

Deep Vein Thrombosis and Pulmonary Embolism in the Perioperative Patient

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Presentation Summary

Approximately 500,000 cases of deep vein thrombosis (DVT) and pulmonary embolism (PE) occur in the United States each year. Of those patients who suffer a massive PE, 70% die within the first hour of symptom onset. Thus, early and aggressive intervention is essential. Clinical evaluation of patients is key in assessing clot risk and is aided by a variety of screening devices, with venography as the gold standard. Patients who undergo hip and knee arthroplasty are at highest risk for DVT and PE. However, appropriate

prophylaxis can reduce the incidence significantly. Although standard low-dose heparin is considered to be ineffective, positive experience with the administration of the low-molecular weight heparin (LMWH) enoxaparin, because of the speed of its efficacy in postoperative patients at high risk for DVT, has been reported. The dosage of enoxaparin is weight-adjusted and is sometimes combined with warfarin. Tools for risk-factor assessment and suggested prophylactic regimens for patients undergoing total hip and knee replacement are presented.

A practical approach to deep vein thrombosis (DVT) prophylaxis is essential because as many as 250,000 total hip and knee arthroplasties are performed in North America each year, and these patients are at a 70% risk of developing DVT postoperatively unless prophylactic measures are taken. Patients who present with lower extremity injuries are also highly susceptible to DVT at a rate of about 30% to 50%. These patients must also be aggressively treated prophylactically.

With good prophylaxis, DVT can be prevented, and some of the treatment issues can be put to rest. Nonetheless,

approximately 500,000 cases of DVT and pulmonary embolism (PE) occur in the United States each year. Approximately 70% of patients who suffer a massive PE die within the first hour of symptom onset.¹⁻⁴ In addition, the disease is unsuspected in most affected patients until after their deaths—up to 70% are diagnosed at autopsy.^{5,6} These disturbing statistics demonstrate the need for early and aggressive interventions with heparins, and the use of low-molecular weight heparins (LMWH) may revolutionize how these patients are treated in the future.

Complications resulting from venous thromboembolisms are severe

and can include death from PE, chronic pain, swelling, and skin ulceration secondary to postphlebitic syndrome. In addition, there may be side effects from treatment, particularly bleeding.

Pathogenesis of DVT

The pathogenesis of DVT in the perioperative period involves several components, including venous stasis, an acquired hypercoagulable state, endothelial injury, and the positioning of the limb during surgery. During hip replacement, for example, a substantial amount of torsion of the femoral vein occurs during insertion of the prosthesis, setting off thrombi intraoperatively. The procedure results in trauma, with the resultant activation of tissue factor and the clotting cascade, with a perioperative drop in antithrombin III levels. Inhibition of the fibrinolytic system also makes patients hypercoagulable, and they

often experience a dramatic reduction in venous capacity and outflow.

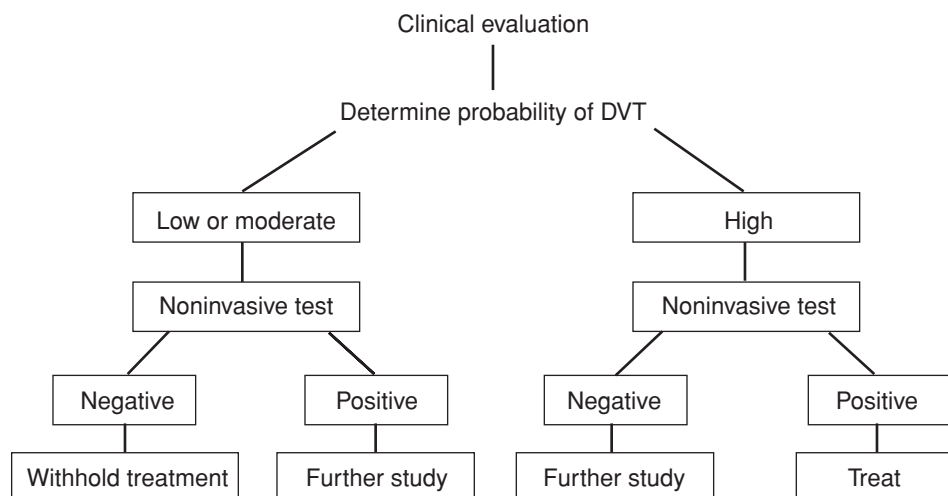
Detection of Venous Thrombosis

There are a variety of diagnostic tests for venous thrombosis, including radioactive fibrinogen scanning, impedance plethysmography, nuclear venography, technetium Tc 99m apcitide, Doppler screening, and venography.

