

reduced for patients with acute myocardial infarctions (odds ratio [OR], 0.48; 95% confidence interval [CI], 0.33-0.71). For the medical conditions studied taken together, mortality in the hospitals with resident-to-bed ratio of 1 compared with those with resident-to-bed ratio of 0 was also less (OR, 0.74; 95% CI, 0.61-0.89). Similarly, mortality was improved in the three other medical conditions excluding acute myocardial infarction (OR, 0.79; 95% CI, 0.63-0.98). Compared with hospitals in the 25th percentile of teaching intensity, hospitals in the 75th percentile of teaching intensity had an 11.1% relative mortality decrease, and those in the 90th percentile of teaching intensity had a 15.9% relative decrease in mortality for all the combined medical conditions.

Comment: This study raises a number of interesting questions about the impact of duty hour reform on in-hospital mortality. There are many possible explanations for the findings, including more attending involvement and more use of mid-level providers in response to the resident work hour restrictions. In addition, the failure of mortality rates to decrease in the surgical patients does not necessarily imply poor care of the surgical patients. Perhaps these patients were already getting excellent care, and this care was not affected by a decrease in work hours by the surgical residents. Nevertheless, surgical program directors must ask themselves whether they are doing well or whether they could be doing better, or perhaps both.

Idraparinux Versus Standard Therapy for Venous Thromboembolic Disease

The van Gogh Investigators. *N Engl J Med* 2007;357:1094-104

Conclusion: Once-weekly subcutaneous idraparinux for 3 to 6 months has efficacy similar to heparin plus a vitamin K antagonist for treatment of deep venous thrombosis (DVT). Idraparinux is inferior compared with standard therapy for treatment of patients with pulmonary embolism (PE).

Summary: Idraparinux is a long-acting synthetic inhibitor of factor X activity. Preliminary studies suggest that for treatment of venous thromboembolism (VTE), a fixed subcutaneous dose of idraparinux given once weekly is as effective and results in less bleeding than vitamin K antagonist (J Thrombosis Homeostasis 2004;2:47-53). In this study, the authors investigated the potential use of idraparinux as a substitute for standard therapy for VTE.

This is a report of two randomized, noninferiority, open-labeled trials comprising 2904 patients with DVT and 2215 patients with PE. Patients received either heparin, followed by adjusted doses of a vitamin K antagonist for 3 or 6 months, or subcutaneous idraparinux (2.5 mg once weekly) for 3 or 6 months. The primary end point was the 3-month incidence of symptomatic recurrent VTE. In the DVT study, the incidence of recurrent VTE at day 92 was 2.9% in the idraparinux group and 3.0% in the standard therapy group (odds ratio [OR], 0.98; 95% confidence interval [CI], 0.63-1.50). This result satisfied a prespecified noninferiority requirement. The rate of clinically important bleeding was 4.5% in the idraparinux group and 7.0% in the standard-therapy group ($P = .004$). At 6 months, the hazard ratio for recurrent VTE with idraparinux was 1.01. At 6 months, the bleeding rates were similar in the standard-therapy and idraparinux groups. In patients with PE, recurrence at day 92 was 3.4% in the idraparinux group and 1.6% in the standard therapy group (OR, 2.14; 95% CI, 1.21-3.78). This finding did not meet the prespecified noninferiority requirement.

Comment: The results suggest idraparinux is equally efficacious in the treatment of DVT as heparin followed by warfarin therapy. It appears to be inferior to heparin followed by warfarin therapy for treatment of PE. If additional studies support differences in clinical efficacy in treatment of DVT vs PE, a long-held concept that the same anticoagulant therapies can be used for DVT and PE will need to be re-addressed. Idraparinux is a promising new anticoagulant for treatment of DVT. The enthusiasm for this very long-acting agent, however, will likely be limited by lack of a specific antidote that can be administered during bleeding episodes.

Extended Prophylaxis of Venous Thromboembolism With Idraparinux

The van Gogh Investigators. *N Engl J Med* 2007;357:1105-12.

Conclusion: During a 6-month period of extended prophylaxis after treatment of venous thromboembolism (VTE), idraparinux effectively prevents recurrent VTE but has an increased risk of major hemorrhage.

Summary: This is one of two articles evaluating idraparinux in treatment of venous thromboembolism. (See also "Idraparinux Versus Standard Therapy for Venous Thromboembolic Disease" in this abstract section.) Because this novel factor Xa inhibitor has a long half-life and does not require laboratory monitoring, its use as an extended method of prophylaxis in patients requiring long-term prophylaxis against VTE seems attractive. This is especially so in that it appears to be as effective as heparin after warfarin therapy for treatment of deep venous thrombosis. In this study, the authors evaluated the efficacy and safety of a 6-month extension of prophylaxis against recurrent VTE using idraparinux in patients who had already received 6 months of prophylaxis with either idraparinux or a vitamin K antagonist. Patients were entered into the study if it was determined that anticoagulation beyond 6 months after an initial episode of VTE was

warranted. Patients were randomized to receive once-weekly injections of 2.5 mg of idraparinux or a placebo for 6 months, without monitoring. The primary efficacy end point was recurrent VTE, and the primary safety end point was major bleeding.

The study enrolled 1215 patients, 594 in the idraparinux group and 621 in the placebo group. The rate of recurrent VTE was 1.0% (6 of 594) in the idraparinux group and 3.7% (23 of 621) in the placebo group ($P = .002$). Patients in the idraparinux group had 11 major bleeding episodes, and the placebo group had none ($P < .001$). Three of the 11 bleeding episodes were fatal intracranial hemorrhages. Patients whose initial treatment after VTE was 6 months of a vitamin K antagonist were compared with patients whose initial treatment after VTE was 6 months of idraparinux. When subsequently treated with placebo, patients initially treated with 6 months of idraparinux had a lower overall incidence of recurrent VTE (0.7% vs 5.9%). Patients who received 6 additional months of idraparinux had a higher incidence of major bleeding (3.1% vs 0.9%).

