Clinical trial establishes catheter-based aortic valve replacement as new standard of care

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One-year data from the PARTNER clinical trial, published today in the *New England Journal of Medicine*, demonstrate that transcatheter aortic-valve implantation, compared with standard therapy, resulted in significantly lower rates of death among patients who cannot undergo surgery for aortic stenosis. The results will be presented tomorrow as a Late Breaking Trial at the 22nd annual Transcatheter Cardiovascular Therapeutics (TCT) scientific symposium.

Transcatheter aortic-valve implantation (TAVI) is a new procedure in which a bioprosthetic valve is inserted through a catheter and implanted within the diseased native aortic valve. The Placement of AoRtic TraNscathetER valves (PARTNER) trial is a multicenter, randomized clinical trial comparing TAVI with standard therapy in high-risk patients with severe aortic stenosis. The co-principal investigators are Martin B. Leon, M.D., and Craig R. Smith, M.D., at NewYork-Presbyterian Hospital/Columbia University Medical Center. The data published today reflect a prespecified cohort of patients who were considered to be unsuitable candidates for surgery.

The primary end point was the rate of death from any cause over the duration of the study. A total of 358 patients with aortic stenosis who were considered to be unsuitable candidates for surgery underwent randomization at 21 centers, including 17 in the United States. Patients randomized for standard therapy received a combination of watchful waiting, medications, and balloon aortic valvuloplasty, which can provide transient clinical benefit but does not alter long-term outcomes.

At one year, patients who underwent TAVI showed a 45 percent reduction in the rate of death from any cause compared with patients who received standard therapy (30.7 percent vs. 50.7 percent) and a 54 percent reduction in the combined end point of death from any cause or repeat hospitalization (42.5 percent with TAVI vs. 71.6 percent with standard therapy). Among survivors at one year, the rate of cardiac symptoms was significantly lower among patients who had undergone TAVI, as compared with those who had received standard therapy (25.2 percent vs. 58.0 percent).

"Based on the reduction in mortality during the first year of the study, balloon-expandable TAVI should be the new standard of care in patients who are not suitable candidates for surgery," said Martin B. Leon, M.D., professor of medicine and director of the Center for Interventional Vascular Therapy at NewYork-Presbyterian Hospital and Columbia University Medical Center. Dr. Leon, founder and chairman emeritus of the Cardiovascular Research Foundation, is the co-principal investigator of the study.

At 30 days, TAVI, as compared with standard therapy, was associated with a higher incidence of major strokes (5.0 percent vs. 1.1 percent) and major vascular complications (16.2 percent vs. 1.1 percent). In the year after TAVI, patients had no deterioration in the functioning of the bioprosthetic valve, as assessed by evidence of stenosis or regurgitation on an echocardiogram.

"This study shows that transcatheter valve replacement is a safe and effective option for this life-threatening illness in patients unsuitable for surgical valve replacement," said Dr. Smith, study co-principal investigator and surgeon-in-chief at NewYork-Presbyterian Hospital/Columbia University Medical Center. Dr. Smith is also the Valentine Mott Professor of Surgery, the Johnson & Johnson Distinguished Professor of Surgery, and chair of the Department of

Surgery at Columbia University College of Physicians and Surgeons. "Additional studies are needed to examine the increased incidence of stroke following TAVI."

According to the study authors, research is already under way on the next generation of TAVI devices that researchers hope will address the vascular complications encountered in the trial.

Treatment of Aortic Stenosis

Aortic valves, which regulate blood flow from the heart into the aorta, can fall victim, typically with age and the onset of cardiovascular disease, to stenosis (failure to open) and insufficiency (which leads blood to flow in the wrong direction back into the heart). Aortic stenosis results in a poor quality of life and a high rate of death, approximately 50 percent, in the first two to three years after diagnosis without surgical intervention. Approximately 300,000 Americans suffer from severe aortic stenosis.

In clinical practice, at least 30 percent of patients with severe symptomatic aortic stenosis do not undergo surgery for replacement of the aortic valve because of advanced age, left ventricular dysfunction, or the presence of multiple coexisting conditions.

The replacement valve used in the PARTNER trial is made of pericardial tissue leaflets hand-sewn onto a metal frame and implanted via a catheter into the left ventricle. It is then positioned inside the patient's existing valve using a balloon to deploy the frame, which holds the valve replacement in place. The procedure is performed on a beating heart, without the need for cardiopulmonary bypass and its associated risks.

The transcatheter valve procedure takes about 90 minutes, compared

with four to six hours for open-heart surgery. In open-heart surgery, the surgeon cuts through the breastbone, stops the heart, removes the valve, and replaces it. Open-heart surgery can require a two- to three-month recovery period, compared with only a few days for the transcatheter approach.

The multicenter PARTNER trial, which has more than 1,000 patients, began in 2007 and will be completed in 2014. The results reported today reflect only the cohort of patients who are not considered candidates for surgery. The other arm of the trial, which compares transcatheter valves with surgically implanted valves, is ongoing. The executive committee of the trial includes two academic co-principal investigators, three interventional cardiologists, and three cardiac surgeons.

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