CPR by Bystanders Infrequent, Often Inadequate

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ORLANDO — A strikingly elevated risk for stroke and total mortality in patients who received the β-blocker metoprolol CR starting a few hours before noncardiac surgery in a trial with more than 8,000 patients triggered a quick change in practice in hospitals across the United States.

“β-Blockers should not be routinely started perioperatively to reduce cardiac events,” Dr. Judith S. Hochman commented at the annual scientific sessions of the American Heart Association. The findings presented at the meeting were a “landmark that will change practice,” added Dr. Hochman, professor of cardiology at New York University School of Medicine.

“Many hospitals have been driven by guidelines to start β-blocker treatment on the morning of surgery. Hospitals will quickly review and re-think these protocols,” commented Dr. Lee A. Flesher, professor and chairman of anesthesiology and critical care at the University of Pennsylvania.

But experts stressed that the new findings do not apply to patients on an established β-blocker regimen at the time they undergo elective, noncardiac surgery, and that it remains unclear whether it is beneficial to titrate patients at risk of cardiovascular complications onto a β-blocker regimen starting a few weeks before surgery.

The Perioperative Ischemia Evaluation (POISE) trial was designed to be the first large-scale test of a prophylactic approach that’s been widely used for several years on at-risk patients undergoing noncardiac surgery. The study enrolled patients at 193 centers in 23 countries during October 2002 to July 2007. Eligible patients were 45 years or older, were scheduled for noncardiac surgery, and had intermediate to high risk for atherosclerotic disease. The mean age of the enrolled patients was 69, and 82% had diabetes or hypertension.

In the β-blocker group, patients were randomized to receive either 100 mg oral metoprolol CR or placebo 2-4 hours before surgery. Patients in the β-blocker group received a second 100 mg oral dose of metoprolol CR within 6 hours after surgery, or 30 days after surgery, but was reduced if the heart rate or systolic pressure dropped too low.

The primary end point was the rate of cardiovascular death, nonfatal myocardial infarction, and nonfatal cardiac arrest occurring the 30 days after surgery. This rate was significantly lower, by 0.9%, in the metoprolol group, Dr. P.J. Devereaux reported.

The difference was largely due to a reduced rate of nonfatal myocardial infarction—5.1% in the placebo group and 3.6% with metoprolol, a significant difference.

Metoprolol treatment was also linked with significantly higher rates of serious adverse effects: a statistically significant twofold boost in the risk of strokes (a 1.0% rate, vs. a 0.5% rate with placebo), most of which were incapacitating, and significant increases with metoprolol in clinically significant episodes of hypotension and bradycardia. Metoprolol treatment was also linked with a significantly higher rate of all-cause death, 3.1% vs. 2.3% with placebo.

“Knowing these data, I certainly would not recommend this treatment for my mother,” said Dr. Devereaux, a cardiologist at McMaster University in Hamilton, Ont., and lead investigator of the study. The study was primarily funded by national agencies in Canada and other countries, but it also received support from Astrazeneca, which markets metoprolol CR (Toprol XL). Dr. Devereaux had no disclosures for the study.

“The analysis also failed to identify any patient subgroup that had less risk and a clearer overall benefit from β-blocker treatment,” commented Dr. Flesher.

The results will force a substantial change in practice. Just a few weeks before surgery, Dr. Devereaux gave his report, a joint AHA/American College of Cardiology task force issued updated guidelines for the perioperative care of patients undergoing noncardiac surgery. The guidelines say “β-Blockers are probably recommended for patients in whom preoperative assessment identifies CHD or high cardiac risk, as defined by the presence of at least one clinical risk factor, who are undergoing intermediate-risk or vascular surgery” (Circulation 2007;116:e418-99). The recommendations for β-blockers were generally consistent with the POISE guidelines that made β-blockers an option, many hospitals have been getting graded on the quality of their care based on part on whether they had a protocol in place to start a β-blocker on virtually all higher-risk, noncardiac surgery patients, said Dr. Flesher, who chairs the ACC/AHA task force. That practice will now have to quickly change, he said in an interview.

“There is a pressing need to find safe treatments to prevent cardiovascular complications of noncardiac surgery,” said Dr. Devereaux in an interview. Currently there is a “large and growing epidemic of perioperative cardiovascular disease,” he said. “Patients die after successful surgery due to their cardiovascular complications.” Other drugs that might be beneficial to start just before surgery, or possibly days before, include statins and aspirin, he said.

Results from another major trial are expected soon that will shed added light on this issue. The Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography (DECREASE)-IV trial has enrolled about 6,000 patients scheduled for noncardiac surgery, and randomized them to treatment with the β-blocker bisoprolol or placebo, and also randomized patients to treatment with statins or statin plus placebo. Unlike POISE, patients in DECREASE-IV could be started on bisoprolol and fluvastatin as much as 30 days before surgery.

A longer ligation time and a β-blocker regimen that’s stable for several days before surgery might improve outcomes, might the use of bisoprolol instead of metoprolol, Dr. Don Poldermans, professor of anesthesiology at Erasmus University, Rotterdam, the Netherlands, and senior investigator for DECREASE-IV, said in an interview.