Valve replacement via catheterization is gaining ground

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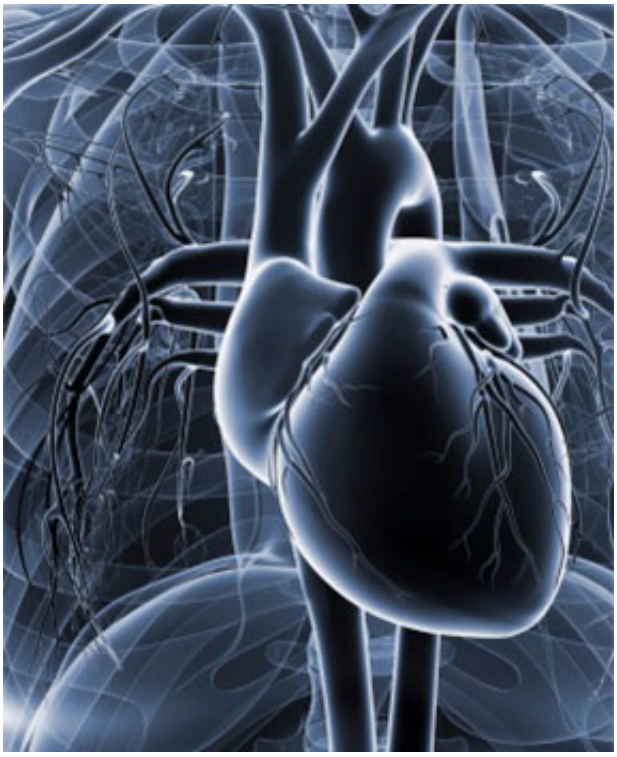

Credit: PIXOLOGICSTUDIO

When Maryann Casey battled breast cancer more than 30 years ago, her doctors warned that the radiation therapy could damage her heart. Still, she was caught off guard when, after an echocardiogram in 2012, she was diagnosed with severe aortic stenosis, a potentially fatal heart-valve disease.

"They were telling me I could drop dead," says Casey, 62, who lives in San Jose with her husband and 20-year-old daughter. Her local doctors said the key valve that carries blood out of the heart into the aorta had severely narrowed, obstructing blood flow and dangerously stressing her heart. "They said, you need to have open-heart surgery immediately." It felt like lightning had struck twice, she says.

Despite that frightening warning Casey, who retired after 24 years as a security manager in Silicon Valley, soon learned that open-heart surgery wasn't her only option. After the shock of receiving her second diagnosis of a potentially fatal disease, she quickly made an appointment with her oncologist, the same Stanford physician who she credits with saving her life and who continues to give her yearly physical examinations and mammograms.

"I was told by my oncologist I would probably never heal correctly after open-heart surgery," Casey says. "He knew about this new treatment at Stanford and recommended I go talk to the heart doctors there."

Casey was lucky. Her Stanford oncologist, Frank Stockdale, MD, PhD, the Maureen Lyles D'Amrogio Professor of Medicine Emeritus, was well-informed about treatment options for aortic stenosis, a calcification of the heart valve. This new nonsurgical approach to valve replacement involves placing an artificial heart valve, made of cow tissue supported by a stainless steel mesh frame, inside the damaged valve. Referred to as "transcatheter aortic valve replacement" or TAVR, the procedure is designed for patients with severe, symptomatic aortic stenosis who have health conditions that make the preferred treatment, open-heart surgery, very high risk.

"The odds were that she would not heal well," says Stockdale. Casey's fast-growing, inflammatory form of breast cancer had required especially high doses of radiation, which he suspected caused additional

long-term damage to the skin and muscles of her chest and to the heart muscle.

ABOUT 300,000 AMERICAN PATIENTS suffer from deterioration of the valve, which forces the heart to work harder to pump blood, often leading to heart failure and sudden death. Each year, about 50,000 of these patients undergo open-heart surgery to replace the valve, which involves cutting through the breastbone, stopping the heart, removing the old valve and sewing a new one into place. Thousands of other patients are turned away, deemed too old or ill to survive the operation, or because they have so many other serious medical problems.

