DVT Preventive Care Should Be Handled More Urgently

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ROME — Many health care providers are inappropriately complacent regarding the long-term sequelae of deep vein thrombosis in the lower extremities, speakers said at the annual meeting of the Cardiovascular and Radiological Interventional Society of Europe.

Deep vein thrombosis (DVT) occurs in more than 250,000 U.S. patients per year. Standard medical management—that is, anticoagulation, compression stockings, and leg elevation—is all about preventing pulmonary embolism, a dreaded acute complication with roughly a 13% in-hospital mortality.

But often, anticoagulation only partially clears the thrombus, and it doesn't fix the delicate venous valves threatened by low or absent blood flow. As a result, many patients develop chronic postthrombotic syndrome (PTS), or "heavy leg," marked by ruptured valves, lifelong chronic deep venous insufficiency, painful leg swelling, and stasis ulceration, according to Dr. Kenneth R. Thomson of the Alfred Hospital, Melbourne.

"We need to educate clinicians to think of [deep venous] thrombus as a valve attack, like a brain attack or a heart attack, and have a more rapid and aggressive treatment," he said.

That will require more accurate diagnosis. Even in premier medical centers, the radiologist continued, it's surprising how often patients who present to the emergency department with a swollen leg get an ultrasound exam that stops at the groin and doesn't include the iliac veins or inferior vena cava.

Dr. Stephen T. Kee stressed that PTS can be as disabling as severe peripheral arterial disease. The direct medical costs of PTS in the United States are estimated at $300 million annually.

"When venous disease is extensive, it is essentially beyond medicine's ability to treat. Anticoagulation alone is not enough. They need our help. Lysis in correct doses is very safe, although in most cases it must be combined with other endovascular techniques with which we are very familiar," said Dr. Kee, chief of interventional radiology at the University of California, Los Angeles, Medical Center.

Interventional radiologists perform catheter-delivered thrombolysis (CDT) for DVT. It provides more complete clot lysis than the systemic infusion used in acute MI, and with much lower risk of bleeding complications. In roughly 90% of cases, there is an underlying anatomic defect that requires adjunctive angioplasty in order to maintain patency, along with stenting in the case of suprainguinal disease, he explained.

These procedures are most effective in acute DVT. Ideally, Dr. Thomson said, CDT ought to be done in the emergency department. The reality is most patients aren't referred for this more aggressive therapy until at least several months of anticoagulant therapy have gone by and the leg remains swollen. By then the thrombus is hardened and desiccated, crosslinked to fibrin, tightly adherent to the vein wall—and the valves are destroyed.

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DR. THOMSON

Dr. Thomson is a coinvestigator in a Cook Inc. project aimed at developing percutaneous bioprosthetic venous valves for use in DVT patients who have experienced "valve attack." The 1-year clinical outcomes reported at the meeting are promising, but better biomaterials are needed to improve valve longevity.

CDT for DVT is an off-label use of lytics. Nonetheless, the Society for Interventional Radiology (SIR) this year issued a position statement declaring CDT as an adjunct to anticoagulation an acceptable initial treatment strategy for carefully selected patients with acute DVT of less than 14 days' duration.

The SIR statement cited registry data suggesting CDT has better outcomes than those obtained with anticoagulation alone, which results in PTS in up to 50% of patients if compression stockings aren't used and 25% if they are.

A SIR research consensus panel concluded that if more aggressive treatment of DVT is to become a multidisciplinary national priority, there is a pressing need for persuasive A-level supporting data. Toward that end, the society has submitted to the National Institutes of Health a detailed protocol for a large randomized trial to be called Acute Venous Thrombosis Removal with Adjunctive Catheter-Directed Thrombolysis (ATTRACT). The trial will compare anticoagulation alone to thrombolysis with or without angioplasty and stenting. The primary end point will be the cumulative 12-month PTS incidence.

If approved by NIH, ATTRACT will start in April 2007 and be led by Dr. Suresh Vedantham of Washington University, St. Louis. ■

Facilitated Thrombolysis Devices Speed DVT Therapy

ROME — Several relatively new percutaneous pharmacomechanical devices may have a major impact on the treatment of deep vein thrombosis, according to speakers at the annual meeting of the Cardiovascular and Radiological Interventional Society of Europe.

Devices such as Bacchus Vascular Inc.'s Trellis and the EKOS Lysus System render tough clots more amenable to low-dose lytic therapy, though through very different mechanisms. The thrombus clears dramatically faster than with conventional catheter-delivered thrombolysis (CDT), which often takes 24-50 hours or more of continuous infusion conducted in an ICU or step-down unit. The faster thrombus clearance translates into lower hospital costs and—in the view of many interventionalists—less risk of lytic-related hemorrhage as well.

