

Chest Physicians Urge Action

Thrombosis from page 1

"For every general hospital, we recommend that a formal, active strategy that addresses the prevention of VTE be developed... in the form of a written, institution-wide thrombo-prophylaxis policy," the guidelines state.

Computer decision support systems, preprinted orders, and periodic audits and feedback mechanisms are advocated by the committee, while "passive methods" such as educational meetings and handouts are deemed inadequate as standalone strategies to increase adherence to thromboprophylaxis.

"Despite very good evidence, prophylaxis is still underutilized in people who would benefit," Dr. Jack Hirsh said in an interview.

Hospitals need to have firm policies and enforce them, he added. "Instead of surgeons or physicians kicking a box, saying they should be used, the box should only have to be kicked when they are not used," said Dr. Hirsh, professor emeritus of medicine at McMaster University and founding director of the Henderson Research Center, both in Hamilton, Ont.

In the new guidelines, the recommendation for VTE prophylaxis has been expanded beyond major general, gynecologic, and orthopedic surgeries to include bariatric and coronary artery bypass surgery.

No prophylaxis is recommended for low-risk patients undergoing laparoscopic surgery or knee arthroscopy, or those taking long airplane flights.

As expected, the new guidelines reaffirm the position of the American College of Chest Physicians that aspirin alone is not sufficient therapy to prevent venous thromboembolism in any patient population, because more effective alternatives are available, including heparin, low-molecular-weight heparin, and a synthetic, selective factor Xa inhibitor, fondaparinux, which was approved by the FDA in 2001.

Many of the guidelines now mentioning fondaparinux as an alternative anticoagulant rate the evidence for its use as 1A, meaning that the supportive data are strong.

Dr. Geno J. Merli, chief medical officer of Thomas Jefferson University Hospital, Philadelphia, welcomed the renewed emphasis on prophylaxis therapy that does not depend solely on aspirin.

"Aspirin is still being widely used for prophylaxis," he said, noting that some consensus-based guidelines for orthopedic surgery still advocate the use of aspirin as a solo preventive agent.

The length of recommended postsurgical prophylaxis has been extended in the guidelines to 28 days (and in some surgeries, 35 days) for most general, gynecologic, and orthopedic procedures, he noted. Previously, prophylaxis was generally advised for 2 weeks following surgery.

A new chapter greatly expands evidence-based guidance concerning the perioperative management of patients on antithrombotic therapy who require emergency or elective surgery. Detailed

sections provide advice for specific conditions and surgical circumstances, ranging from minor dermatologic surgery to hip fracture.

"This [publication] is not meant to be read from cover to cover," Dr. Hirsh said. "It is an encyclopedic reference to be used by physicians if the patient has had a stroke, is at risk of stroke, has had a heart attack, is at risk of heart attack, has atrial fibrillation, has an inherited thrombophilia, or is pregnant and on antithrombotic therapy."

Among the most pivotal changes in the recommendations are guidelines on patients with atrial fibrillation, management of pregnant women and children, and treatment of DVT.

► **Atrial fibrillation.** Antithrombotic therapy in patients with atrial fibrillation is awarded the strongest evidence grade (1A), reflecting widespread agreement of findings from randomized, controlled trials.

Target international normalized ratios, drug choices, and dosages are detailed in the new guidelines in the



'It's good to have choices' for treatment of acute DVT.

DR. MERLI

hopes that primary care physicians will use the document to guide therapy, Dr. Hirsh said.

"There is marked underutilization of warfarin [in atrial fibrillation patients], not by cardiologists, but by family physicians. The logistics of monitoring are difficult," he said.

As a result, the guidelines include one entire section that addresses the nuts and bolts of monitoring. Evidence is cited that affirms the rationale for using computer assistance to adjust dosages based on monitoring data.

► **Pregnant women.** Dr. Hirsh identified new guidelines for pregnancy as among "the most controversial and, I think, the most important" in the document.

Randomized trials are difficult to conduct in this population, so most of the recommendations receive a 2C grade that reflects weak evidence, noted Dr. Shannon M. Bates, who oversaw the chapter on pregnancy issues.

Nonetheless, "a great deal of work has gone into making sure that our recommendations are unbiased and clearly reflect the available data," said Dr. Bates, director of the adult hematology residency training program at McMaster University Medical Centre in Hamilton, Ont.

"By distilling this information into clear recommendations that include a reflection of the quality of available data, we hope to make it easier for physicians to provide the best evidence-based care to their patients," she added.

Key elements of the pregnancy guidelines include a recommendation against

routine prophylaxis other than early mobilization in patients undergoing cesarean section; a recommendation against testing for inherited hypercoagulable states in women with a history of pregnancy complications; and deletion of a previous recommendation advocating antithrombotic therapy in women with pregnancy complications and a known inherited hypercoagulable state.

