Who Should Get Long-Term Venous Prophylaxis?

Studies are needed to identify the risk factors for the recurrence of pulmonary embolism.

ARTICLES BY
JANE SALODOF MACNEIL
Southwest Bureau

NICE, FRANCE — Now that safe and effective thrombolytic agents are available for short-term treatment of venous disease, Patrick Mismetti, M.D., has two questions he would like to see answered.

The first is how long to treat venous disease in high-risk patients. The second is, how can clinicians identify those high-risk patients who need long-term preventive therapy?

"We have to evaluate optimal duration of treatment, because there is a place between 6 months and indefinitely," Dr. Mismetti said at the annual meeting of Cardiovascular and Interventional Radiological Society of Europe. He also called for an epidemiological study to identify patients at high risk of pulmonary embolism.

Physicians need to be able to individualize treatment, balancing the risk of disease recurrence against the risk of bleeding, according to Dr. Mismetti of the Thrombosis Research Group in Saint-Etienne, France.

"We have to try to identify patients at high risk of deep venous disease advancing in order to be aggressive in these patients and to use moderate treatment in other patients," he said in an interview.

For short-term treatment, he told meeting attendees that low–molecular weight heparin or fondaparinux is preferred. Both are effective and as safe as unfractionated heparin in most patients. Although it is more difficult to administer, he said, unfractionated heparin should be used in patients at risk of major bleeding or severe renal insufficiency.

'We have to try to identify patients at high risk of deep venous disease advancing in order to be aggressive in these patients and to use moderate treatment in other patients.'

Long-term treatment reduced recurrences of venous disease in several studies cited by Dr. Mismetti. In one trial, comparing 1 month of therapy after a first episode with 3 months, the rate of recurrence at 1 year fell from 11.4% to 6.4% with the longer treatment (Thromb. Haemost. 1995:74:605-11).

In another study, comparing 1.5 months and 6 months of treatment, the recurrence rates at 2 years were 18.1% and 9.5%, respectively (N. Engl. J. Med. 1995:332:1661-5).

"In both cases, longer duration was associated with significant decrease in deep venous disease recurrences," Dr. Mismetti said. "However, in certain circumstances, this short treatment of 3 months is not sufficient. We know people who need more treatment."

For patients who have had a second episode, he cited a study comparing 6 months of treatment to indefinite therapy. Recurrences fell from 20.7% to 2.6% at 4 years with the longer treatment. Risk of major bleeding increased, however, from 2.7% to 8.6% (N. Engl. J. Med. 1997; 336:393-8).

Another placebo-controlled trial was stopped in patients with ideopathic venous disease, he added, because of the high rate of recurrence in patients who did not receive long-term treatment: 27.4% vs. 1.3% (N. Engl. J. Med. 1999;340:901-7).

Although 12 months is now recommended for some patients with idiopathic disease or a second episode, Dr. Mismetti questioned whether that was enough for those at high risk.

Use of a vena cava filter is another issue that needs further study, according to Dr. Mismetti. He was an investigator in the PREPIC (Prévention du Risque d'Embolie Pulmonaire par Interruption Cave) trial, which this summer reported filters reduced risk of pulmonary embolism but increased risk of deep venous thrombosis (Circulation 2005;112:416-22).

Studies are needed to identify the risk factors for recurrence of pulmonary embolism, he said, adding that the group hopes to start a second clinical trial next year.

Scott O. Trerotola, M.D., chair of the meeting session on venous disease, questioned why Dr. Mismetti did not support use of catheter-directed thrombolysis. Dr. Trerotola, of the University of Pennsylvania in Philadelphia, said a randomized study has shown "dramatic improvement" with the technique (Eur. J. Vasc. Endovasc. Surg. 2002;24:209-14).

"I have to present evidence-based medicine, and I try to do it," Dr. Mismetti replied. "But we have some little experience with this technique, and the weight of deep venous disease recurrence is very high in our small clinical experience."

"Clearly, for us in the DVT lysis community, the challenge is there to do these trials," said Dr. Tretorola, noting that several clinical studies are underway.

