Data Back Medical Therapy for Stable Angina

BY JEFF EVANS
Senior Writer

Optimal medical treatment—with or without percutaneous coronary intervention—improved quality of life significantly in most patients with stable angina, according to an analysis of the quality of life of patients in the COURAGE trial. But PCI may be worthwhile in patients with treatment-refractory symptoms who are initially treated with medical therapy alone.

The combination of PCI plus optimal medical therapy improved patients' quality of life slightly more than did optimal medical therapy alone. Patients with the most frequent symptoms accrued most of the benefits seen with combination treatment, but these were significant for only 6-24 months.

This quality of life subanalysis of the COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) trial "demonstrates that both treatment strategies can have a profoundly positive effect on patients' health status and suggests complementary roles—optimal medical therapy as first-line therapy, with PCI reserved for patients who do not have a response or who have severe baseline symptoms," Dr. Eric D. Peterson and Dr. John S. Rumsfeld wrote in an editorial accompanying the study (N. Engl. J. Med. 2008;359:751-3).

In the trial, Dr. William S. Weintraub of the Christiana Care Health System, Newark, Del., and his associates in the COURAGE Trial Research Group randomized 2,287 patients to either treatment arm. The patients were required to have stenosis of more than 70% in at least one major epicardial coronary artery, with objective evidence of myocardial ischemia or stenosis of at least 80% in at least one coronary artery and classic angina without provocative testing.

The main findings of COURAGE, presented at the annual meeting of the American College of Cardiology in March 2007 and published simultaneously, showed no difference between PCI plus optimal medical therapy versus optimal medical therapy alone on the primary end point of death or myocardial infarction during the study's median follow-up period of 4.6 years (N. Engl. J. Med. 2007;356:1503-16).

In the present analysis, mean scores on all domains of the Seattle Angina Questionnaire significantly improved in both groups after 1-3 months, and did not change substantially thereafter. The questionnaire measures physical limitations resulting from angina; any recent change in the severity of angina; satisfaction with treatment; and quality of life. After 6-24 months of follow-up, scores on some domains of the 19-item questionnaire had im-

proved significantly more among the patients who underwent PCI. This difference was lost at the final 36-month assessment (N. Engl. J. Med. 2008;359:677-87).

Patients who were treated with medical therapy alone (including patients who did not cross over to undergo PCI) also had "significant and rapid improvement" of scores on the Seattle Angina Questionnaire, which "shows that PCI is not always essential for the relief of symptoms in patients with stable angina," wrote Dr. Peterson of the Duke Clinical Research Institute, Durham, N.C., and Dr. Rumsfeld of the Denver Veterans Affairs Medical Center.

> **Percutaneous coronary intervention is not always essential for the relief of stable angina symptoms.**
>
> DR. PETERSON

For the first 6 months of follow-up, a greater percentage of PCI-treated patients had "clinically significant" improvement in the domains of physical limitation, angina frequency, and quality of life than did patients who received medical treatment alone. This difference did not persist beyond 6 months.

Baseline scores on the questionnaire were worse for 68 patients treated with medical therapy alone who crossed over to the other group to undergo PCI within 3 months after randomization, compared with the 895 patients in the trial arm who did not cross over within the first 3 months. The scores of these 68 patients rapidly improved following revascularization, "confirming that some patients have an especially marked benefit from PCI," Dr. Weintraub and his coinvestigators wrote.

Analyses of the patients who had complete data through 36 months showed that most of the improvement in angina frequency occurred during the first 3 months. PCI-treated patients who had the most frequent angina symptoms (multiple episodes of angina per week) had the largest clinical improvement in that period. No improvement occurred among patients who rarely had angina.

During the first 24 months of follow-up, a significantly greater proportion of patients who received PCI and optimal medical therapy were totally free from angina symptoms, compared with those who received optimal medical therapy alone. (See box.) But this result was driven by patients with the most frequent angina symptoms.

