

Diagnosis of Lower-Extremity Deep Vein Thrombosis in Outpatients

A 68-year-old man was referred to your outpatient clinic following a cemented right hip arthroplasty procedure 3 weeks before your examination. He reports that he has had pain in his right calf and thigh since being discharged from the hospital and that these symptoms limit his ability to ambulate. He also reports difficulty getting in and out of bed. You find that he has a swollen right lower extremity and that he complains of pain when you palpate his right posterior calf and knee. You suspect that he may have a deep vein thrombosis (DVT), but you also consider that it is likely that the lower-extremity symptoms are attributable to the recent surgical procedure. Do you contact the patient's physician?

The diagnosis of DVT in patients who are hospitalized is well recognized, but DVT associated with outpatient care is less frequently discussed.¹ The purpose of this update is to summarize evidence-based approaches to the clinical examination of outpatients who are at risk for DVT. We also review radiological and laboratory-based diagnostic tests used to confirm or refute the diagnosis of DVT.

Venous thromboembolism (VTE) is a vascular disease that manifests as DVT or pulmonary embolism (PE). Both DVT and PE can be symptomatic or asymptomatic. Newly diagnosed cases of symptomatic VTE are estimated to occur in approximately 250,000 Americans per year, and DVT accounts for approximately two thirds of these cases.² Deep vein thrombosis most commonly appears in the lower extremity and is typically classified as being either proximal (affecting the popliteal and thigh veins) or distal (affecting the calf veins). Proximal deep vein thrombosis (PDVT) is the more dangerous form of lower-extremity DVT because it is more likely to cause life-threatening PE and may result in a greater risk of postthrombotic syndrome.^{3,4} Calf DVT, although less serious than PDVT, must be considered because the thrombus extends proximally in approximately 30% of cases.⁴

[Riddle DL, Wells PS. Diagnosis of lower-extremity deep vein thrombosis in outpatients. *Phys Ther.* 2004;84:729–735.]

Key Words: *Diagnosis, Venous thrombosis.*

Daniel L Riddle, Philip S Wells

Because PDVT is a potentially life-threatening disorder, physical therapists should be highly skilled at identifying outpatients who are at risk for PDVT.

Proximal deep vein thrombosis has a major impact on quality of life and can lead to death. The estimated case fatality rate is 5.1% following anticoagulant therapy.⁵ Postthrombotic syndrome, a chronic disorder characterized by leg swelling, pain, venous stasis, skin ulcers, and, in severe cases, amputation, is reported to occur in 17% to 50% of patients following PDVT.⁶ The costs associated with the examination and management of patients with PDVT are substantial. Hull and colleagues⁷ reported in 1997 that the costs associated with the diagnosis and management of PDVT are approximately \$4,000 per episode. Costs will presumably be higher for patients in whom a diagnosis of PDVT is missed.

Much research has been done to identify risk factors for PDVT, and these studies have been summarized in a recent article.⁸ Among the outpatients who are at highest risk for PDVT are those who have had major general surgery, major orthopedic surgery, and major trauma (Tab. 1). For example, PDVT is reported to be the most common complication following hip or knee arthroplasty and traumatic orthopedic injuries.⁹ In many cases, PDVT does not appear until after a patient has been discharged from the hospital and is being managed as an outpatient.^{10–12} If outpatients with PDVT can be identified earlier rather than later, the risk for severe morbidity and mortality potentially can be lessened.^{13,14}

Clinical Examination for PDVT

Most clinicians attempt to identify outpatients suspected of having PDVT by considering the patients' signs and symptoms and associated risk factors. For example, patients with symptomatic PDVT tend to complain of lower-extremity pain, calf tenderness, and lower-extremity swelling.^{14,15} However, approximately 75% of all patients who are suspected of having PDVT are found not to have PDVT when formal diagnostic testing is completed.^{16,17} Table 2 summarizes the various clinical conditions that potentially mimic symptoms associated with PDVT.¹⁸

Given that PDVT is a serious disorder with potentially life-threatening consequences, tests used by physical therapists to identify patients with PDVT should have a very high sensitivity (proportion of patients with the disorder who have a positive test) so that negative tests

would indicate that the clinician can confidently rule out the disorder.¹⁹ False negative tests would be potentially catastrophic in this case because the patient would actually have a PDVT even though the test result was negative. The therapist would potentially falsely conclude that referral to a physician is unnecessary.