Dr. Thomas O. McNamara said both the Trellis and Lysus devices are so new that their optimal roles aren't defined yet, but he has used both devices and believes that both are particularly well suited for treating subacute DVT of about 8-90 days' duration.

Fresh thrombus not more than a week old is often readily cleared using slow-drip CDT. But subacute clot that has begun to harden and cross-link with fibrin is much more resistant to conventional CDT. The pharmacomechanical devices thus broaden the spectrum of DVT amenable to lysis, explained Dr. McNamara, professor of radiology at the University of California, Los Angeles.

The Trellis device consists of a lytic-infusion catheter with an oscillating wire and occluding balloons at either end. The catheter is passed across the clot, the balloons above and below the thrombus are inflated, and the oscillating wire is activated for 15 minutes, during which a small quantity of a thrombolytic agent is administered at 5-minute intervals.

The oscillating wire macerates the clot, breaking it up into smaller fragments with far greater surface area, which enhances the effectiveness of lytic therapy. Meanwhile, the balloons trap the clot so it can't embolize. They are also supposed to trap the lytic so it can't become systemic and cause bleeding. "The device does that, but not completely," he said.

After the oscillating wire has been fired up for several 15-minute bursts, the dissolved clot is sucked out through the catheter and the balloons are deflated.

Dr. Stephen T. Kee, chief of interventional radiology at UCLA Medical Center, noted that total Trellis procedure time, from access site puncture to sheath removal, is typically 1 hour to just over 2 hours, even when stenting or other adjunctive procedures are performed.

Dr. McNamara said interventionalists who have difficulty getting patients into the ICU for lengthy CDT may use the Trellis routinely as a single-session treatment. But he added that the system is too expensive to use as initial therapy for most of his patients.

But the device is clearly justified in the postop patient with DVT, he continued. He has used the Trellis in 24 such patients and found it quite effective, though it's not foolproof. One spinal fusion surgery patient required transfusion after bleeding into the buttock, which was believed to be caused by systemic escape of the lytic triggering bleeding at the donor bone site.

The Lysus System combines high-frequency, low-power ultrasound with simultaneous CDT. It includes a catheter with multiple ultrasound transducers 1 cm apart. The same catheter emits a thrombolytic agent in a continuous infusion through a separate channel.

The radially delivered ultrasound waves loosen the clot and drive the lytic agent deep within it. That accelerates thrombolysis, with an average infusion time of 24 hours or less and uses lower lytic doses than in conventional CDT, said Dr. McNamara, an EKOS consultant. ■

Metabolic Syndrome, Elevated Biomarker Compound Heart Risk

BARCELONA — Elevated lipoprotein-associated phospholipase A2 and metabolic syndrome are additive in their predictive power for future cardiovascular events, Dr. Margaretha Persson said at the joint congress of the European Society of Cardiology and the World Heart Federation.

Lipoprotein-associated phospholipase A2 (Lp-PLA2) is a novel biomarker reflecting a proinflammatory state. Findings show it is an independent predictor of cardiovascular risk in the Atherosclerosis Risk in Communities Study (Circulation 2004;109:837-42) and the Rotterdam Study (Circulation 2005;111:570-5). Metabolic syndrome (MS) is also associated with systemic inflammation and increased cardiovascular risk.

Dr. Persson analyzed 10-year follow-up data on 4,480 healthy middle-aged nondiabetic participants in the Malmo (Sweden) Diet and Cancer Cardiovascular Cohort. The baseline prevalence of MS was 14% in women and 20.5% in men. Mean plasma Lp-PLA2 activity was 51 nmol/mL per minute in those with MS and 43 nmol/mL per minute in those without. Of those with MS, 51% had an Lp-PLA2 level in the top tertile, compared with 30% of those without.

The more components of MS an individual had, the higher the Lp-PLA2.

The presence of MS and high Lp-PLA2 were independent of age, gender, smoking status, and LDL-cholesterol level. Subjects with high Lp-PLA2 had an adjusted 50% increased relative risk of having a first MI or ischemic stroke during 10 years of follow-up, compared with those with an Lp-PLA2 in the lower two tertiles. Those with MS had a 67% increased risk, compared with those without MS. Subjects with both MS and high Lp-PLA2 had a 118% increase in risk, compared with those with neither, according to Dr. Persson of Malmo University Hospital.

Her study was sponsored by GlaxoSmithKline. The company's Diadexus PLAC blood test is Food and Drug Administration–approved for measurement of Lp-PLA2. ■