# Are ACE Inhibitors Needed in All CAD Patients?

*'The PEACE trial should make us reconsider ... treating large numbers of patients for small benefits.'*

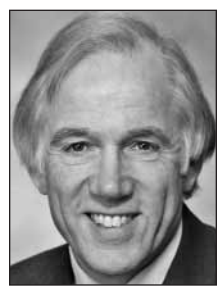
BY BRUCE JANCIN
*Denver Bureau*

NEW ORLEANS — No sooner had the ink dried on new American College of Physicians practice guidelines calling for ACE inhibitor therapy in patients with coronary artery disease than the document was rendered outdated by a new megatrial.

The trial—an 8,290-patient trial sponsored by the National Heart, Lung, and Blood Institute—was the Prevention of Events With Angiotensin-Converting Enzyme Inhibition (PEACE) trial, the results of which were presented by Marc A. Pfeffer, M.D., at the annual scientific sessions of the American Heart Association.

PEACE showed that in patients with stable CAD and preserved left ventricular function who are receiving contemporary management—usually including coronary revascularization, lipid-lowering therapy, aspirin, and good blood pressure control—the addition of an ACE inhibitor doesn't further reduce clinical atherosclerotic events.

A median of 4.8 years after 8,290 PEACE participants at 187 sites were randomized in double-blind fashion to a target dose of 4 mg/day trandolapril or placebo, the incidence of the primary end point—a composite of cardiovascular death, acute MI, or coronary revascularization—was virtually identical in the two groups: 21.9% in the ACE inhibitor arm, and 22.5% with placebo. No identifiable patient subgroup benefited from trandolapril, reported Dr. Pfeffer, PEACE cochair and interim chairman of the department of medicine at Brigham and Women's Hospital, Boston.



"I guess we're getting to the point where some of our therapies are redundant," observed Dr. Pfeffer, who is also professor of medicine at Harvard Medical School, Boston. "This is going to liberalize physicians' choices. When people go to the pharmacy and have a choice of either filling this prescription or filling that, this study is certainly going to help."

The impact of PEACE on clinical practice is likely to be substantial. "The PEACE-type population represents the majority of patients with CAD," Dr. Pfeffer observed.

Initial reaction to PEACE was one of open surprise. After all, two earlier landmark trials—the Heart Outcomes Prevention Evaluation (HOPE) and European Trial on Reduction of Cardiac Events With Perindopril in Stable Coronary Artery Disease (EUROPA)—had convincingly shown that ACE inhibitor therapy resulted in roughly a 20% reduction in atherosclerotic events in patients with coronary or other vascular disease but no history of heart failure.

**'We have three very-well-conducted clinical trials with conflicting results.'**

**DR. GIBBONS**

No one was more surprised by PEACE than Raymond J. Gibbons, M.D., chairman of the AHA Scientific Sessions Program Committee, and coauthor of the recent ACP guidelines (Ann. Intern. Med. 2004;141:562-7) that, on the strength of HOPE and EUROPA, recommended routine ACE inhibition in certain patients with asymptomatic CAD.

"We've got a real problem. We have three very-well-conducted clinical trials with conflicting results," Dr. Gibbons, the Arthur and Gladys D. Gray Professor of Medicine at the Mayo Medical School, Rochester, Minn., told this newspaper.

Dr. Pfeffer admitted that he, PEACE cochair Eugene Braunwald, M.D., and the other investigators were initially taken aback by the unexpected outcome. Upon further analysis, however, they found an explanation: The PEACE population was at lower global cardiovascular risk than those in HOPE and EUROPA, hence the opportunity for therapeutic benefit was also smaller.

PEACE patients had better blood pressure control at baseline (mean 133/78 mm Hg) and higher rates of lipid-lowering therapy and aspirin use than in the other two trials. Their 72% rate of coronary revascularization prior to enrollment was much higher.

Moreover, the combined atherosclerotic event rate in the placebo arm of PEACE was actually lower than in the ACE inhibitor–treated arms of both HOPE and EUROPA. Annualized all-cause mortality in PEACE was a mere 1.6% per year, which is equivalent to the age- and gender-matched U.S. general population, despite the fact that all PEACE patients had CAD and more than half had a prior MI.

Discussant John G.F. Cleland, M.D., predicted "PEACE may mark the beginning of the end of the megatrial."

"The clinical relevance of any intervention that requires a large long-term study to show a statistically significant effect must be questioned. ... The PEACE trial should make us reconsider the whole medical philosophy of treating large numbers of patients for small benefits. Accurate targeting of highly effective therapy should be the goal of modern medicine," added Dr. Cleland, professor of medicine at the University of Hull (England). ■

# PET/CT May Prove to Be an Alternative to Angiography

BY KERRI WACHTER
*Senior Writer*

PHILADELPHIA — The race to find clinical cardiology applications for combined PET/CT technology is officially on, now that the results from the first round of studies have been presented at the annual meeting of the Society of Nuclear Medicine.

