PCI or Drug Therapy: Consider Ischemic Burden

BY DIANA MAHONEY
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BOSTON — In the ongoing debate over whether patients with chronic, stable angina are better served by revascularization with percutaneous coronary intervention in addition to drug treatment or optimal medical therapy alone, the key variable appears to be ischemic burden, Dr. Daniel S. Berman reported at the annual meeting of the American Society of Nuclear Cardiology.

Last year, investigators in the Clinical Outcomes Using Revascularization and Aggressive Drug Evaluation (COURAGE) trial reported that adding percutaneous coronary intervention (PCI) to optimal medical therapy in patients with stable coronary artery disease did not improve clinical end points, compared with optimal medical therapy alone (N. Engl. J. Med. 2007;356:1503-16).

More recently, however, a substudy of the COURAGE trial comprising 314 patients equally distributed between groups treated with PCI plus optical medical therapy and optimal medical therapy alone showed that the PCI strategy produced a greater ischemia reduction than the optimal medical therapy–only (OMT-only) intervention—particularly among patients with moderate to severe ischemia at baseline, said Dr. Berman, chief of cardiac imaging and nuclear cardiology at Cedars-Sinai Heart Center in Los Angeles. "Importantly, patients in both groups who experienced ischemia reduction had a significantly lower risk for death or myocardial infarction than patients without ischemia reduction, and the magnitude of residual ischemia was proportional to the overall risk of subsequent cardiac event," he said.

The main COURAGE trial included 2,287 patients, with a history of angina or documented myocardial ischemia and at least one significant coronary lesion, who were stable on medical therapy. Participants were randomized to continue their medication alone or with PCI, and the study's combined end points were death or nonfatal myocardial infarction. The composite rates of death or nonfatal MI over 4.6 years of follow-up were statistically similar in both groups, at 19.0% and 18.5%, respectively, for PCI and OMT-only.

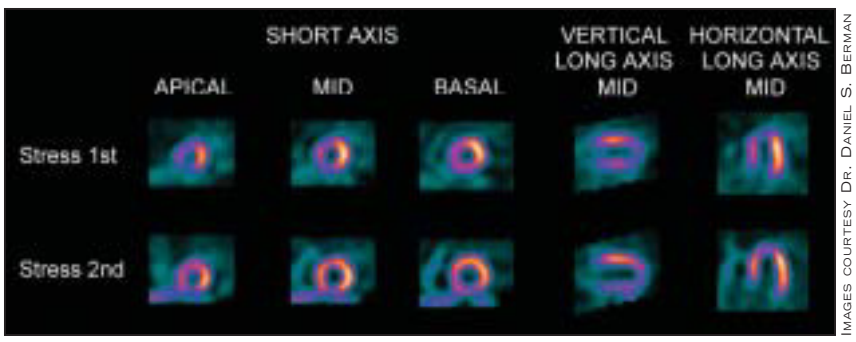
In the nuclear imaging substudy, the 314 patients were equally distributed between the PCI and OMT groups and they were well matched with respect to demographics and risk factors, said Dr. Berman. All of the patients were on medication for a mean 374 days from baseline and all underwent serial myocardial perfusion single-photon emission computed tomography (MPI SPECT) studies 6-18 months following the baseline examination to assess the extent and severity of the perfusion defect in the global myocardium, he said.

COURAGE patients with moderate to severe ischemia showed greater improvement after PCI than after medical therapy.

DR. BERMAN

With myocardial ischemia defined as the total perfusion deficit at stress minus the perfusion deficit at rest, 33% of patients in the PCI group and 20% in the OMT-only group showed a 5% or greater reduction in ischemia. Among patients with moderate to severe pretreatment ischemia, defined as a perfusion defect involving 10% or more of myocardium, "78% of the PCI patients demonstrated 5% improvement or greater, compared to 52% of the [OMT-only] patients," Dr. Berman reported.

In considering these changes in terms of their relationship to subsequent outcomes, "we looked at the myocardial infarction rates in patients with and without ischemia reduction and determined that patients in both groups with 5% improvement in ischemia had approximately 50% lower cardiac event rate," Dr. Berman said. A similarly reduced cardiac event rate was observed in the 105 patients from both groups with moderate to severe ischemia and a greater than 5% reduction post treatment, he said.



IMAGES COURTESY DR. DANIEL S. BERMAN

MPI-SPECT image shows the first and second stress myocardial perfusion in a patient who received optimal medical therapy only. Total perfusion deficit was reduced from 16% to 6%.