The Homans sign is perhaps the most common clinical test for identifying patients who may have PDVT. Studies^{20,21} have demonstrated that the Homans sign has essentially no diagnostic value with sensitivities on the order of 50%. Other isolated clinical findings such as calf tenderness, swelling, and redness have been shown not to have diagnostic value for detecting PDVT.^{20–22} Because most physical therapists cannot prescribe formal diagnostic tests such as compression ultrasound, therapists need a method for determining when a patient with lower-extremity symptoms potentially attributable to PDVT should be referred for a diagnostic workup.

Use of Clinical Decision Rules for PDVT Diagnosis

Prior to the 1980s, research indicated that clinical diagnosis for PDVT was fraught with error and that clinicians were almost entirely dependent on radiological diagnostic tests to make the diagnosis of PDVT. More sophisticated methods for combining risk factors and signs and symptoms into a clinical diagnostic index (called clinical decision rules [CDRs] or clinical prediction rules) began to evolve in the 1980s and have become a commonly accepted evidence-based approach to diagnosis.^{23,24} A *clinical decision rule* is defined as a clinical tool that quantifies the contributions that various components (clusters) of the patient's history and physical examination make toward the diagnosis.²⁵ These more sophisticated approaches to diagnosis many times do not rely on sensitivity or specificity estimates for clinical application

DL Riddle, PT, PhD, FAPTA, is Professor, Department of Physical Therapy, Medical College of Virginia Campus, Virginia Commonwealth University, Richmond, VA 23298-0224 (USA) (dlriddle@vcu.edu). Address all correspondence to Dr Riddle.

PS Wells, MD, Canada Research Chair in Thromboembolic Disease, is Professor, Department of Medicine and Clinical Epidemiology Unit, University of Ottawa and the Ottawa Health Research Institute, Ottawa, Ontario, Canada.

Both authors provided concept/idea, writing, and fund procurement.

This work was supported by a grant from the Agency for Healthcare Research and Quality (#RO3 HS13059–01).

Table 1.
Risk Factors for Deep Vein Thrombosis^a

Strong risk factors	
Fracture (pelvis, femur, tibia)	
Hip or knee replacement	
Major general surgery	
Major trauma	
Spinal cord injury	
Moderate risk factors	
Arthroscopic knee surgery	
Central venous lines	
Chemotherapy	
Congestive heart or respiratory failure	
Hormone replacement therapy	
Malignancy	
Oral contraceptive therapy	
Cerebrovascular accident	
Pregnancy/postpartum	
Previous venous thromboembolism	
Thrombophilia	
Weak risk factors	
Bed rest >3 days	
Immobility due to sitting (eg, prolonged air travel)	
Increasing age	
Laparoscopic surgery	
Obesity	
Pregnancy/antepartum	
Varicose veins	

^a Modified with permission from: Anderson FA Jr, Spencer FA. Risk factors for venous thromboembolism. *Circulation*. 2003;107(23 suppl 1):I9–I16.

but rather provide an estimate of the probability that a disorder is present. Instead of interpreting sensitivity or specificity for a test result and applying it to a clinical decision, the therapist using a CDR would determine the probability that the disorder of interest is present. Quantifying the degree of uncertainty associated with a clinical decision is considered a strength of CDRs. Because most of the clinically important information is incorporated into the CDR score, the clinician can be confident that the probability derived from the CDR is accurate.²⁶

A variety of CDRs have been developed to guide the examination of outpatients suspected of having a PDVT.^{12,17,27–30} Several important limitations exist for 3 of these CDRs.^{12,27,28} Landefeld and colleagues²⁷ reviewed the medical records of 355 patients with symptomatic PDVT who underwent ascending venography. Data on 76 clinical items were collected, and venograms (a gold standard diagnostic test for DVT) were interpreted according to standard criteria. Using data collected on 236 patients, the authors found 5 independent clinical predictors of PDVT: swelling above the knee of the affected lower extremity, swelling below the knee, recent immobility, presence of cancer, and fever. This study was not prospective and had a relatively small sample size. In addition, both inpatients and outpatients were studied, so the results may not be generalizable specifically to outpatients.²⁷

