ADVISER'S VIEWPOINT

Probability Assessment Key to PE

Use of validated pretest probability assessments to predict the likelihood of a patient's having a pulmonary embolism offers a high-quality approach to care at a relatively low cost. But a recent study presented at the international conference of the American Thoracic Society and highlighted in this issue of HOSPITALIST NEWS ("Scans for PE Done Without Suitable Risk Assessment," p. 1) shows that this is often not the approach taken in the hospital.

BY ROBERT PENDLETON, M.D.

The 8-year, single-center study conducted by Dr. Subani Chandra and her colleagues at the Long Island Jewish Medical Center in New Hyde Park, N.Y., found that only about 2%-3% of physicians who ordered computed tomography pulmonary angiography (CTPA) for suspected acute PE documented a pretest probability (PTP) assessment. While this study was conducted only at a single center, it is certainly consistent with what most physicians in clinical practice observe. The question is, does taking time to assess PTP matter?

The evidence is strong in favor of making PTP assessments for suspected PE the standard of care. Major diagnostic errors occur when we don't use PTP assessments. Most nonexpert clinicians are inaccurate in their "gestalt" of the likelihood of PE. Also, studies have shown that about 40% of patients with a high PTP score but a negative CTPA will have a PE that is missed during imaging (N. Engl. J. Med. 2006;354:2317-27). Conversely, about 40% of patients who have a positive CTPA and a low PTP assessment actually have false-positive studies. This carries its own potential for harm, such as when patients with false-positive studies are exposed to anticoagulants.

The study by Dr. Chandra and her colleagues drives home the point that when it comes to PE, the stakes are high. This is not only about providing the highest-quality care, but doing so in the most cost-conscious manner. For example, a complete PTP assessment (e.g., Well's score or Geneva score) costs approximately $100-$300. If you couple that with the $30 for a D-dimer blood assay, the total cost for ruling out PE in up to a third of patients is only $130-$330. This is a striking contrast to CTPA, which can cost up to $1,800. When we fail to take an evidence-based approach, we are not only making poor clinical decisions, we are also doing so at greater cost.

There is a need for more education to make hospitalists and other physicians aware of the data supporting the benefits of PTP assessments. Developing methodology to allow for the seamless incorporation of PTP assessments into clinical work flow also is paramount. Until those two barriers are addressed, we'll continue to see a gap between what physicians should be doing and what is actually happening in clinical practice.

Key national organizations like the Society of Hospital Medicine and the North American Thrombosis Forum have an opportunity to exert real influence and shape the educational content and outreach in this area. But they must reach out, including to hospitals in rural areas with few hospitalists. Reaching those hospitals is a major challenge, but one that has to be addressed if we're ever going to achieve real change in the assessment of PE. ■

DR. PENDLETON is director of the University of Utah's thrombosis service and codirector of its hospitalist program in Salt Lake City.

Pretest Before Scanning

Risk Assessment *from page 1*

fear of missing the diagnosis of PE that is very real. That governs their decision to just get a CAT scan without conducting a pretest probability assessment."

She and her associates evaluated the use of CTPA in the diagnosis of suspected acute PE in 850 patients who presented to Long Island Jewish Medical Center, New Hyde Park, N.Y., in 2000, 2005, and 2008. Then they used the Revised Geneva Score to retrospectively assign pretest probability of PE to each patient.

The total number of CTPAs performed for suspected PE stood at 87 in 2000 but jumped to 1,115 in 2005 and to 1,883 in 2008, reported Dr. Chandra, a second-year fellow in the division of pulmonary and critical care at the medical center. In contrast, the percentage of CTPAs that were positive for PE declined during the same period, from 30% in 2000 to 20% in 2005 to 15% in 2008.

In 2000, 47% of CTPAs ordered in the emergency department were positive for acute PE, compared with 26% in the department of medicine and 21% in the department of surgery. In 2005, the CTPA yield decreased to 22% in the emergency department and to 17% in the department of medicine, but increased to 28% in the department of surgery. In 2008, the CTPA yield dropped further to 14% in the emergency department and to 16% in the department of medicine, but remained 28% in the department of surgery.

