Venous Thromboembolic Disease

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Physicians understand the importance of prompt diagnosis and therapy of venous thromboembolism. This is a common and potentially deadly disease. Many patients may have no symptoms of this disorder, yet face a significant risk of serious complications if undiagnosed and untreated. Venous duplex ultrasonography has become the diagnostic test of choice for deep venous thrombosis. Quantitative d-dimer levels may be very helpful in establishing the diagnosis of venous thrombosis. Helical (spiral) computed tomographic scans have replaced nuclear medicine ventilation-perfusion imaging for pulmonary embolus. So, the evolution of diagnostic methods has helped to identify patients with venous thromboembolism at an earlier stage of the disease. Treatment of venous thromboembolism has rapidly evolved over the past 40 years. Patients are often treated with subcutaneous low-molecular-weight heparins as outpatients, rather than admitted to hospital for continuous intravenous infusions of unfractionated heparin. This change in practice grew from a body of scientific literature supporting this advance.

Jaff MR. Venous Thromboembolic Disease. The Ochsner Journal 2002;4:6-8.

Venous thromboembolism (VTE) is the third most common cardiovascular disorder, behind myocardial infarction and stroke (1). It is estimated that over six million Americans will suffer from some manifestation of VTE. Methods of diagnosis have become more sophisticated, yet it is the understanding of the epidemiology, presentation, and natural history that ultimately leads to early diagnosis and treatment.

In a study of Swedish men born in 1913, the incidence of deep venous thrombosis (DVT) was 182 per 100,000 patient observation-years (2). The probability of a venous thromboembolic event was estimated to rise from 0.5% at age 50 years to 10.7% by age 80 years. The mortality associated with deep venous thrombosis is estimated to be 30% at 3-years after discharge (3).

Several risk factors predispose patients to develop venous thromboembolism (Table 1). These risk factors identify subsets of patients in whom the risk of venous thromboembolism formation is significant. Patients are divided into low, moderate, high, and very high risk (Table 2). In patients who are classified as very high risk for the formation of venous thromboemboli (i.e. patients undergoing total joint replacement), the incidence of proximal DVT is 10%-20%, with fatal pulmonary embolism rates of 1%-5%. In one study of outpatients with clinically suspected DVT, the presence or absence of risk factors was identified. Approximately 50% of 426 patients referred for evaluation of potential DVT had a major risk factor of immobilization, trauma, or recent surgery (4).

One would suspect that, given these identifiable risk factors for DVT, physicians would develop risk profiles for patients and provide aggressive prophylaxis against DVT. Unfortunately, this has not been found to be true. In a 30-year autopsy study of patients in a large medical center in Sweden, the incidence of venous thrombosis, pulmonary embolus, or fatal pulmonary embolism did not decrease over the 30-year period (5). Improvement in physician utilization of effective prophylactic measures is critical for the future reduction in morbidity and mortality from venous thromboemboli.

In a recent retrospective series of patients with a first DVT in Olmstead County, Minnesota over a 10-year period, the average annual incidence of in-hospital DVT was more than 100 times greater than the incidence among community based residents. The incidence did not decrease over the 10-year period, despite increasing awareness about the efficacy of prophylaxis (6).

The natural history of DVT has been clarified by a prospective series of 355 consecutive patients with a first episode of symptomatic DVT. The incidence of recurrent venous thromboembolism was 30.3% after 8 years. Hypercoagulable states and malignancy were major risks for recurrent events (7).

Table 1. Risk factors for venous thromboembolism.

- Increasing age
- Prolonged immobility/paralysis
- Prior episodes of venous thromboembolism
- Malignancy
- Major surgery (i.e. abdomen, pelvis, lower extremity orthopedic)
- Obesity
- Venous varicosities
- Major co-morbid medical illness (congestive heart failure, myocardial infarction, stroke with paralysis)
- Fracture of the pelvis or long bones of the lower limbs
- Oral contraceptive use

Table 2. Incidence of venous thromboembolism based on risk. Adapted from Geerts WH, Heit JA, Clagett GP, et al. Prevention of venous thromboembolism. Sixth ACCP Consensus Conference of Antithrombotic Therapy. Chest 2001;119 (suppl):132S-175S.

Level of Risk	Proximal DVT (%)	Pulmonary Embolus (%)	Fatal PE (%)
Low Risk	0.4	0.2	0.002
Moderate Risk	2-4	1-2	0.1-0.4
High Risk	4-8	2-4	0.4-1.0
Highest Risk	10-20	4-10	0.2-5

DVT= deep vein thrombosis; PE= pulmonary embolism

Diagnosis of DVT has evolved to center around venous duplex ultrasonography. This is the primary noninvasive screening test. It is reliable, inexpensive, and relatively easy to perform. Several series comparing duplex ultrasonography to ascending contrast venography in patients with suspected DVT demonstrated a sensitivity of 93% and specificity of 98% (8). Other potentially helpful diagnostic modalities include quantitative D-dimer assays and 3-dimensional 'spiral' computerized tomographic studies of the pulmonary arteries to more effectively diagnose pulmonary emboli.

The treatment of venous thromboemboli has rapidly changed over the past 10 years. The standard therapy, intravenous anticoagulation with unfractionated heparin, was first introduced as primary treatment of pulmonary emboli in 1960 (9). This landmark randomized trial resulted in extrapolation of the efficacy of heparin in pulmonary emboli to DVT. Improved understanding of heparin pharmacokinetics (10) and safer, more effective dosing regimens with weight-based nomograms (11), and optimal oral anticoagulant dosing with warfarin (12) revolutionized the therapy for this potentially lethal disorder. However, with the results of well-designed randomized clinical trials demonstrating equivalent efficacy and safety of low molecular weight heparins when compared with unfractionated heparin, a new era of antithrombotic therapy for venous thromboembolic disease arose (13).

Advantages of low molecular weight heparin compared with unfractionated heparin are numerous and include predictable dose-response curves, excellent subcutaneous absorption, lack of need for repeated measurements of anticoagulant effect, and the ability to treat appropriate patients out of hospital for their venous thromboembolic events. There also appears to be lower risk of heparin-induced thrombocytopenia (14) and heparin-associated osteoporosis (15).

The future of intervention for venous thromboembolic disease will include mechanical thrombectomy and thrombolytic therapy, novel antithrombotic agents, and potentially surgical intervention. This monograph is designed to provide a state-of-the-art analysis of current strategies for the diagnosis and management of deep vein thrombosis and pulmonary embolus.

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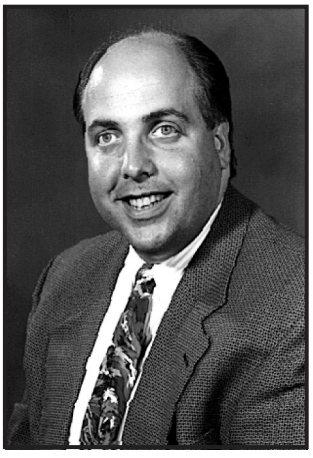

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