Radioactive Fibrinogen Scanning.

Radioactive fibrinogen scanning is an outdated test, yet, it is nonetheless relevant because it serves as the foundation for most general surgery studies performed in the past. It is moderately sensitive in calf veins but less sensitive in femoral and iliac veins. The test poses a small risk of hepatitis from pooled serum and a potential risk for infection with the human immunodeficiency virus (HIV). In addition, the test is difficult to perform, there are frequent

Figure 1. Clinical Evaluation Algorithm to Determine Probability of DVT



DVT = deep vein thrombosis.

false positives, and the results are sometimes unavailable for 24 to 48 hours.

Impedance Plethysmography (IPG). IPG is an inexpensive and portable tool that detects alterations in the flow or volume response of the venous system. Reasonably sensitive from the knee up, it functions poorly in the detection of calf thrombi. The test is used to determine if a patient's blood flow has returned to baseline following treatment or prophylaxis. It is, however, limited in that it cannot distinguish between old thrombi and acute thrombi.

Nuclear Venography. Nuclear venography uses a radioactive tracer and gamma camera to detect thrombi. Somewhat less accurate than a venogram, which is considered the gold standard, nuclear venography is not useful for detecting clots in small vessels below the knee. However, the test poses no iodine allergy problem and allows the provider to check ventilation perfusion with a lung scan test while assessing the leg.

Technetium Tc 99m Apcitide. Technetium Tc 99m apcitide is a diagnostic radiopharmaceutical based on a synthetic peptide that binds to the GPIIb/IIIa adhesion-molecule receptors found on activated platelets. It is indicated for scintigraphic imaging of acute venous thrombosis in the lower extremities and may be an option for use in difficult patient types such as those who are obese or those with deep iliac clots.

Doppler Screening. Doppler screening, which uses Doppler-augmented ultrasound and IPG, is considered the "silver standard" of care, with sensitivity and specificity that is almost equivalent to that of the venogram. It is portable, with sensitivity greater than 90% in patients presenting with symptoms. However, Doppler screening is

much less reliable in asymptomatic patients and may be insensitive for use in calf vein thrombosis.

Venography. Venography is the gold standard in venous thrombus detection and can detect thrombi

In addition to diagnostic screenings, clinical evaluation of patients is critical in assessing clot risk.

from the ankle to the pelvis. The most highly sensitive and specific of all detection devices, it is able to detect constant intraluminal filling defects, abrupt termination of vessels, and collateralization of blood vessels. However, the test requires a skilled interpreter. Other disadvantages include its high cost (\$800 to \$1000), the potential for problems with iodine, the possibility of poor mixing of blood with dye, and a 1% incidence of phlebitis.

Clinical Evaluation of Probability of DVT

In addition to diagnostic screenings, clinical evaluation of patients is critical in assessing clot risk. The algorithm illustrated in Figure 1 is offered to determine from a clinical stand-point the probability of a patient having a clot. Frequently, the most difficult aspect of DVT is not prophylaxis or treatment, but rather diagnosis, primarily because tests are often inconclusive.

Epidemiology and Consequences

Patients who undergo hip and knee arthroplasty are routinely

given prophylaxis because they are at highest risk for DVT and PE, with rates as high as 40% to 60% if not treated. Up to 15% to 25% of patients experience proximal DVT, and 0.5% to 2% suffer fatal PEs when not treated prophylactically.^{7,8} The long-term economic implications of DVT are substantial. Approximately 25% to 50% of patients experience post-phlebotic syndrome 3 years after their initial episode, resulting in numerous readmissions and time lost from the workplace.

Postoperative DVT most often begins in the small veins in the calf, where it typically is small, silent, and asymptomatic. After a hip operation, 20% to 30% of cases originate in the proximal iliofemoral veins. The same proportion of calf vein DVTs propagate proximally.

Patients who develop DVT despite prophylaxis are at an increased risk for PE. The significance of calf thrombi after total knee replacement was investigated in a study of 1257 patients conducted by Haas et al in 1992.⁹ Using preoperative and postoperative ventilation perfusion scans and postoperative venograms to detect thrombi, the group found that the 655 patients with calf thrombi were at significantly higher risk for both symptomatic and asymptomatic PE, with 6.9% exhibiting a positive lung scan compared with 2% of patients with no venographic thrombi ($P < 0.001$). Of the 489 patients with a negative venogram, 2% had a positive lung scan and 0.2% had symptomatic PE, indicating that patients with negative venograms may still be at risk for PE.