Table 2.
Conditions That May Mimic Symptoms Associated With Proximal Deep Vein Thrombosis^a

Category of Condition	Specific Examples
Musculoskeletal	Trauma, hematoma, myositis, tendinitis, Baker's cyst, synovitis, osteoarthritis, osteomyelitis, tumors, fractures
Neurological	Sciatica, lower-limb paralysis
Venous	Phlebitis, postthrombotic syndrome, compressed veins
Arterial	Acute arterial occlusions, a-v fistula
Generalized edema	Cardiogenic, nephrogenic, dysproteemic
Cutaneous	Dermatitis, cellulitis, lipoedema, panniculitis
Localized edema	Pregnancy, oral contraceptive intake, limb immobilization

^a Modified with permission from: Prandoni P, Mannucci PM. Deep vein thrombosis of the lower limbs: diagnosis and management. *Baillieres Best Pract Clin Haematol*. 1999;12:533–554.

Nypaver et al²⁸ also examined a relatively small sample of both inpatients and outpatients (N=299), and the examiners were not blinded to the diagnostic ultrasound results. Perrier and colleagues¹² prospectively examined 474 consecutive patients seen at the emergency wards of several hospitals. The preliminary diagnosis by the emergency department physician was DVT. The authors asked the physicians to rank the probability of DVT as low, moderate, or high “on the basis of risk factors for venous thromboembolism, symptoms and signs commonly encountered in PE or DVT, and the likelihood of an alternative diagnosis.”^{12(p191)} The study by Perrier et al has 2 limitations. The diagnostic approach was not validated on a second group of patients. Validation on a second sample is traditionally a required step in CDR validation.²⁵ In addition, the authors did not provide operational definitions for the items in the CDR. Clinicians would be unable to replicate the criteria for categorizing patients, because the authors did not provide definitions of the criteria to use to make probability judgments.

The CDR described by Wells and colleagues^{17,29,30} (Tab. 3) is the CDR that has been most commonly recommended for outpatients suspected of having PDVT.^{31–33} Wells and colleagues^{17,29,30} incorporated signs, symptoms, and risk factors for PDVT from the literature and from clinical experience to develop the CDR. The patient group used to develop the CDR consisted of 529 outpatients with a variety of disorders, and all patients were tested for the presence of PDVT by use of venography in all of the participating centers.¹⁷ Criteria for admission in all 3 studies^{17,29,30} were consecutive outpatients with lower-extremity pain or swelling in

Table 3.
Clinical Decision Rule Developed by Wells and Colleagues²⁹

Clinical Finding	Score ^a
Active cancer (within 6 months of diagnosis or palliative care)	1
Paralysis, paresis, or recent plaster immobilization of lower extremity	1
Recently bedridden >3 days or major surgery within 4 weeks of application of clinical decision rule	1
Localized tenderness along distribution of the deep venous system ^b	1
Entire lower-extremity swelling	1
Calf swelling by >3 cm compared with asymptomatic lower extremity ^c	1
Pitting edema (greater in the symptomatic lower extremity)	1
Collateral superficial veins (nonvaricose)	1
Alternative diagnosis as likely or greater than that of deep vein thrombosis ^d	-2

^aScore interpretation: ≤0=probability of proximal lower-extremity deep vein thrombosis (PDVT) of 3% (95% confidence interval [CI]=1.7%–5.9%), 1 or 2=probability of PDVT of 17% (95% CI=12%–23%), ≥3=probability of PDVT of 75% (95% CI=63%–84%).

^bTenderness along the deep venous system is assessed by firm palpation in the center of the posterior calf, the popliteal space, and along the area of the femoral vein in the anterior thigh and groin.

^cMeasured 10 cm below tibial tuberosity.

^dMost common alternative diagnoses are cellulitis, calf strain, and postoperative swelling.

whom diagnosis of PDVT could not be excluded by the referring physician based on clinical findings. The original CDR required the assessment of 12 signs, symptoms, or medical history findings such as whether the patient had calf swelling of greater than 3 cm (measured 10 cm below the tibial tuberosity), pitting edema, and the presence of paralysis.¹⁷ The authors used criteria established prior to the study to group patients into low-, moderate-, and high-probability groups based on the presence or absence of the 12 clinical findings. They found that the CDR could be used to group patients into a high-probability group (85% risk of PDVT), a moderate-probability group (33% risk of PDVT), or a low-probability group (5% risk of PDVT).