Comment: The two abstracts on idraparinux in this month's issue of the *Journal of Vascular Surgery* indicate idraparinux is an effective anticoagulant for treatment of DVT and for extended prophylaxis of VTE. This article in particular, however, highlights a significant drawback of this drug, which is the lack of an effective antidote to administer during hemorrhagic episodes.

Prediction of Cerebral Hyperperfusion after Carotid Endarterectomy Using Cerebral Blood Volume Measured by Perfusion-Weighted MR Imaging Compared with Single-Photon Emission CT

Fukuda T, Ogasawara K, Kobayashi M, et al. *Am J Neuroradiology* 2007; 28:737-42.

Conclusion: In patients without contralateral internal carotid artery (ICA) occlusive disease, cerebral blood flow volume (CBV), as measured by perfusion-weighted magnetic resonance imaging (PWI), may identify patients at risk for cerebral hyperperfusion after carotid endarterectomy (CEA).

Summary: Cerebral hyperperfusion after CEA may result in intracranial hemorrhage and perhaps even impairment of cognitive function without associated intracranial hemorrhage (*J Neurosurg* 2005;102:38-44). Magnetic resonance imaging can characterize cerebral hyperperfusion using timed boluses of contrast agents and can provide quantitative hemodynamic values, such as CBV (*Stroke* 2006;37:388-92). In this study, the authors measured CBV using PWI in patients undergoing CEA for unilateral >70% ICA stenosis. Patients in this study did not have significant contralateral ICA occlusive disease. Fifty-four of the 70 patients had coexisting hypertension. With respect to their ICA stenosis, 46 were symptomatic and 24 were asymptomatic. Cerebral blood flow was measured using single-photon emission computed tomography (SPECT) before and immediately after CEA and on the third postoperative day.

There was a significant correlation between preoperative CBV as measured by PWI and increases in cerebral blood flow immediately after CEA ($R = 0.785$, $P < .0001$). Using a definition of hyperperfusion as a >100% increase in cerebral blood flow compared with preoperative values, hyperperfusion was observed in 7 of 15 patients (47%) with elevated preoperative CBV values. No patients with normal preoperative CBV values exhibited hyperperfusion after CEA. Elevated preoperative CBV was the only significant independent predictor of post-CEA hyperperfusion. A clinical hyperperfusion syndrome developed in two of the seven patients who displayed hyperperfusion immediately after CEA.

Comment: SPECT using an acetazolamide challenge can identify patients at risk for cerebral hyperperfusion after CEA (*Stroke* 2001; 32: 1567-73). Limited availability and high cost limits routine clinic use of SPECT. Perfusion weighted imaging, however, requires short scanning times and can be incorporated into clinical MRI examinations. This study suggests that patients at risk for cerebral hyperperfusion after intervention for high-grade ICA stenosis may potentially be identified using currently widely available technology.

Upper Extremity Deep Vein Thrombosis: A Community-Based Perspective

Spencer FA, Emery C, Lessard D, Goldberg RJ, and the Worcester Venous Thromboembolism Study Investigators. *Am J Med* 2007;120:678-84.

Conclusion: Upper extremity venous thrombosis (UEDVT) has different risk factors, incidents of pulmonary embolism (PE), and differences of timing and location of recurrent venous thromboembolism (VTE) compared with patients with lower extremity deep venous thrombosis (DVT).

Summary: The authors sought to compare risk factors, magnitude of venous thrombus, and management strategies in persons with UEDVT vs lower extremity DVT diagnosed in 1999. This population-based investigation involved review of medical records from Worcester, Massachusetts (population 478,000) that had had International Classification of Disease (9th revision) codes consistent with possible DVT during 1999. The age adjusted rate of UEDVT was 16 per 100,000 population (95% confidence

interval [CI], 13-20) compared with 91 per 100,000 population for lower extremity DVT (95% CI, 83-100). Compared with patients with lower extremity DVT, patients with UEDVT were more likely to have undergone recent central venous access, a cardiac procedure, or to have been in an intensive care unit. Short-term and 1-year recurrence rates of VTE and all-cause mortality were not different in patients with upper vs lower extremity DVT. Patients with UEDVT, however, were less likely to have PE at presentation or at follow-up compared with patients with lower extremity DVT. None of the patients presenting with UEDVT were diagnosed with simultaneous PE, whereas PE was recognized clinically in 15% of patients presenting with lower extremity DVT. At 30 days, only one patient with UEDVT was diagnosed with PE, and no other clinically recognizable PE occurred during a 1-year follow-up in the patients with UEDVT. Five patients with lower extremity DVT had a newly diagnosed PE within the first month, and clinically recognizable PE developed in seven patients by 1 year.

Intravenous heparin was used to treat 47.8% of patients with UEDVT vs 61.8% of those with lower extremity DVT ($P = .03$). Subcutaneous low-molecular-weight heparin was used in 69.6% of patients with UEDVT vs 70.5% of patients with lower extremity DVT ($P = .87$). At hospital discharge, warfarin therapy was more frequent in patients with lower extremity DVT than in those patients with UEDVT (73.7% vs 56.5%, $P = .004$).

Comment: The American College of Chest Physicians suggests UEDVT should be treated similarly to lower extremity DVT (Chest 2004; 126:401S-428S). The observations presented here suggest that despite a lower use of long-term anticoagulation, UEDVT may have a more benign prognosis than lower extremity DVT in terms of PE. Prospective randomized studies are clearly needed to optimize potential prophylactic treatment for patients at risk for UEDVT and therapeutic treatment for those who develop the disease.