The short-term prognosis of DVT is good when patients are treated with adequate doses of heparin followed by warfarin for 3 months, with recurrence rates of less than 5% in patients with proximal DVT, 2% within the initial treatment period, and 2% within the next 3 months.

LMWHs: Prophylaxis of Choice

Unfractionated heparin is often not much more effective than placebo in orthopedic populations, and standard low-dose heparin should not be used in hip and knee replacement. Some investigators have used adjusted-dose heparin, but extensive monitoring is required and it is being used much less frequently, making LMWHs the prophylaxis of choice for many clinicians for use in hip and knee replacement patients. LMWHs offer several advantages over conventional heparin, including their predictable action, which does not require laboratory monitoring; their subcutaneous route of administration; and their lessened effects on bleeding, platelets, and microvascular permeability.

Within a group of 60 orthopedic surgeons performing 20,000 surgeries annually at Baylor College of Medicine in Houston, Texas, positive experience was noted with enoxaparin in postoperative patients at high risk for DVT. Enoxaparin is rapidly effective, acting within 30 to 45 minutes.

Treatment Based on Risk-Factor Assessment

To determine risk, Methodist Hospital in Houston, Texas, uses a DVT prophylaxis risk factor assessment form, as shown in Figure 2. Patients are systematically assigned a score based on the number of risk factors present and are assigned to a risk category to determine a suggested but elective prophylaxis regimen.

Patients classified as moderate risk (Type I) are fairly active patients in the perioperative period and are typically discharged at day 3 to 5 following total knee or hip arthroplasty. They are normally active at home, have only one risk factor other than age, and have no prior history of DVT. Patients with multiple risk factors (Type II) are

Figure 2. The Methodist Hospital Deep Vein Thrombosis Prophylaxis Risk Factor Assessment

Assessment:
 (Check all pertinent factors; each risk factor has value of 1 point unless otherwise noted.)

Age 40 to 60 (1 point)
 Age 61 to 70 (2 points)
 Age over 70 (3 points)
 Documented history of DVT or PE (3 points)
 Family history of DVT or PE
 Leg swelling, ulcers, stasis, varicose veins
 History of pelvic or long bone fracture
 Lower extremity arthroscopy in patients > 50 years of age
 History of, or anticipated bed confinement/immobilization > 12 hours
 Confining air/ground travel (4 hours within 1 week of admission)
 Spinal cord injury with paralysis
 Stroke with paralysis
 Myocardial infarction / congestive heart failure
 Obesity (greater than 20% over ideal body weight)
 General anesthesia time > 2 hours
 Pregnancy, or postpartum < 1 month
 Multiple trauma
 Inflammatory bowel disease
 Inherited thrombophilia (3 points)
 Activated protein C resistance (factor V Leiden mutation)
 Antithrombin III deficiency
 Protein C or S deficiency
 Plasminogen or plasminogen activator deficiency
 Dysfibrinogenemia
 Antiphospholipid antibodies or Lupus anticoagulant (3 points)
 Nonhemorrhagic myeloproliferative disorders including polycythemia vera
 Hyperviscosity syndromes
 Estrogen hormone replacement therapy
 Name _____
 Dosage _____
 Other _____

Total Risk Factor Score _____

Risk Assignment Category			
Low Risk Score of ≤ 1, <i>or</i>	Moderate Risk Score of ≥ 2, <i>or</i>	High Risk Score of 3 or 4, <i>or</i>	Very High Risk Score of ≥ 3
Minor surgery	Major surgery and age ≥ 40 with no additional risk factors	Age ≥ 40 and major surgery; myocardial infarction and additional risk factors	Major surgery in patients age ≥ 40 and any of the following: <ul style="list-style-type: none"> • History of venous thromboembolism; • Hip fracture or total joint procedures of leg; • Stroke/spinal cord injury; • Visceral malignancy; • Additional risk factors

DVT = deep vein thrombosis; PE = pulmonary embolism.