Although the substudy was not sufficiently powered to generalize that reducing ischemia will prevent later cardiac events, "we did see a striking relationship between amount of residual ischemia and the subsequent death or myocardial infarction rate," Dr. Berman said. This observation is "definitely a hypothesis generator," warranting a controlled trial comparing the PCI-based strategy with OMT alone in patients with chronic stable angina who would be randomized based on the presence of moderate to severe ischemia, he said. "We should be studying patients with 10% or more ischemia to determine if there is a subset of patients who would have improved angina and quality-of-life outcomes with revascularization." The findings would be especially important to those patients with documented large amounts of jeopardized myocardia in whom medical therapy does not provide adequate relief, he concluded.

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Anemia, Renal Impairment Increase Post-PCI Mortality

BY MITCHEL L. ZOLER
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TORONTO — Both anemia and renal impairment raise the risk of death in patients undergoing percutaneous coronary interventions.

In a review of 572 patients, those whose serum creatinine level spiked by 25% or more following percutaneous coronary intervention (PCI) for a myocardial infarction had about a threefold increased risk of dying during the first 15 months after their procedure, compared with patients who didn't have this sign of renal dysfunction, Dr. Alexander Goldberg said at the 14th World Congress on Heart Disease. Patients faced an increased risk for death post-PCI regardless of whether their rise in serum creatinine was transient or prolonged, noted Dr. Goldberg, director of interventional cardiology at Sieff Government Hospital in Safed, Israel.

Patients who were anemic and had impaired left ventricular function were about four times more likely to die following PCI than were patients who were not anemic (but also had a low left ventricular ejection fraction) in a review of 120 patients, Dr. Amit Varma reported in a separate talk at the congress. Patients with iron-deficiency anemia were especially at risk for cardiac mortality, and patients with malignancy-associated anemia had the highest risk for noncardiac death, said Dr. Varma, a cardiologist at Virginia Commonwealth University in Richmond.

The impact of a rise in serum creatinine after PCI was examined in consecutive patients who underwent primary PCI for a myocardial infarction at Sieff Government Hospital. Stable renal function, defined as a serum creatinine level that did not rise by more than 25% after the procedure, was seen in 76% of the patients. Persistently impaired renal function occurred in 13%, which meant their serum creatinine rose by more than 25% after PCI and remained elevated over time, while 11% had transient worsening that resolved, with their serum creatinine briefly rising by more than 25% but falling before they left the hospital.

During a median follow-up of 15 months, the mortality rate was 16% in patients with transiently impaired renal function, 12% in those with persistent renal impairment, and 4% in those with no renal impairment. The increased mortality rates in the two groups with substantial rises in creatinine were significantly higher than the rate in the patients without this rise. In a multivariate analysis that controlled for differences in age, gender, baseline creatinine levels, hypertension, diabetes, Killip class on hospital admission, and other variables, patients with transient worsening renal function had a significant, 3-fold increased risk of dying, and those with persistently worse renal function had a significant, 2.6-fold increased risk of death, compared with the patients whose creatinine level did not spike, Dr. Goldberg said at the congress sponsored by the International Academy of Cardiology.

It was surprising that transient renal impairment led to a prognosis as poor as persistent impairment, he said. It is also unclear how renal impairment can be avoided in these patients. "Many factors play a role," he continued. Patients with myocardial infarctions who are treated with thrombolytic therapy instead of primary PCI also can develop worsening renal function, and patients who get no reperfusion therapy are even more vulnerable to renal impairment, he said.

The impact of anemia in patients undergoing PCI was examined in 120 patients with a left ventricular ejection fraction of less than 45% who were treated with PCI during April 2003–December 2005 at Virginia Commonwealth University. All patients received drug-eluting stents. Twenty-nine patients (24%) were anemic, defined as a hemoglobin level of less than 12 g/dL in men and postmenopausal women. The anemic patients were further subdivided by their type of deficiency: 13 patients (11%) had iron-deficiency anemia, 9 (8%) had anemia of chronic disease, and 7 (6%) had malignancy-associated anemia (total adds up to 25% because of rounding).

During a median follow-up of 30 months, the mortality rate was 8% in the nonanemic patients and 34% in the anemic patients, Dr. Varma reported, and anemia remained a significant predictor of mortality even after adjusting for baseline differences in the patient groups. In patients with the worst anemia, a hemoglobin level of 10 g/dL or less, the mortality rate was 45%.

The incidence of cardiac mortality was greatest, about 60%, in patients with iron deficiency anemia. None of the patients had bleeding complications following PCI; the iron deficiency anemia was not the result of bleeding. The incidence of noncardiac death was greatest, also about 60%, in patients with malignancy-associated anemia. In contrast, the patients with anemia of chronic disease did "remarkably well," with none of these patients dying during follow-up, Dr. Varma said.

The findings suggest that "the underlying cause of anemia rather than the anemia itself" may play an important role in post-PCI mortality in patients with impaired left ventricular function, Dr. Varma said. ■