In an interview, he added that a challenge to validating deep vein thrombolysis is that it works best in clots that are 7-10 days old. Given that many patients are now sent home with low–molecular weight heparin, he said, interventional radiologists often are not called until 2 and 3 weeks later in difficult cases.

"We used to have the opportunity to capture these patients while they were in the hospital and offer treatment for DVT," he said. "Now we don't, because they're out." ■

Look for DVT When Diagnosing Pulmonary Embolism

NICE, FRANCE — When pulmonary embolism is suspected, clinicians also should be looking for thromboembolic disease in the venous system, Christian J. Herold, M.D., said at the annual meeting of the Cardiovascular and Interventional Radiological Society of Europe.

"In my experience, there is limited awareness regarding the role of the lower-extremity venous system as the prime source of pulmonary embolism," said Dr. Herold, a radiologist at the University of Vienna Medical Center.

'There is limited awareness regarding the role of the lower-extremity venous system as the prime source of pulmonary embolism.'

Pulmonary embolism and deep venous thrombosis are components of the same thromboembolic disease complex, Dr. Herold stressed.

He explained that as many as 70% of patients with proven pulmonary embolism also have proximal deep vein thrombosis.

Dr. Herold said the probability of pulmonary embolism should be assessed for every patient where the condition is suspected.

Imaging studies must be done in every patient with a moderate to high probability of pulmonary embolism.

"Diagnosis is very important because mortality is very high in undiagnosed and untreated patients," he warned, putting the death rate in these patients at 10%-30% and emphasizing that the first week can be critical. "Unfortunately … many patients go unrecognized."

Clinicians at his institution last year examined 4,250 patients for venous thromboembolic disease, Dr. Herold reported at the meeting.

The process relies heavily on CT and an easy to follow algorithm that is taught to medical residents at the hospital.

He said alternative diagnoses should be considered since ruling out pulmonary embolism does not mean the patient is disease free.

In one study, Dr. Herold noted, 70% of patients with suspicion of pulmonary embolism did not have pulmonary embolism.

"Many had alternative diagnoses, and CT provides you this information," Dr. Herold advised, adding that "CT has evolved into an unofficial gold standard for analyzing pulmonary arteries."

He urged that CT angiography and CT venography both be used when venous disease is suspected. "There is information in the body that you can retrieve using the same examination, the same bolus," he said.

His group does CT venography 3 minutes after the pulmonary artery examination. "We prefer to do discontinuous slices with 3- to 4-cm gaps," he said. "We don't miss clots with this technique."

According to the medical literature, he added, CT venography has a sensitivity of 95%-100% and specificity of 97%-100%. He said studies in more than 5,300 patients have shown CT angiography to have a negative predictive value of 99%-100%, and that, therefore, it can be used to rule out treatment.

The radiologist cautioned, however, that in some patients, this rule does not always hold true. "All those guidelines and rules do not really account for 100% of patients. You may have individualized exceptions. And each patient has to be treated as an individual," Dr. Herold advised. ■

Diagnosing Thromboembolic Disease: Keep the Process Simple

Many combinations of tests have been promoted as ideal algorithms for diagnosing pulmonary embolisms, Dr. Herold said.

Most are too complex. He urged institutions to develop their own simple approaches. As an example, he offered the following:

► All patients with intermediate or high clinical probability of pulmonary embolism (independent from any other clinical or laboratory result) must be imaged.

► Clinical symptoms determine the region to be imaged.

► No further imaging is required to institute treatment in a patient whose primary examination is positive.

► If the patient has a moderate or high clinical probability for pulmonary embolism and the primary imaging exam is negative, assess the complementary region with CT angiography, CT venography, and ultrasound.

► If the patient has a low clinical probability of pulmonary embolism, D-dimer tests can help determine whether imaging is necessary.

Dr. Herold noted that most algorithms involve CT angiography, D-dimer testing, and ultrasound. Lung ventilation-perfusion scanning and pulmonary angiography are rarely used, he said.