Figure 3. Suggested Prophylaxis Regimens and Contraindications to Anticoagulation Therapy Based on the Methodist Hospital Risk Factor Assessment

Suggested Regimens for Prophylaxis in Each Risk Category			
Low Risk	Moderate Risk	High Risk	Very High Risk
<input type="checkbox"/> Early ambulation <input type="checkbox"/> Consider elastic stockings	<input type="checkbox"/> LDUFH every 8-12 hours <i>or</i> <input type="checkbox"/> SCD or +/- elastic stocking	<input type="checkbox"/> LDUH (5000 U every 8 hours and 2 hours preop) <i>or</i> <input type="checkbox"/> SCD or LMWH	<input type="checkbox"/> LMWH <i>or</i> <input type="checkbox"/> Oral anticoagulation with target INR 2.0-3.0 <i>or</i> <input type="checkbox"/> SCD + heparin (LMWH or LDUFH)
Contraindications to Anticoagulation Therapy: Relative (check if applicable) <ul style="list-style-type: none"> <input type="checkbox"/> Cerebral hemorrhage at any time previously <input type="checkbox"/> GI, GU bleed or stroke within past 6 months <input type="checkbox"/> Thrombocytopenia <input type="checkbox"/> Coagulopathy <input type="checkbox"/> Active intracranial lesions/neoplasms <input type="checkbox"/> Proliferative retinopathy <input type="checkbox"/> Vascular access/biopsy sites inaccessible to hemostatic control Absolute (check if applicable) <ul style="list-style-type: none"> <input type="checkbox"/> Active hemorrhage from wounds, drains, lesions <input type="checkbox"/> Heparin use in HITT <input type="checkbox"/> Warfarin use in pregnancy <input type="checkbox"/> Severe trauma to head, spinal cord, or extremities with hemorrhage within 4 weeks 			

GI = gastrointestinal; GU = genitourinary; HITT = heparin-induced thrombocytopenia and thrombosis; INR = international normalized ratio; LDUFH = low-dose unfractionated heparin; LMWH = low-molecular weight heparin; SCD = sequential compression device.

Table. Warfarin Prophylaxis Options for Total Knee and Hip Replacements

- Initiate either the night before, or the night of, surgery
- Target INR of 2.0 to 3.0 by day 5 postoperative
 - Keep in the lower range for the elderly or those at risk for bleeding
- Length of therapy: 4 to 6 weeks from initiation of therapy and to be completed as an outpatient
- Protime/INRs to be done Mondays and Thursdays as an outpatient for the first 2 weeks and then weekly afterward until therapy is completed
- If risk factors persist after 4 to 6 weeks, it is optional to continue anticoagulation for longer (3 months)

INR = international normalized ratio.

typically transferred to a rehabilitation service or skilled nursing facility before discharge. These patients are somewhat slower in rehabilitating and recovering range of motion. Type II patients possess at least 2 or 3 risk factors other than the surgery, including obesity and inactivity. This group includes orthopedic patients with 3 or more risk factors or with a prior history of documented DVT, and patients with a congenital or acquired thrombophilic state.

Suggested prophylaxis regimens and contraindications to anticoagulation therapy are outlined in Figure 3. Enoxaparin is administered based on weight and age guidelines. Patients are typically treated prophylactically with 30 mg of enoxaparin subcutaneously bid or every 12 hours, usually started the morning after surgery but within 24 hours unless bleeding is present. Enoxaparin dosages are weight-adjusted, based on experience that most bleeding following enoxaparin occurred in patients who weigh less than 100 lb.

Type I risk patients are given enoxaparin for 7 to 10 days and are discharged with instructions for self-administration of the drug. Patients with multiple risk factors or prior history of DVT (Type II) require extended prophylaxis with enoxaparin for 2 to 3 weeks to prevent thromboembolic complications.¹⁰ This should be followed by combined enoxaparin and warfarin until the patient becomes therapeutic on warfarin alone, which should be continued for 4 to 6 weeks or until risk factors disappear. Other therapeutic options for the use of warfarin are presented in the Table.

As part of the Houston Arthritis Institute pathway, enoxaparin is generally not administered on the day of surgery, but 18 to 30 hours after surgery. Previous attempts to administer the drug before surgery

resulted in some bleeding, leading the group to move toward postoperative administration of enoxaparin. To defray the risks of delaying drug therapy, the group uses intermittent pneumatic compression devices—a grade A, level 1 recommendation from the American College of Chest Physicians for patients undergoing total knee replacements. With the advent of LMWH, vena cava filters are used less frequently. However, when filters are used, warfarin anticoagulation may be necessary.

Conclusion

Clinicians need to look at every patient individually and practice prophylaxis for the patient, not the procedure. Diagnosing DVT is often difficult, but careful clinical assessment that may be complemented with diagnostic testing is crucial. Prophylaxis is key to preventing DVT, and LMWHs have revolutionized how patients are treated.

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