In comparison with optimal medical therapy alone, Dr. Weintraub and his colleagues calculated that 11-17 patients would have to be treated with PCI plus optimal medical therapy in order for 1 patient to obtain a clinically significant improvement in angina frequency, physical function, or quality of life.
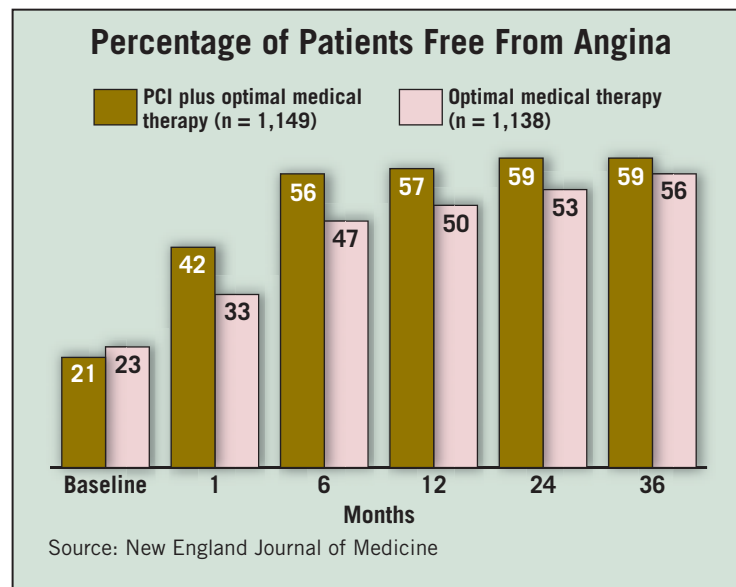
But this calculation does not take into account the harms associated with PCI, according to Dr. Peterson and Dr. Rumsfeld. The current in-hospital mortality associated with elective PCI is about 0.2%, based on data from the National Cardiovascular Data Registry. The periprocedural rate of myocardial infarction in the COURAGE trial was 2.8%. Based on the calculations of the COURAGE trial investigators and these figures, "for every 1,000 patients treated with a PCI-first strategy, approximately 2 would die, 28 would have a periprocedural myocardial infarction, 60 to 90 would have an incremental, transient gain in health status, and 800 or more would see neither harm nor benefit," Dr. Peterson and Dr. Rumsfeld wrote. This estimation makes it "difficult to assert that a PCI-first strategy should clearly be adopted routinely in patients with stable angina."

Measurement of the patients' general health status with the RAND 36-Item Health Survey largely corroborated the results found with the Seattle Angina Questionnaire.

Nearly 25% of the follow-up assessments were not available for analysis, but the investigators performed sensitivity analyses, which did not detect any potential biases.

Dr. Peterson reported receiving consulting fees from Bayer and Pfizer Inc., and grant support from Sanofi-Aventis, Bristol-Myers Squibb Co., Schering-Plough Corp., and Merck & Co. Dr. Rumsfeld disclosed that he is a scientific advisory board member at UnitedHealthcare and is chief science officer of the National Cardiovascular Data Registry.

Dr. Weintraub and some of his coinvestigators reported financial ties to a variety of pharmaceutical companies, which provided funding for the trial. The U.S. Department of Veterans Affairs Cooperative Studies Program and the Canadian Institutes of Health Research also funded the study. ∎

Percentage of Patients Free From Angina

PCI plus optimal medical therapy (n = 1,149) | Optimal medical therapy (n = 1,138)

Months	PCI plus optimal medical therapy	Optimal medical therapy
Baseline	21	23
1	42	33
6	56	47
12	57	50
24	59	53
36	59	56

Source: New England Journal of Medicine

ELSEVIER GLOBAL MEDICAL NEWS

Obesity Linked to Higher Morbidity After Coronary Bypass

BY MITCHEL L. ZOLER
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TORONTO — Obesity was linked to an increased risk for postsurgical complications in a study of more than 11,000 patients who underwent coronary bypass surgery.

But in this series, obesity did not result in a significantly increased risk for postsurgical mortality, Dr. Mahboob Alam said at the 14th World Congress on Heart Disease.

Obesity also was linked to a significant 38% reduced risk for repeat operations for postoperative bleeding, an unexpected finding that requires further study to understand, said Dr. Alam, a cardiologist at Baylor College of Medicine, Houston.

The retrospective study included 11,417 consecutive patients who underwent coronary artery bypass surgery at St. Luke's Episcopal Hospital in Houston during 1996-2006. The series included 2,257 patients (20%) who were obese, which is defined as having a body mass index of 30 kg/m² or greater.

The nonobese patients were older, with an average age of 64 years, compared with an average age of 61 in the obese patients. But the obese patients had more comorbidities, with higher rates of unstable angina, coronary artery disease, hypertension, heart failure, and diabetes.

The primary end point for the analysis was mortality during the first 30 days fol-

> **Obesity was linked with increases in renal insufficiency, myocardial infarction, and respiratory failure.**
>
> DR. ALAM

lowing bypass surgery, and although the obese patients had an 8% increased risk for death in a multivariate analysis, this difference was not statistically significant relative to the nonobese patients, Dr. Alam said at the congress sponsored by the International Academy of Cardiology.

The multivariate analysis showed that obesity was linked with significant increases in the rate of several new-onset morbidities, compared with nonobese patients following coronary artery bypass, including a 43% increased rate of renal insufficiency, a 71% increased rate of myocardial infarction, a 46% rise in respiratory failure, a 2.9-fold increased rate of sternal wound infections, and a 2.1-fold boost in the rate of leg wound infections.

Obesity was linked with a significantly increased duration of postoperative hospitalization. Nonobese patients spent an average of 10.5 days hospitalized, compared with an average of 11.85 days of postoperative hospitalization for the obese patients. ∎