patients that we see have the most common form of valvular heart disease, which is aortic stenosis, a disease that affects up to 1.5 million people in the United States. We have achieved superior outcomes using these innovative approaches, which make valve replacement possible for many patients who cannot tolerate conventional heart surgery.”

Indeed, the Center is cognizant that many of its older patients come from throughout the tri-state area accompanied by a family member. “We pride ourselves in minimizing the stress on our older patients and try to keep their evaluation to one visit if possible,” adds Dr. Krieger.

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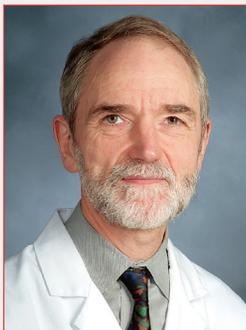
also minimize bleeding risk and damage to the vessel at the access site.”

A number of cerebral embolic protection devices – deflectors and filters – are also beginning to come under study. “These devices may either be deployed in the aortic arch or used to cover the cranial branches during the procedure,” says Dr. Leon. “We should start to see them being used in clinical trials in the U.S in the next 12 months.”

Valves are also being made available for implantation inside a previously placed surgical valve that has deteriorated. Says Dr. Salemi, “We do not remove the old valve because a reoperation poses a much higher risk, and it appears that the valve within the valve provides similar blood flow.”

A Transcatheter Valve Therapy Registry

After FDA approval of a device, a post-approval study follows. “A rarified environment of a randomized trial sometimes does not uncover all of the safety issues related to new therapies,” says Dr. Leon. “The Society of Thoracic Surgeons and the American College of



According to Dr. Geoffrey W. Bergman (left) and Dr. Arash Salemi (right), one of the exciting advantages in the treatment of aortic valve disease via the transcatheter approach is that several different platforms for access are being made available.

Cardiology have worked together to develop the Transcatheter Valve Therapy Registry. This gives us an opportunity to consecutively collect data on all cases performed in the U.S. to be able to monitor for safety, as well as to generate new research that potentially could be used to expand the clinical indications. This is the first time in the interventional world that such a registry has been created.”

This registry has been linked to the Centers for Medicare and Medicaid Services (CMS) and to a national coverage determination on reimbursement.

PARTNER Training and Publishing

NewYork-Presbyterian/Columbia is now the main training site for the commercial release of the Edwards SAPIEN valve, and to date, has trained some 40 percent of the physicians who perform TAVR in the United States and Canada. NewYork-Presbyterian/Columbia, in collaboration with the Cleveland Clinic, is also the key site for the PARTNER Publications Office, a repository and clearinghouse for manuscripts related to substudies and analysis of PARTNER data. There are currently 30 to 40 manuscripts underway.

Remarks of Dr. Craig Smith – Past President, American Association for Thoracic Surgery



At the 92nd Annual Meeting of the American Association for Thoracic Surgery held in May 2012 in San Francisco, Craig R. Smith, MD, Chairman of Surgery, NewYork-Presbyterian/Columbia, addressed the attendees as outgoing President (2011-2012). Reflecting on a wide range of subjects, Dr. Smith also commented on advances and innovations in surgery and medicine today and, as one example, transcatheter aortic valve replacement.

Innovation is driven by people who generate ideas. By people who are constitutionally incapable of focusing on tiny inflections along the asymptotic part of the technology curve, where quality becomes the primary, innovation-stifling objective. These are people, by the way, who often chafe under the yoke of what many call education. Specific forecasting matters little when you know where to look for these people. Find them, and you know where the next big idea will come from, even if you do not know what it is.

On these points, transcatheter aortic valve replacement is instructive. In the idea stage, and in early experimental development, it seemed a reckless fantasy for which the most common forecast was a 100 percent stroke rate. In a surprisingly short time, it has become available for commercial use for certain situations, and the forecast everyone wants to hear is how soon it will completely replace surgical aortic valve replacement. We missed the chance to learn from history, and again sat on the sidelines, driving surgical aortic valve replacement along its quality asymptote, mistaking mini-this and mini-that for innovation, while cardiologists had all the fun.

We awoke from our slumber in time to form exciting new

collaborative relationships with our cardiology colleagues, who began teaching interventional skills to a small cadre of cardiac surgeons. We have now proved that fully trained cardiac surgeons can learn, and practice cardiac surgery and interventional cardiology, in all their flavors. As we mint more and more of these chimera, their creativity will take us in new and surprising directions, on both sides of the former cardiology/surgery divide. Where did these pioneering chimera come from, and where will their successors come from? They will come from this audience in front of me.

The men and women who will carry our specialty and this Association forward after we have gone will be very similar to those who preceded them. Not because they will be performing the same procedures we perform, in the same way, but because they will have the same traits and share similar values. They will not need to be engineers or biochemists or geneticists. They will be men and women for whom the multifaceted excitement of uncertainty is irresistible. They will be men and women who infinitely prefer haggling in a sweaty marketplace of unanswered questions to lounging in a temple of unquestioned answers. Combine that with restless curiosity, imagination, creativity, persistence, and risk-embracing boldness, and the development of revolutionizing treatments of disease in the thorax and blood vessels will come from us.

For a complete transcript of Dr. Smith's remarks, see the October 2012 issue of The Journal of Thoracic and Cardiovascular Surgery.

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