Guidelines were eased for patients who have inherited hypercoagulable states because the association of these conditions and pregnancy complications is backed by scant evidence, while screening and interventions are costly, might carry some degree of risk, and might provoke needless anxiety for women, Dr. Bates said.

The new guidelines also provide detailed recommendations for management of women with prosthetic heart valves who are considering pregnancy.

► **Children.** Greatly expanded guidelines "pretty well cover every conceivable thrombotic issue" in neonates and children, Dr. Hirsh noted.

Stroke is one of the 10 leading causes of death in childhood, but it is difficult to diagnose and predict based on risk factors. Therefore, the new guidelines recommend that any child with arterial ischemic stroke receive initial antithrombotic therapy until the underlying causes are understood, followed by maintenance therapy to prevent recurrence.

Detailed sections offer guidelines on the prevention of thrombotic events in children with congenital heart disease, including sections on ventricular assist devices and prosthetic heart valves.

► **Treatment of DVT.** The guidelines offer two options—one monitored and one unmonitored—for subcutaneous heparin administration for acute DVT, Dr. Merli said in an interview.

The first regimen calls for an initial dose of 17,500 U or a weight-adjusted dose of about 250 U/kg every 12 hours, with the dose adjusted to achieve and maintain an activated partial thromboplastin time (aPTT) prolongation that corresponds to plasma heparin levels of 0.3-0.7 IU/mL anti-Xa activity when measured 6 hours after injection (rather than beginning therapy with the smaller initial dose).

The second option is a fixed-dose, unmonitored regimen that calls for an initial dose of 333 U/kg followed by a twice-daily dose of 250 U/kg.

"It's good to have choices," Dr. Merli said.

The guidelines also suggest for the first time the use of catheter-directed thrombolysis with thrombus fragmentation and/or aspiration in "selected patients with extensive acute proximal DVT who have a low risk of bleeding," but advocate this pharmacomechanical approach only if "appropriate expertise and resources are available."

The guidelines also acknowledge the feasibility of reducing international normalized ratio monitoring during anticoagulation therapy in very low risk patients with an unprovoked DVT who have been intensively monitored for 3 months following standard protocols, Dr. Merli noted. ■

Prolonged QRS Predicts Adverse Events

BY MARY ANN MOON
Contributing Writer

A prolonged QRS duration predicts high mortality and morbidity after discharge in patients hospitalized for heart failure who also have reduced left ventricular ejection fraction, according to an analysis of the EVEREST trial.

"This high morbidity and mortality was observed even though patients were well treated with standard medical therapy that included β -blockers and ACE inhibitors or angiotensin receptor blockers," said Dr. Norman C. Wang of Northwestern University, Chicago, and his associates.

Measuring QRS duration on ECG is "relatively inexpensive, simple to perform, and yields an instant result," the investigators noted.

The EVEREST (Efficacy of Vasopressin Antagonism in Heart Failure Outcome Study With Tolvaptan) investigators reported their main conclusions last year. They now report the results of a retrospective, post hoc analysis of data on a subset of 2,962 subjects hospitalized for heart failure at more than 350 medical centers around the world and followed for a median of 10 months. This study was supported by Otsuka Pharmaceutical Group.

Patients underwent ECG evaluation at admission and at several intervals during hospitalization. About 45% of the patients had a prolonged QRS (duration of 120 milliseconds or more).

A prolonged QRS on admission was associated with a significantly increased risk of death within 3 months (12% incidence) and at the end of follow-up (28% incidence), compared with a normal QRS on admission (7% and 19%, respectively). This represents a 24% increased risk of death with a prolonged QRS duration.

Similarly, the composite end point of cardiovascular death or rehospitalization for heart failure was significantly more common in patients with a prolonged QRS on admission, Dr. Wang and his associates said (JAMA 2008;299:2656-66).

Also, if a prolonged QRS developed during hospitalization, it was associated with increased event rates after discharge.

However, "one must be cautious in attributing mechanistic significance to the QRS widening itself" as study patients with a wide QRS consistently had a higher prevalence of many known risk factors, including older age, lower ejection fraction, faster heart rate, and higher serum blood urea nitrogen, creatinine, and brain natriuretic peptide levels, Dr. Barrie Massie said in an interview. "Importantly, they were less often treated with β -blockers and much more frequently receiving amiodarone," added Dr. Massie, professor of medicine at the University of California, San Francisco, and chief of cardiology at the San Francisco VA Medical Center.

Most patients who died during follow-up succumbed to progressive heart failure or sudden cardiac death, Dr. Wang reported. ■