

Groups Address GI Effects of Antiplatelets, NSAIDs

BY SHARON WORCESTER

Southeast Bureau

Identifying and treating the potentially life-threatening problem of gastrointestinal complications in patients who use the combination of antiplatelet therapy and NSAIDs are the focus of a new scientific statement by the American College of Cardiology Foundation, the American College of Gastroenterology, and the American Heart Association.

Practical clinical guidance for reducing the risk of ulceration and related bleeding—including the use of gastroprotection, either with proton pump inhibitor therapy or treatment of *Helicobacter pylori* infection—was included in the consensus document.

Ulcerations and gastrointestinal bleeding are recognizable risks in individuals who use antiplatelet agents and NSAIDs, with these patients having up to a fourfold increased risk of such complications, compared with those who are not using the medications, according to Dr. Deepak L. Bhatt, document cochair, and his colleagues on the consensus document writing committee (J. Am. Coll. Cardiol. 2008 [doi:10.1016/j.jacc.2008.08.002]).

Considering that NSAIDs, including aspirin, are the most widely used class of medication in the United States, and that more Americans are surviving and living with heart disease in addition to conditions that require them to take NSAIDs (such as arthritis, inflammation, and related musculoskeletal pain), the management of GI risk will become an increasingly important part of cardiovascular care, according to an American College of Cardiology (ACC) statement on the consensus document.

"Doctors are uncertain about how best to prevent bleeding complications in patients receiving antiplatelet therapy and NSAIDs, which are both commonly used,

and can cause erosions in the stomach lining," Dr. Bhatt, chief of cardiology at VA Boston Healthcare System, noted in the statement. "These recommendations represent the collective expertise of leading cardiologists and gastroenterologists, as well as an extensive review of the literature, and provide specialists with practical measures to manage competing risks and help improve patient safety."

In addition, Dr. David Johnson, the immediate past president of the American College of Gastroenterology and professor of medicine and chief of gastroenterology at Eastern Virginia Medical School, Norfolk, stressed the importance of "proactive assessment" of individual risk, and of the need for improved communication between cardiologists, gastroenterologists, and primary care physicians to improve patient safety.

Likewise, patients must be informed of the importance of disclosing all medication information to ensure that appropriate measures can be taken to reduce risk, he noted.

The organizations made recommendations for the following clinical scenarios:

► **GI complications of aspirin and of combined aspirin and nonaspirin NSAIDs.** Gastroprotective therapy should be prescribed for at-risk patients who use low-dose aspirin, and for those using any NSAIDs in conjunction with cardiac-dose aspirin. Because the risk of upper gastrointestinal events increases with aspirin dose escalation, doses greater than 81 mg should not be routinely prescribed for chronic phase therapy.

► **GI effects of combined aspirin and anticoagulate therapy.** There is a "clinically meaningful and significantly increased risk of major extracranial bleeding events, a large proportion from the upper GI tract" in those on this combination, and the combination should be used with an "established vascular, arrhythmic, or

valvular indication." Concomitant proton pump inhibitor (PPI) therapy is advised.

► **GI effects of clopidogrel and clopidogrel plus anti-coagulant therapy.** Clopidogrel should not be substituted for aspirin as a strategy to reduce recurrent ulcer bleeding in high-risk patients, because it is inferior to the combination of aspirin plus PPIs. Also, the combination of clopidogrel and warfarin therapy is associated with an increased incidence of major bleeding, compared with monotherapy; this combination should be considered only when the benefits are likely to outweigh the risks. An international normalized ratio of 2.0-2.5 is recommended when warfarin is added to aspirin or to aspirin and clopidogrel.

► **Treatment and prevention of aspirin and NSAID-related gastroduodenal injury.** PPIs should be used for both the prevention and the treatment of NSAID- and aspirin-associated GI injury.

► **H. pylori testing and eradication.** Before initiating chronic antiplatelet therapy in patients with a history of ulcer disease, test for and eradicate *H. pylori*.

► **Discontinuation of antiplatelet therapy because of bleeding.** The decision to discontinue aspirin therapy in the setting of acute ulcer bleeding should be individualized based on cardiac risk and GI risk assessments to discern potential thrombotic and hemorrhagic complications.

► **Endoscopy in patients on mono or dual antiplatelet therapy.** High-risk cardiovascular patients who are on dual therapy may benefit from endoscopic therapy. Collaboration between the cardiologist and endoscopist is important to assess the risk of bleeding against the risk of thrombosis in regard to the timing of antiplatelet therapy cessation.

