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 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), the Global Registry of Acute Coronary Events (GRACE), or the Platelet IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy (PURSUIT) scoring methods.

'A physician who chooses a conservative strategy is not a pariah. It's an acceptable strategy.'

DR. WENGER

"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.

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 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.

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. ■

Value of Circadian Blood Pressure Variations Confirmed

BY PATRICE WENDLING
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CHICAGO — Treated hypertensive patients who have either extreme or very slight dips in nighttime blood pressure are at greater cardiovascular risk than are those with moderate dips, according to a study in 1,472 patients.

Prior research has shown that people whose blood pressure fails to dip at night ("nondippers") are at much higher risk for cardiovascular events than are patients whose BP follows the normal diurnal pattern and falls by 10%-20% during sleep. The new data extend these findings to include "extreme dippers," or those whose nighttime systolic and/or diastolic BP dips by at least 20%.

"Circadian blood pressure pattern influences cardiovascular outcome in treated hypertension and its evaluation allows a better prognostic stratification and may suggest a more appropriate pharmacological management," lead investigator Dr. Sante D. Pierdomenico and associates reported in a poster at the annual meeting of the American Society of Hypertension.

The investigators studied 388 patients with a dipper BP pattern (systolic and diastolic nighttime BP reduction of at least 10% and less than 20%), 745 with a nondipper BP pattern (systolic and/or diastolic reduction of less than 10%), and 339 with an extreme-dipper BP pattern. Blood pressure measurements were taken with a 24-hour ambulatory blood pressure monitoring system.

Cardiovascular risk was significantly higher in nondipper patients (RR 1.7) and in extreme-dipper patients (RR 2.2), compared with dipper patients.

Nondippers (mean age 61 years) were significantly older than dippers (58 years) or extreme dippers (55 years), and were more likely to have diabetes (8%) than were dippers (4.4%) or extreme dippers (4%). However, nondippers were significantly less likely to be smokers (17%) than were dippers (25%) or extreme dippers (22%).

During an average of 5 years of follow-up, there were 116 cardiovascular events. The event rate per 100 patient-years was 0.91, 1.93, and 1.73 in dipper, nondipper, and extreme-dipper patients, respectively. Event-free survival was significantly different among the groups, reported Dr. Pierdomenico, professor of medicine and aging science at G. d'Annunzio University in Chieti, Italy.

A Cox regression analysis that adjusted for various covariates, including 24-hour BP and drug therapy, showed that cardiovascular risk was significantly higher in nondipper patients (relative risk 1.7) and in extreme-dipper patients (RR 2.2), compared with dipper patients.

"This and many other studies would argue for 24-hour blood pressure monitoring at least in the subgroup of people at very high risk of being nondippers," said Dr. George Bakris, director of the hypertension center at the University of Chicago, in a statement, "for example, those with kidney disease [glomerular filtration rate less than 60 mL/min per 1.73 m^2]; those who are obese, with or without sleep apnea; blacks with hypertension; and those with insulin resistance." ■