EVEREST II: 2-Year Data Show MitraClip Safety

Although percutaneous repair is safer than surgery, it does not reduce mitral regurgitation as completely.

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FROM THE ANNUAL MEETING OF THE AMERICAN COLLEGE OF CARDIOLOGY

NEW ORLEANS – The durability and safety of treating mitral regurgitation with a percutaneous device as compared with that of surgical repair or replacement persisted at 2 years, according to an updated analysis of the EVEREST II trial results presented at the meeting.

"Our fundamental finding is that outcomes are very stable between 1 and 2 years of follow-up," Dr. Ted Feldman, principal investigator, announced at a press briefing.

'Stability is the major message in the examination of 2-year outcomes' of percutaneous repair.

DR. FELDMAN

"The Kaplan-Meier curves for mortality and reoperation remain literally and completely flat through that time period, and clinical outcomes are durable," he said.

On the basis of data from the first year of the study, percutaneous repair with the MitraClip was safer than surgery, but surgery yielded more complete reduction in mitral regurgitation (N. Engl. J. Med. 2011;364:1395-1406).

The 2-year results, presented at the meeting, show that both approaches reduced mitral regurgitation, and meaningful clinical benefits persisted, said Dr. Feldman, who is director of the cardiac catheterization laboratory at the NorthShore University HealthSystem in Evanston, Ill.

Clinical outcome measures at 2 years' follow-up showed that mitral regurgitation grade and left ventricular volumes remained stable between 1 and 2 years in both groups. The intergroup comparison showed a more favorable reduction in mitral regurgitation and a greater reduction in left ventricular diastolic volume with surgery at 1 and 2 years, and no difference in systolic volume reduction.

Also, New York Heart Association (NYHA) functional class was stable between years 1 and 2.

"Interestingly, the intergroup comparison showed a more favorable NYHA class outcome at both years with the clip," Dr. Feldman reported.

The safety profile continued to be favorable, as well. "We saw no percutaneous device embolization; no device fracture, erosion, or migration; and no additional occurrence of single leaflet device attachment," he reported.

"Stability is the major message in the examination of 2-year outcomes," Dr. Feldman said.

"The randomized trial represents our very early experience with the device. Our procedural rate was 86% in the trial but in the postrandomization registry is in the 96% range. We are certainly going to get better at doing this."

At a panel convened to comment on the study results, Dr. Gregg W. Stone, professor of medicine at New York Presbyterian Hospital and Columbia University, New York, said that the follow-up analysis of EVEREST II is "very well done" and has, "for the most part, shown stability and fairly comparable mortality, though 22% of patients still need surgery if they take the route of the percutaneous option."

Dr. Steven F. Bolling, professor of surgery at the University of Michigan, Ann Arbor, maintained that while EVEREST II "suffers a little from awkward analyses," the results are promising, pending the right patient selection and longer follow-up.

Patients at high surgical risk and those with cardiomyopathy-associated MR would be the appropriate subset for further study in order to refine the optimal use of the device, said Dr. Bolling.

EVEREST II (Endovascular Valve Edge-to-Edge Repair Study) is a prospective, multicenter, randomized controlled phase II trial comparing the safety and efficacy of the MitraClip System with mitral valve surgery in the treatment of mitral regurgitation. The study enrolled 279 patients with 3+ or 4+ mitral regurgitation who were either symptomatic or were asymptomatic with a baseline left ejection fraction of 60%; 27% had functional mitral regurgitation and 73% had degenerative mitral regurgitation. Approximately half of the patients had NYHA functional class III or IV heart failure.

The patients were randomized 2:1 to receive the MitraClip device ($n = 184$) or mitral valve (MV) repair or replacement ($n = 95$). More than 90% of the study cohort was available for the 2-year analysis.

Outcomes through 1 year (primary safety and efficacy end points) were recently reported (N. Engl. J. Med. 2011; 364:1395-406), showing increased safety with the MitraClip device compared to surgery, but greater reduction in mitral regurgitation with surgery. At 30 days, major adverse events occurred in 15% of the percutaneous arm versus 48% of the surgical arm. Left ventricular function improved in both groups, as did NYHA functional class and quality of life at 1 year.

At the meeting, Dr. Feldman presented two analyses of the 2-year data. The first was an intention-to-treat analysis, in which any mitral valve surgery following percutaneous repair was considered an end-point event.

VITALS

Major Finding: At 2 years, the composite primary efficacy end point of freedom from death, MV surgery for valve dysfunction (for device patients) or reoperation (for surgery patients), and MR greater than 2+ at 12 months was met by 52% of the percutaneous group and by 66% of the surgery group.

Data Source: A prospective, multi-center, randomized controlled phase II trial of 279 patients with 3+ or 4+ mitral regurgitation.

Disclosures: Dr. Feldman reported consulting fees, honoraria, and research grants from Abbott Vascular. Dr. Stone reported consulting fees and honoraria from Abbott Vascular and numerous other pharmaceutical and device companies. Dr. Bolling reported no relevant disclosures.

The second analysis was a comparison of treatment strategies, in which MV surgery following unsuccessful in-hospital percutaneous repair was not considered an end point event. In the latter analysis, subsequent surgery within 90 days of the percutaneous procedure was still considered a "success" for the MitraClip.

The composite primary efficacy end point was freedom from death, MV surgery for valve dysfunction (for device patients) or reoperation (for surgery patients), and mitral regurgitation greater than 2+ at 12 months.

Patients at high surgical risk and those with cardiomyopathy-associated MR would be the appropriate subset for further study in order to refine the optimal use of the device.

In the intention-to-treat analysis, the primary composite end point was met at 2 years by 52% of the percutaneous group and by 66% of the surgery group; in the 1-year analysis, these figures were 55% and 73%, respectively.

More patients receiving the clip later had MV surgery (22%), compared with the few patients in the surgery arm who required reoperation (3.6%). There was no significant difference in mortality or recurrent mitral regurgitation.

In the second analysis, there was no statistical difference in the effectiveness end point between the two arms of the study.

"When subsequent surgery within 90 days on device patients is considered a success, we see similarly stable results at 1 and 2 years," he noted.

In this analysis, the primary end point was met at 2 years by 63% of the percutaneous group and by 66% of the surgery group.

When the subsequent need for MV surgery is removed as an end-point event, 6.2% of the percutaneous group and 3.6% of the surgery group had MV surgery or reoperation.

There was no difference in the Kaplan-Meier mortality plot for the intention-to-treat analysis at any time point, he stressed. At 1 year, 95% of the patients in each arm were alive; at 2 years, 91% of the surgery arm and 90% of the percutaneous arm were still alive.

The Kaplan-Meier plot for freedom from MV surgery/reoperation, however, favored the surgical arm: 96% versus 78% at 2 years.

The "need for surgery in patients in the clip group was almost entirely in the first several months after therapy, and after 6 months the curves overlapped at 1 and 2 years," he observed.

"Importantly, 78% of device patients are free from MV surgery at 2 years," noted Dr. Feldman.

When these early failures were excluded, there were no differences in the need for MV surgery or for reoperation.

At the press conference, Dr. Feldman explained that the two analyses "answer different questions."

"The intention-to-treat analysis gives the patient the odds of success with the clip at the end of the year," he explained. "It tells them that 78% will be free of the need for surgery at 2 years, and 97% will have NYHA functional class I or II."

The second analysis answers the question, "What if I am in the 20% needing surgery?" That analysis counts the combined strategy of the clip, with surgery as needed. ■