The consensus document is considered to be part of "an ongoing dialogue" and will be updated "as more definitive data are accrued," according to the ACC statement. ■

STAT Registry: Acute Severe Hypertension Is Poorly Managed

BY BRUCE JANCIN

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MUNICH — Acute severe hypertension is a common, suboptimally treated condition with a high recurrence rate and surprisingly high morbidity and mortality.

These are the principal lessons of the just-completed large national Studying the Treatment of Acute Hypertension (STAT) registry, Dr. Christopher B. Granger said at the annual congress of the European Society of Cardiology.

The STAT observational registry documented 90-day mortality and readmission rates following an episode of acute severe hypertension (ASH), rates comparable with those typically encountered in patients with acute heart failure or an acute coronary syndrome.

These and other sobering STAT findings "reinforce the major need to improve prevention and treatment of this understudied condition," stressed Dr. Granger, a cardiologist at Duke University, Durham, N.C., and chairman of the STAT steering committee.

ASH involving blood pressures in excess of 180/110 mm Hg, or greater than 140/90 mm Hg with subarachnoid hemorrhage, occurs in 1%-2% of the 72 million Americans with chronic hypertension. At some busy urban emergency departments, ASH accounts for up to 25% of all patients seen. Yet little contemporary information is available about the

characteristics of affected patients, their treatment, or outcomes. This was the impetus for STAT.

Dr. Granger reported on 1,588 adults who received intravenous antihypertensive agents for ASH within 24 hours of presenting at 25 nationally representative participating U.S. hospitals.

The mean age of STAT registry participants was 58 years. About one-half were women, and 56% were African American. Overall, 89% of participants had a history of chronic hypertension, 35% were diabetic, 31% had chronic kidney disease, 15% had a history of drug abuse, and 27% had previously been hospitalized for ASH. Nonadherence to medications for chronic hypertension was deemed a contributing factor in 25% of ASH episodes.

Roughly one-quarter of patients were admitted for acute hypertension, another quarter for stroke or other neurologic complications, and one-quarter for heart failure or other cardiovascular conditions.

The median hospital length of stay was 5 days. Roughly half of patients were admitted to the intensive care unit. During their stay, 48% of patients had brain imaging by CT or MRI and 45% had an echocardiographic examination—yet dis-

turbingly, a mere 13% had a documented funduscopic exam, Dr. Granger noted.

Among the key STAT findings:

► **Poor outcomes.** In-hospital mortality was 6.9% and 90-day mortality was 11%. The 90-day readmission rate was 37%, and 9.3% of patients were rehospitalized within 90 days for recurrent ASH.

► **Lengthy time to blood pressure control.** The median time to drive systolic blood pressure below 160 mm Hg was 4 hours. Moreover, following initial control, fully 60% of patients experienced a rebound to greater than 180 mm Hg.

Also, 4% of patients had iatrogenic hypotension, in most cases requiring vasopressors.

► **Variable treatment approaches.** Intravenous antihypertensive therapy was administered within 1 hour in 47% of patients and within 3 hours in 74%. Two-thirds of patients required two or three intravenous antihypertensive drugs. The first intravenous drug employed was labetalol in 32% of cases and metoprolol in 17%, followed in descending order by nitroglycerin, hydralazine, nicardipine, and sodium nitroprusside. Nicardipine was the only drug that served as monotherapy in the majority of treated patients.

► **Inadequate follow-up.** ASH is a life-threatening condition, yet 65% of patients had no documentation in the medical record of a follow-up appointment being scheduled or attended.

"Although this may be an overestimate of the true degree of the problem, I think it does illustrate what is probably the single most important opportunity to improve care that we've seen in this study," Dr. Granger noted.

Ongoing STAT analyses include efforts to identify risk factors for recurrence, as well as the most effective ways to lower high blood pressures without exacerbating damage to the kidneys and other organs.

"We're trying to analyze the relationship between patterns of control and outcome. There are interesting data from the ECLIPSE [Evaluation of Clevidipine in the Postoperative Treatment of Hypertension Assessing Safety Events] trial showing that it appears patients with perioperative hypertension who get into and stay within a target blood pressure range have better outcome; it was an independent predictor. Whether that's the case in this population with acute severe hypertension is a very important question we currently lack information on," he continued.

Both the STAT registry and ECLIPSE were funded by the Medicines Company. Dr. Granger has received research grants and served as a paid consultant to the company. ■



These findings reinforce the need to improve prevention and treatment of this understudied condition.

DR. GRANGER