Combined PET/CT scanners have stimulated interest in imaging circles by offering clinicians the ability to combine noninvasive assessments of anatomy and function in one imaging session.

**'We found excellent agreement [between the] two techniques for determining whether revascularization was needed or not.'**

Based on the studies presented at the meeting—which showed the technology to be more sensitive at detecting stenotic/ischemic coronary artery disease (CAD) than coronary angiography and proved it useful in usually hard-to-image obese patients—combined PET/CT seems to be living up to all of the excitement the prospect of its use had generated.

In a study of 25 patients with known CAD, researchers at University Hospital Zurich (Switzerland), evaluated the feasibility and image quality of integrated PET/CT to assess coronary anatomy and perfusion.

Patients underwent contrast-enhanced CT angiography with retrospective ECG gating and rest, and adenosine stress myocardial perfusion PET scans using N-13 ammonia. The patients were also assessed by coronary angiography. Six patients already had undergone coronary artery bypass graft procedures. Of note, 22 of the 25 were male.

For each patient, the researchers evaluated a total of 100 segments from four vessels—left main coronary artery, left anterior descending coronary artery, left circumflex artery, and right coronary artery. They also analyzed the 12 bypass grafts. The CT scans take only a few minutes, and the PET scans take about an hour.

With conventional angiography, the researchers found 65 normal vessel segments, compared with 51 normal vessels identified by CT. "A few of the lesions considered as not significant by angiography, revealed ischemia on the PET scan," said P.T. Siegrist, M.D., of the hospital. Overall PET/CT imaging had a sensitivity of 90% and a specificity of 98%.

The researchers also compared the decision whether to revascularize based on the PET/CT findings to the clinical decision for revascularization obtained by using PET alone to assess myocardial perfusion and coronary angiography to assess anatomy. Only the combination of a stenotic lesion and ischemia prompted a decision to revascularize.

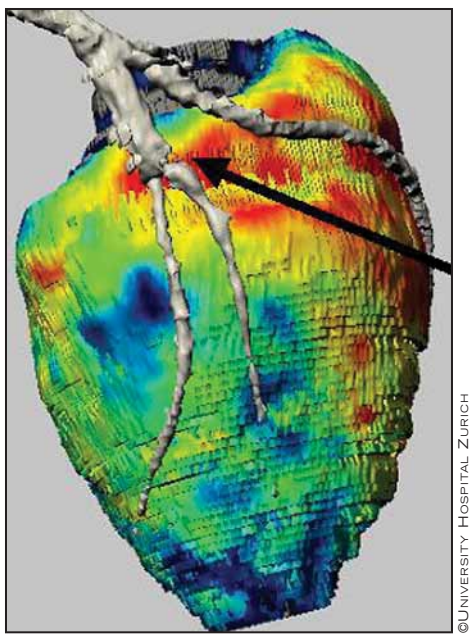
With conventional angiography, 11 vessel segments qualified for revascularization. Likewise, PET/CT identified 11 vessel segments that qualified for revascularization. "We found excellent agreement [between] two techniques for determining whether revascularization was needed or not," Dr. Siegrist said.

The study was funded in part by GE Medical Systems and Amersham Health.

In a similar study, researchers at Brigham and Women's Hospital in Boston combined rubidium-82 PET scans to assess myocardial perfusion and CT to assess anatomy in patients known or suspected of having CAD.

Marcelo F. Di Carli, M.D., and his colleagues from Brigham and Women's Hospital, Boston, performed gated rest/stress $^{82}$Rb PET/CT myocardial perfusion imaging on 94 consecutive patients (41 women) with known (21 patients) or suspected (73 patients) CAD. Stress imaging was performed with dipyridamole, adenosine, or dobutamine infusions. The studies were completed in about 45 minutes.

Most patients were overweight or obese, with an average body mass index of 30. In spite of this, the image quality was very good or excellent for all of the patients. In all, 38 patients were found to have abnormal myocardial perfusion, and 2 patients had probable myocardial perfusion abnormalities. Myocardial perfusion was normal in 53 patients and probably normal in 1 patient, Dr. Di Carli said.



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**This PET/CT depiction of an in-stent thrombosis (arrow) shows the perfusion deficits in the distal left anterior descending artery in blue.**

PET/CT assessment of myocardial perfusion using $^{82}$Rb appears to provide a good alternative to SPECT assessment of perfusion, especially for overweight and obese patients. ■