New Evidence Fuels Rewrite

Guidelines *from page 1*

agement options; longer use of the antiplatelet drug clopidogrel, for up to 1 year in all patients; and a broadening of the anticoagulant drug options to include two newer agents, fondaparinux and bivalirudin, in addition to the older drugs low-molecular-weight heparin and unfractionated heparin.

"It's a totally rewritten guideline, with 5 years worth of new evidence," Dr. Wenger said in an interview.

Some of that evidence spoke to the efficacy of a conservative, noninvasive management strategy and a recognition that one approach does not fit all when treating patients with unstable angina or non-STEMI who do not have hemodynamic or electrical instability or persistent angina.

A key to making the conservative approach work is an early start to a broad range of medications during the first 24 hours of hospitalization, including aspirin, clopidogrel (Plavix), an anticoagulant, an oral β-blocker, and an oral ACE inhibitor. Other important steps include making sure that the patient is truly not at high risk by checking ventricular function with echocardiography or a nuclear test, and possibly by measuring serum levels of B-type natriuretic peptide, Dr. Wenger said.

"A lot of things, applied early, contribute to the safety of conservative management, which is what makes it an acceptable option," said Dr. Wenger. "It's a sizable medical cocktail in the first 24 hours."

The guidelines noted that "use of aggressive anticoagulant and antiplatelet agents has reduced the incidence of adverse outcomes in patients managed conservatively."

As backing for the conservative strategy, the guidelines cited results reported from the Invasive versus Conservative Treatment in Unstable Coronary Syndrome (ICTUS) trial, which showed that after 1 and 3 years of follow-up patients randomized to a selective invasive strategy had similar outcomes compared with patients managed with a routine invasive strategy (Lancet, 2007;369:827-35).

But the guidelines also noted that despite this finding in favor of a conservative strategy, a meta-analysis of seven trials including ICTUS found that overall an early invasive strategy led to fewer deaths or new coronary events (J. Am. Coll. Card. 2006;48:1319-25).

The guidelines call the conservative strategy preferable for certain patients, such as women who are at low risk of death or STEMI. That is because in low-risk women, the risk of complications from coronary catheterization, such as puncture site bleeding, exceeds the potential benefit from a percutaneous intervention, she said.

An important step when deciding between an invasive or conservative strategy is an early risk assessment of the patient. Although the guidelines allow physicians to make a qualitative assessment of high, intermediate, or low risk, on the basis of factors such as cardiac markers (especially troponin level), ECG, clinical findings, pain, and history, they recommend going further and using one of the formal scoring systems that have been validated during the past few years: the Thrombolysis in Myocardial Infarction (TIMI), Global Registry of Acute Coronary Events (GRACE), or Platelet IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy (PURSUIT) scoring methods.

"We thought it was a little early to say that everyone has to use a formal scoring system on every patient, but we're pushing people in that direction," said Dr. Jeffrey L. Anderson, the associate chief of cardiology at LDS Hospital in Salt Lake City and also the chairman of the guidelines committee.

"We hope that people will become more familiar with scoring over the next few years and that eventually" it will be used routinely, he said in an interview.

'A lot of things, applied early, contribute to the safety of conservative management.'

DR. WENGER

Other important, new elements in the guidelines deal with antiplatelet and anticoagulant therapy.

In addition to daily aspirin, which is continued indefinitely, all patients should start on clopidogrel as soon as possible and continue on it for a year if they are treated conservatively or get a bare-metal coronary stent, and continue for at least a year on clopidogrel if they receive a drug-eluting coronary stent.

Two new anticoagulant drugs have been introduced since the 2002 guidelines, fondaparinux (Arixtra) and bivalirudin (Angiomax), and these are deemed alternatives to the low-molecular-weight heparin enoxaparin (Lovenox) and unfractionated heparin.

The new set of guidelines also call for treatment with a glycoprotein IIb/IIIa inhibitor, for example eptifibatide (Integrilin), tirofiban (Aggrastat), or abciximab (ReoPro) for recurrent angina or prior to diagnostic angiography or coronary stenting.

Overall, the antiplatelet and anticoagulant options are numerous and complex. The guidelines "try to walk a physician through, step by step, but in some cases they can choose one option or another. To simplify things, I recommend that a physician, group, or hospital decide on a particular strategy and try to focus on using just that to make it easier for everyone," commented Dr. Anderson, who is also a professor of medicine at the University of Utah.

The guidelines also call for aggressive, ongoing medical management after the patient is discharged. At the core of the regimen is an ACE inhibitor, or an angiotensin receptor blocker for ACE inhibitor–intolerant patients.