Enter TAVR, a procedure that many in the field refer to as a game changer. In the first year after FDA approval in late 2011, about 7,000 U.S. patients with severe aortic stenosis were treated with transcatheter valve replacement. Doctors are grateful for this new alternative, but they warn that the obvious appeal of a less invasive procedure should not be the overriding factor in choosing a treatment plan for severe aortic stenosis.

"This has been an incredible advance for patients who wouldn't have had options in the past," says Stanford heart surgeon Michael Fischbein, MD, PhD, assistant professor and residency program director in cardiothoracic surgery. "But this device isn't for everyone. It's important to consider the risks and benefits in each individual patient. There are downsides."

TAVR has emerged from the trend over the past three decades toward less invasive heart treatments—catheter-based procedures instead of open-chest surgery. The artificial tissue valve is a feat of engineering able to fold up into a fraction of its functional size. To get it inside the heart, it's compressed and placed in the tip of a thin catheter, about as wide as a pen. This gets inserted into a blood vessel, usually an artery in

the leg, then threaded up through the aorta and down into the heart. At the site of the diseased valve, the artificial valve is released from the delivery catheter and expanded with a balloon. This pushes open the damaged valve and lodges the bioprosthetic one within its cavity where it immediately starts opening and closing, allowing blood to leave the heart and preventing it from leaking back in.

The U.S. Food and Drug Administration first approved a TAVR valve in 2011, allowing it to be used for patients who were deemed too sick to be candidates for open-heart surgery. In 2012, the FDA added an approval for TAVR for patients who, like Casey, are considered at high risk of complications or death from open-heart surgery. Both approvals were based on the results from the PARTNER 1 clinical trial, which was sponsored by the company that makes these bioprosthetic heart valves, Edwards Lifesciences Corp., based in Irvine, Calif. In the fall of 2015, the results of the PARTNER 2 clinical trial are due out, and they could once again move that line. This new randomized trial is testing the use of the minimally invasive technique in patients with severe stenosis at moderate risk for open-heart surgical aortic valve replacement.

Until this year, the Sapien valve produced by Edwards Lifesciences had been the only transcatheter aortic valve with FDA approval. Each of these valves costs about $33,000, but with competition the price is expected to drop. In January the FDA granted approval to a second device for use in extreme-risk patients—Medtronic's CoreValve system—and other companies are expected to jump in within the next few years with their own valves.

THE DECISION

Casey is far from the average TAVR patient. She's much younger and healthier. Most patients are in their 80s or older. Typical TAVR candidates are much more weakened by the valve narrowing, which

impedes the delivery of blood to the body and stresses the heart. Casey hadn't even yet realized that the swelling in her ankles and the "fuzziness" or light-headed feeling she experienced were results of her weakened heart. She was still exercising regularly on a treadmill right up until her diagnosis, when her doctors told her it was too dangerous to continue.

At the recommendation of her much-loved oncologist Stockdale, she went to the Stanford Transcatheter Heart Valve Clinic where she was seen by William Fearon, MD, associate professor of medicine and director of interventional cardiology, and by Fischbein. Her doctors categorized Casey as high risk for open-heart surgery because of the radiation therapy she underwent in her 30s. The radiation, which probably caused the damage to her heart valve, also impaired the ability of the muscles and skin of her chest to heal. Unlike open-heart surgery, TAVR would not require a sternotomy, an incision in the center of the chest, which meant an easier recovery. And because the heart continues to beat throughout the procedure, no heart-lung machine would be required.

"I was scared about the skin healing, having my chest broken open, the lengthy recovery," Casey says. "My doctors showed me the valve. I took a picture of it. I thought this might be a better way to go."

Stanford Hospital is one of only a handful of hospitals in Northern California to offer the transcatheter procedure; the team here has performed more than 300 since October 2008 as part of clinical trials and now under commercial use guidelines. Each new patient with aortic stenosis who comes to Stanford and is a potential candidate for TAVR, like Casey, undergoes consultations with both a cardiologist and a cardiac surgeon as part of a team approach to determine which treatment is best—TAVR, surgical aortic valve replacement, which would require open surgery or, in certain cases, medications alone. This team approach

is not new to the world of heart disease management, but it has been forgotten for decades, heart doctors say. Treatments such as inserting stents through catheters are done by the cardiologists and open operations are performed by cardiovascular surgeons. Usually the two specialties operate in separate worlds.

