

Unstable Angina, Non-STEMI Get New Guidelines

BY MITCHEL L. ZOLER
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Early invasive and conservative strategies for managing unstable angina or non-ST-segment-elevation myocardial infarction both received endorsements in the first guidelines on the topic from the American College of Cardiology and the American Heart Association since 2002.

Recommendation of a conservative, medically based option is a substantial change from the 2002 guidelines. The choice between an invasive or conservative strategy depends on patient stability, disease severity, other patient characteristics, and patient and physician preference. In contrast, the 2002 version presented the early-invasive strategy as the main option for most patients. The new guidelines were developed in collaboration with the American College of Physicians and other organizations (*J. Am. Coll. Cardiol.* 2007;50:652-726).

"What we're now saying is that a physician who chooses a conservative strategy is not a pariah. It's an acceptable strategy, except for unstable patients," said Dr. Nanette K. Wenger, professor of medicine at Emory University, Atlanta, and a member of the guideline writing committee.

Other notable updates to the guidelines include a suggestion to use a formal scoring system to assess patient risk and help guide the choice between the two management options; longer use of the antiplatelet drug clopidogrel (for up to 1 year in all patients); and a broadening of 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 man-

agement 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 the conservative approach 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 key 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," Dr. Wenger said. "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."

The guidelines cited results 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 as patients managed with a routine invasive strategy (*Lancet* 2007;369:827-35). But the guidelines also noted that 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. Cardiol.* 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. 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.

Early risk assessment is crucial. The guidelines let physicians 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, but 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, associate chief of cardiology at LDS Hospital in Salt Lake City and 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.

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.

The two new anticoagulant drugs, fondaparinux (Arixtra) and bivalirudin (An-

giomax), are deemed alternatives to enoxaparin (Lovenox) and unfractionated heparin. The guidelines also call for treatment with a glycoprotein IIb/IIIa inhibitor, such as 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," said 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.

The discharge regimen follows established U.S. guidelines for managing blood pressure and serum lipids. 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 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 an NSAID is needed at discharge, it should be used at the lowest effective dose for the shortest possible time. ■

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Value of Presurgery Revascularization Is Still Unresolved

BY MITCHEL L. ZOLER
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BALTIMORE — The jury remains out on the safety and efficacy of coronary revascularization for very high-risk patients before they have major vascular surgery.

A pilot study that randomized 101 adult patients to revascularization or medical therapy before major vascular surgery failed to show (and was underpowered to show) a significant overall outcome difference between these two options, Dr. Olaf Schouten said at the Vascular Annual Meeting. A definitive test of the idea that selective revascularization before vascular surgery yields better outcomes would need to screen about 9,000 patients and find at least 600 to enroll in the randomized trial, said Dr. Schouten, a vascular surgeon at Erasmus Medical Center, Rotterdam, the Netherlands. It's unclear whether such a large and expensive study will ever occur.

However, the study did raise questions about the best sequence of treatments in patients with advanced coronary disease who also need major vascular surgery, such as repair of an abdominal aortic aneurysm. That's because the results of a subgroup analysis showed that among the patients who survived the first 30 days after vascular surgery, the mortality rate among those who first had coronary

revascularization was 46% less than those who did not have revascularization, a statistically significant difference. This finding suggests that the long-term benefit of performing revascularization first is undercut by an acute risk, probably stent thrombosis, Dr. Schouten said in an interview. But he stressed that this subgroup analysis from limited data does not support initial revascularization; it just highlights the complex interplay between the benefits and adverse effects of initial revascularization in these patients.

In the study, 32 of the 49 revascularization patients underwent a percutaneous coronary intervention and coronary stenting; 30 of these 32 patients received drug-eluting stents. The other 17 patients in this subgroup had coronary bypass surgery. The average interval between revascularization and vascular surgery was about 30 days, and patients who were on dual antiplatelet therapy continued the regimen during vascular surgery.

Another study, the Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echo (DECREASE)-V pilot study, was done during 2000-2005 at six hospitals in six countries (*J. Am. Coll. Cardiol.* 2007;49:1763-9). The investigators screened 1,880 consecutive patients scheduled to undergo elective, open reconstruction of their abdominal aortic or infrainguinal arteries.

The primary end point was all-cause death and nonfatal

MI during 30 days after vascular surgery. The rates were 43% in the revascularized patients and 33% in those managed medically, a difference that was not significant. At 1 year, the rate of death or MI was 49% and 44%, respectively, also a nonsignificant difference. No patient in the medical therapy group had revascularization during the first year.

The study focused on extremely high-risk patients because they are the most likely to benefit from coronary revascularization before vascular surgery, Dr. Schouten said. Patients were screened for risk factors, including age over 70, angina, prior MI, heart failure, diabetes, and renal dysfunction. Patients with at least three risk factors underwent cardiac stress testing. All 101 patients who showed extensive, stress-induced cardiac ischemia were enrolled in the trial. About a quarter of the patients had two-vessel coronary disease; the remainder had triple-vessel disease.

All patients were maintained on β -blockers, either continuing their preexisting regimen or starting on bisoprolol (Zebeta). The dosage for all patients was adjusted to achieve a resting heart rate of 60-65 beats per minute. Fifty-two patients were managed medically only, and 49 underwent revascularization; all then underwent scheduled vascular surgery. Two patients, both of whom had coronary bypass surgery, died from a ruptured aneurysm before their vascular surgery occurred. ■