A new addition in the guidelines is use of an aldosterone receptor blocker, either spironolactone or eplerenone (Inspra) for patients with a left ventricular ejection fraction of 40% or less and either symptomatic heart failure or diabetes, as long as they don't also have significant renal dysfunction or hyperkalemia.

Other elements of the discharge regimen include following established U.S. guidelines for managing blood pressure and serum lipids, and a strong push for smoking cessation.

Hormone therapy should not be started in postmenopausal women, and in general should stop in postmenopausal women who were on hormonal therapy at the time of their coronary event.

Supplements with antioxidant vitamins C and E and folic acid should not be used. Treatment with an NSAID (aside from aspirin) should be stopped when a patient is first admitted.

If a drug of this type is required by the patient at discharge, it should be used at the lowest effective dose for the shortest possible time. ■

Diabetes Raises Mortality in ACS Patients

BY KATE JOHNSON
Montreal Bureau

Patients with diabetes have increased 30-day and 1-year mortality following acute coronary syndromes, compared with patients without diabetes, according to an analysis of more than 60,000 patients.

At 30 days after acute coronary syndrome (ACS), diabetes was a significant independent factor associated with all-cause mortality for patients presenting with ST-segment-elevation myocardial infarction (STEMI) and for those with unstable angina/non-STEMI (UA/NSTEMI), with adjusted odds ratios of 1.40 and 1.78, respectively. At 12 months, diabetes remained a significant independent predictor of mortality for both patient groups, with adjusted hazard ratios of 1.22 and 1.65, respectively. The data were adjusted for baseline characteristics, as well as features and management of the index ACS event.

Also at 12 months, "patients with diabetes and presenting with UA/NSTEMI had a mortality that approached patients without diabetes and presenting with STEMI (7.2% vs. 8.1%)," the researchers reported (JAMA 2007;298:765-75).

The analysis pooled 62,036 ACS patients from 11 independent Thrombolysis in Myocardial Infarction (TIMI) Study Group clinical trials. A total of 46,577 patients presented with STEMI, and the remaining 15,459 patients presented with unstable angina/non-STEMI (UA/NSTEMI). A total of 10,613 patients had diabetes by self-report, wrote lead author Dr. Sean M. Donahoe of Cornell University Medical Center, New York, and colleagues.

Long-term use of therapies for the traditional coronary risk factors must be promoted for patients with diabetes, particularly after ACS.

"The burden of cardiovascular risk inherent among the patients presenting with UA/NSTEMI marked the index ACS presentation as a sentinel event in a chronic, progressive course that was more accelerated among patients with diabetes," they wrote. "The UA/ NSTEMI population is enriched with this high-risk diabetic population."

Limitations to the study included the possibility of intertrial variability in ACS management, and the self-reporting of diabetes status.

Given "the increasing burden of cardiovascular disease attributable to diabetes worldwide," the authors noted "the need for a major research effort to identify aggressive new strategies to manage unstable ischemic heart disease among this high-risk population" and wrote "long-term, targeted, intensive use of proven therapies for the traditional coronary risk factors must be widely promoted for patients with diabetes, particularly following ACS."

"Collaboration between medical societies, national health care organizations, and industry will be vital to halt the epidemic of diabetes-related cardiovascular disease," they wrote. ■

Post-MI Depression Affects More Women Than Men

ORLANDO — A higher incidence of depression after a myocardial infarction in women, compared with men, contributes to the worse outcomes that women face, according to a study.

"It's important to identify and treat symptoms of depression at the time of hospitalization for myocardial infarction," Dr. Susmita Parashar said at a conference on cardiovascular disease epidemiology and prevention sponsored by the American Heart Association.

Dr. Parashar, of Emory University, Atlanta, and associates used data on 2,411 acute MI patients at 17 U.S. centers during January 2003-June 2004 in the Prospective Registry Evaluating Myocardial Infarction Events and Recovery study. Patients with a documented MI were assessed for depression at initial hospitalization and at follow-up with the Patients Health Questionnaire (PHQ).

During initial hospitalization, 29% of 752 women in the registry were diagnosed with depression by the PHQ, compared with a prevalence of 19% among 1,531 men, a statistically significant difference.

In an analysis that adjusted for age at baseline, women were 18% more likely to need rehospitalization during 12 months of follow-up, versus men, a significant difference. In a second analysis that adjusted for age and race and several clinical factors at baseline including diabetes, hypertension, and smoking history, women were 20% more likely to be hospitalized during follow-up, compared with men.

—Mitchel L. Zoler