

COURAGE Patients Lacked High-Risk Lesions

BY MITCHEL L. ZOLER
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NEW ORLEANS — Many physicians may have received the wrong message from the major 2007 trial that compared optimal medical therapy with immediate coronary stenting in patients with stable coronary artery disease.

The message many physicians took away was that results from the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial showed that it is safe and good practice to first test optimal medical therapy in patients with stable coronary disease, and if that doesn't work, a patient can later be sent for percutaneous coronary intervention (PCI).

But that's not how the COURAGE trial worked, Dr. Paul S. Teirstein said at the annual scientific sessions of the American Heart Association. What's often forgotten is that all patients screened for the study first underwent diagnostic angiography, and the patients who were randomized to either immediate PCI or optimal medical therapy were primarily the minority of patients with coronary lesions that did not put them at immediate risk.

"All patients [screened for COURAGE] had angiography, and many were excluded. My strong suspicion is that patients at high risk for death and myocar-

dial infarction were excluded," based on their high-risk angiogram results, said Dr. Teirstein, chief of cardiology and director of interventional cardiology at the Scripps Clinic in La Jolla, Calif.

The COURAGE investigators assessed more than 35,000 patients, and identified slightly more than 3,000 who met the study criteria (N. Engl. J. Med. 2007; 356:1503-16). As of late 2008, the research team had not released any data on what the angiograms looked like in the more than 35,000 patients screened, Dr. Teirstein said. He suspects that a substantial number of patients were excluded because their cardiologists weren't comfortable with not immediately stenting a life-threatening stenosis.

He reported conducting a small survey at 7 of the 50 COURAGE sites, where he asked a lead cardiologist at each site whether patients were enrolled into the randomized study if they had high-grade, proximal, left anterior descending (LAD) artery lesions. At five of the seven sites the answer was no. Patients like these were not considered safe candidates to randomize to initial medical therapy. These investigators, as well as many other cardiologists, consider proximal lesions like these to be potential killers that require immediate PCI, Dr. Teirstein said.

Another indication of the risk posed by proximal LAD lesions lies in the results

from the COURAGE nuclear substudy, which used myocardial perfusion imaging in a small subset of the COURAGE patients, slightly more than 300 patients, to compare the ability of PCI and medical therapy to reduce myocardial ischemia. The results showed that PCI plus optimal medical therapy led to a 5% or greater reduction in ischemia in 33% of patients, compared with a similar reduction in just 20% of patients treated medically. The importance of this difference was underscored by a further finding: Among the 105 patients in this substudy with moderate to severe ischemia at baseline, relief of ischemia cut the subsequent rate of death or MI in half compared with patients who did not have ischemia relief (Circulation 2008;117:1283-91).

This dramatic difference in the rate of death or MI between PCI and medical treatment was not seen in the full COURAGE study. A major explanation is that in the overall study about a third of the patients had proximal LAD disease (although not necessarily high-grade lesions). But in the nuclear substudy, nearly half of the patients had such coronary lesions. By chance, the substudy included more patients with what may have been severe and dangerous stenoses, and up-front treatment with PCI led to fewer deaths and MIs, Dr. Teirstein noted.

After the COURAGE results were re-

ported in April 2007, some defenders of the study stressed that COURAGE enrolled "high-risk" patients, based on factors such as a 34% prevalence of diabetes, a 5% prevalence of heart failure, and a 70% prevalence of multivessel disease. But Dr. Teirstein took issue with the idea that these parameters are important determinants of high risk. A high-grade, proximal LAD lesion is a much clearer indicator of high risk, and the COURAGE investigators often did not enroll these patients, he said.

Dr. Teirstein acknowledged that COURAGE was an important study and that it changed his practice. "I learned that you don't need to stent every little blockage in every little vessel," he said. "I leave the small distal side branches alone unless the patient has recalcitrant angina."

But, he stressed, the COURAGE results are not proof that PCI of major, proximal lesions can be safely deferred while medical therapy is tried. Patients with lesions like these were underrepresented in the study because many physicians agree that in these patients postponing PCI is too dangerous.