Typically the heart team would recommend open-heart surgery for patients with aortic stenosis who, like Casey, are in their 60s.

"Most of the patients we treat are in their 80s or 90s," says Fearon. "But occasionally we treat younger patients, like Maryann, because they have a condition that makes traditional aortic valve replacement surgery too risky."

Weighing the pros and cons between the two procedures for each individual patient is essential, the physicians say. According to the PARTNER 1 trial, the risk of stroke is higher with the TAVR procedure, as is vascular bleeding at the site of catheterization. Recovery time is clearly shorter after TAVR, but the valve's longevity remains an important unknown.

The two types of valves used for open-heart surgery have known life spans. Mechanical valves are expected to last the life of the patient. Valves made of animal tissue are estimated to last 10 to 15 years or more if the patient is over 80. Currently there are only preliminary data showing that TAVR valves may last at least five years, without any signs of early degeneration. This adds to the risk, particularly for younger patients, that another replacement valve will be needed.

"We decide which is the right valve for each patient based on the research we have so far," says Fischbein, who, along with Fearon and D. Craig Miller, MD, the Doelger Professor of Cardiovascular Surgery, and Alan Yeung, MD, the Li Ka Shing Professor of Medicine and chief of

cardiovascular medicine, has been involved with the clinical trials used to test TAVR.

"This is another option, an incredible option, for those too high-risk for surgery," Fischbein says. "Now this opens the door for them."

THE PROCEDURE

On Oct. 16, 2012, Casey became one of the more than 120 patients that year at Stanford to undergo the TAVR procedure. The first catheter-based aortic valve transplant was in 2002 in France. It has been approved for use for the past six years in 40 other countries including most of Europe, with a total of 45,000 procedures conducted worldwide.

In the United States, institutions such as Stanford, the Cleveland Clinic, Columbia University and the University of Pennsylvania have been leaders in introducing the new procedure and determining its effectiveness through the clinical trials.

Careful patient selection is key to the successful use of the procedure, says Miller, and that sometimes means not recommending TAVR for a patient who is too old or too sick with other illnesses to benefit from the device.

"That's a very sobering point," says surgeon Miller. For patients who are too old or ill, undergoing the procedure may not increase their quality of life or life expectancy; Miller says that the boundary line between TAVR "utility and futility" is still being defined. For younger, relatively healthy patients like Casey, the unknown longevity of the valve is a major concern.

The TAVR procedure is performed by a team that includes an interventional cardiologist, cardiothoracic surgeon, echocardiographer

and cardiac anesthesiologist. The procedure takes about 45 minutes. Once inserted, the new valve immediately starts working.

"Unlike most open-heart operations, the heart is beating throughout the TAVR procedure," says interventional cardiologist Fearon. "During the actual valve deployment, we use a temporary pacemaker to briefly speed the heart up so that it cannot contract effectively and dislodge the valve."

Recovery from the TAVR procedure is on average about a three- to-five day hospital stay compared to an average seven-day stay for open-heart surgery.

Casey, again, not your average TAVR patient, recovered more rapidly.

She checked into Stanford the night before the procedure on Oct. 15 and checked out on Oct. 17. Stockdale came to visit her in the hospital, where she was up and walking before she checked out. Now, instead of having a 6-inch scar down her chest, she is scar-free. She recovered at home after about two weeks and started exercising, back on the treadmill, after a month. Throughout the entire procedure and recovery period, she never felt any pain in her chest.

"I took a high dose of Tylenol, that was it," Casey says. "I never even filled the pain pill prescription. I was in and out of the hospital in 46 hours."

Casey is concerned about how long the valve will last before she needs another replacement, but she's confident this was the right decision for her. She's got more energy now and exercises three to four times a week, either walking outside or on her treadmill for 30 minutes. She's on her feet constantly, cooking, cleaning, caring for her family.

"I got the call saying I had breast cancer, I'll never forget, on New Year's

Eve," Casey says, remembering back. "I had a good cry." But both times she received those potentially fatal diagnoses, she never really believed she was going to die. "I guess I've beaten the odds a second time."

Provided by Stanford University Medical Center