Dr. Chandra also reported that few physicians who ordered a CTPA for suspected acute PE documented assessment of pretest probability (2% in 2005 and 3% in 2008; data were not available for 2000).

"After retrospective assignment of pretest probability of PE, only a minority of patients in the low and intermediate probability group had D-dimer levels checked (20% in 2005 and 23% in 2008)," the researchers wrote in their poster. "None of the patients with a low or intermediate pretest probability of PE and a negative D-dimer had PE on CTPA. This highlights inappropriate use of CTPA."

She went on to note that in cases where CTPA was negative for PE, a previously unknown alternative diagnosis was found on CTPA in about one-fifth of patients.

Dr. Chandra had no conflicts to disclose.

Rivaroxaban Cut VTE Plus Death After Hip, Knee Surgery

BY MITCHEL L. ZOLER

BERLIN — Rivaroxaban, an investigational oral anticoagulant, significantly cut the combined rate of symptomatic venous thromboembolism and death, compared with enoxaparin, in orthopedic surgery patients in an analysis of four trials involving more than 12,000 patients.

Rivaroxaban produced this and other efficacy benefits vs. enoxaparin without causing a significant increase in most bleeding measures, Dr. Sylvia Haas said at the annual congress of the European Hematology Association.

The RECORD (Regulation of Coagulation in Orthopedic Surgery to Prevent Deep Vein Thrombosis and Pulmonary Embolism) trials 1-4 included two studies that enrolled patients following hip surgery, and two that enrolled knee surgery patients (N. Engl. J. Med. 2008; 358:2765-75; 2776-86; Lancet 2008; 372:31-9; 2009;373:1673-80).

Based on the evidence in these four studies with 6,000 orthopedic surgery patients treated with rivaroxaban, the Cardiovascular and Renal Drugs Advisory Committee of the Food and Drug Administration voted 15-2 in favor of approving the drug for this indication. Ortho-McNeil, which is developing the drug with Bayer, later announced that the FDA sent the company additional questions about the application, but did not ask for any new studies. In countries where it has been approved, rivaroxaban has been marketed as Xarelto.

Dr. Haas, a hematologist and professor of medicine at the Technical University of Munich, said she is a consultant to Bayer Schering Pharma, and is a consultant to, or serves on data and safety monitoring boards for, other drug companies.

A direct inhibitor of coagulation factor Xa, rivaroxaban has high oral bioavailability, rapid onset of action, a 5- to 9-hour half-life, and—importantly—a predictable anticoagulant effect that, unlike warfarin, requires no monitoring.

The primary outcome of the combined analysis was the incidence of symptomatic venous thromboembolism (VTE) and all-cause death during active treatment. This occurred in 0.6% of 6,183 patients on rivaroxaban and 1.3% of 6,200 patients on enoxaparin, a 58% relative risk reduction with rivaroxaban.

Rivaroxaban was significantly better than enoxaparin on a composite of death, MI, stroke, symptomatic VTE, and major bleeds. The composite occurred 96 times in the rivaroxaban patients and 139 times among those on enoxaparin, a 31% relative risk reduction with rivaroxaban.

Although patients on rivaroxaban had more major bleeds, surgical-site bleeds, and clinically relevant nonmajor bleeds, most of these categories showed no significant difference between the rivaroxaban and enoxaparin subgroups. The only exception was the combination of major bleeds and clinically relevant nonmajor bleeds, which occurred in 2.55% of patients on enoxaparin and 3.19% of those not on the drug. (See box.) ■

Rivaroxaban Compared With Enoxaparin

Measure	Rivaroxaban (n = 6,183)	Enoxaparin (n = 6,200)
Incidence of symptomatic VTE and all-cause death (primary end point)		
During treatment	0.6%*	1.3%
During first 12 days of treatment	0.5%*	1.0%
During treatment and follow-up (70 days)	0.8%*	1.6%
Incidence of death, MI, stroke, symptomatic VTE, and major bleeds during 70 days of follow-up	1.6%*	2.2%
Major bleeds during treatment	0.39%	0.21%
Major bleeds and clinically relevant nonmajor bleeds during treatment	3.19%	2.55%

* Significantly different from enoxaparin group.
Note: Data are from 12,383 patients in four RECORD trials.
Source: Dr. Haas