Dr. Teirstein reported receiving grant support from and serving as a consultant to Cordis Corp., Boston Scientific Corp., Abbott Laboratories, and Medtronic Inc. He also receives royalty income from Boston Scientific. ■

Survey: Patients Vastly Overestimate Benefits of Elective PCI

BY BRUCE JANCIN
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NEW ORLEANS — Most individuals undergoing elective percutaneous coronary intervention have highly unrealistic expectations about the procedure's benefits, according to a patient survey.

Two-thirds of survey respondents believed their elective percutaneous coronary intervention (PCI) would extend their life span. An even larger percentage thought it would reduce their chances of having an MI. Neither belief is valid, of course, Dr. John Lee noted at the annual scientific sessions of the American Heart Association.



Moreover, only 31% of those surveyed thought their procedure was done to reduce their anginal symptoms, which is the one evidence-based reason for performing elective PCI, added Dr. Lee of the Mid-America Heart Institute, Kansas City, Mo. "The implication of this study is that better patient communication is needed prior to elective PCI to convey the evidence-based risks and benefits and elicit a more truly informed consent," he said.

Dr. Lee sent his brief single-page questionnaire survey to 498 consecutive patients who underwent elective PCI at two Kansas City hospitals between January 2006 and October 2007; 350 patients responded.

Surprisingly, one-third of the patients were under the mistaken impression that their PCI had been done on an emergency basis (see box). Sixty-eight percent indicated that no treatment option other than PCI was discussed with them. Eighteen percent said they were offered medical management, and 13% recalled coronary artery bypass graft surgery being discussed.

Dr. Lee observed that his survey results were quite similar to those of an 8-year-old survey led by Dr. Eric S. Holmboe, a general internist who today serves as senior vice president for quality research and academic affairs at the American Board of Internal Medicine in Philadelphia. Three-quarters of respondents to Dr. Holmboe's survey believed their elective PCI would prevent a future MI, and 71% thought it would prolong their life (J. Gen. Intern. Med. Sept. 2000; 15:632-7).

Surprisingly, 68% of patients said that no treatment option other than PCI was discussed with them.

DR. LEE

Since that survey, however, considerable additional evidence has accrued as to what elective PCI can and cannot accomplish. A meta-analysis of 11 randomized trials comparing it with conservative management in patients with chronic stable coronary artery disease showed no advantage for elective PCI in terms of death, MI, or need for repeat revascularization (Circulation 2005;111:2906-12).

This meta-analysis was followed by the widely publicized 2,287-patient randomized Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial, which showed no difference between elective PCI and medical management in rates of death, MI, stroke, or hospitalization for acute coronary syndrome (N. Engl. J. Med. 2007; 356:1503-16).

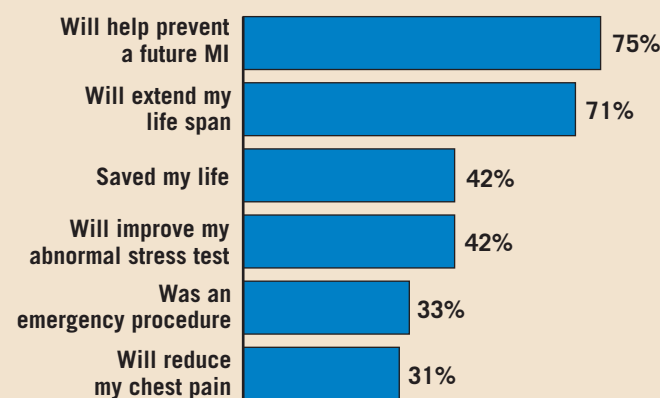
COURAGE was published while Dr. Lee was conducting his survey. He found no significant difference between patient responses obtained pre- versus post-COURAGE.

"It's not surprising that we'd see no differences in patient perceptions of benefit, because most patients don't read the medical literature. But the lack of a difference in the treatments being offered post-COURAGE was a little more surprising," he commented.

One audience member asked whether the disturbing survey results reflect wishful thinking on the patients' part or if physicians are misinforming them.

"Patients really go down a line of physicians before they end up in the cath lab," Dr. Lee replied. "They start off with their primary care doctor, who suspects [coronary artery disease] and sends them off to get a stress test. Then they may go to the interventionalist's office for a consultation, then to the cath lab. There are many steps along the line where they can get their information. It's probably the responsibility of every single one of those physicians to educate the patient." ■

Patients' Perceptions Regarding Elective PCI



Note: Based on a survey of 350 patients.
Source: Dr. Lee