In a follow-up study³⁰ to their 1995 study,¹⁷ Wells et al used multiple logistic regression, a statistical approach for identifying several variables that can independently predict disease status, to simplify the CDR. Each item in the CDR was weighted (either 1 or -2) based on the significant beta coefficients that were kept in the logistic regression model. The authors found that 9 of the original 12 items were kept in the model (Tab. 3). All items in the model, with one exception, are clinical examination or medical history data. The “alternative diagnosis as likely or greater than that of DVT” item is not an examination finding, but requires a clinical decision of its own. Determining this requires knowledge

about signs, symptoms, and probabilities of other diagnoses. If a clinician is unable to make a reasonably accurate estimate of the likelihood of DVT relative to other disorders, the developers of the CDR recommend taking a conservative approach and assigning this item a score of 0. By giving this item a score of 0, a patient’s true probability of DVT may be overestimated, but this strategy would enhance the likelihood that PDVTs will not be missed.

In a third study,²⁹ Wells et al examined an additional 593 outpatients to prospectively validate the CDR developed in the second study.³⁰ The examiner sums the items in the CDR to create a total score (Tab. 3). Patients who had a score of 0 or less had a probability of PDVT of 3% (95% confidence interval [CI]=1.7%–5.9%), those who had a score of 1 or 2 had a probability of PDVT of 17% (95% CI=12%–23%), and those with a score of 3 or higher had a probability of PDVT of 75% (95% CI=63%–84%). The reliability of the judgments of probability (low, moderate, or high) was examined by comparing judgments made by physicians and nurses who participated in the study. The weighted kappa statistic value was .75, suggesting that physicians and nonphysicians can reliably administer the CDR. The probability estimates generated by Wells and colleagues have been confirmed by other groups of researchers.^{34,35}

Wells and colleagues^{29,30} recommend that the CDR be used in all cases in which the clinician suspects a patient’s signs or symptoms may be attributable to PDVT. For example, the clinician might apply the CDR to an outpatient who has undergone recent thoracic surgery if the patient is found to have unilateral lower-extremity swelling and calf pain. In this case, application of the CDR appears straightforward because alternative explanations for the lower-extremity symptoms are unlikely. Use of the CDR is less clear when a patient with a recent lower-extremity surgery or traumatic injury is being seen. This type of patient may have lower-extremity symptoms and signs that are consistent with PDVT, but these findings may be attributable to routine recovery following an injury or surgery. According to Wells and colleagues,^{29,30} whenever the clinician has some doubt about whether clinical findings are attributable to PDVT or routine recovery following surgery or an injury, the CDR should be used. Because of the serious consequences of potentially missing a PDVT, formal diagnostic testing is recommended whenever the clinician suspects that PDVT may be present.^{14,23,36}

Radiologic and Laboratory Testing for PDVT

Clinical practice guidelines^{31–33} suggest that the diagnostic accuracy of the CDR developed by Wells and colleagues^{29,30} in combination with radiological or laboratory diagnostic tests is superior to more traditional

methods of diagnosis. Outpatients with a low probability of PDVT, based on use of the CDR by Wells and colleagues,^{29,30} are most effectively and efficiently diagnosed by use of D-dimer testing, a simple blood test of fibrin degradation.³⁷⁻³⁹ D-dimer levels in the blood are increased by any condition that produces fibrin (eg, PDVT) and have been found to be the most useful blood markers of fibrinolysis.⁴⁰ D-dimer tests are generally highly sensitive but not highly specific, suggesting that negative tests are much more useful for ruling out PDVT than are positive tests for ruling in PDVT.^{36,41,42} The negative predictive value (proportion of patients with a negative test who do not have PDVT) for patients with a negative D-dimer blood test and a low clinical probability of PDVT is higher than 99%.^{38,42,43} Several different D-dimer assays are available, and some have been found to have better diagnostic capability than others.³⁶ When a patient has had a recent surgical procedure and is receiving anticoagulant treatment, the use of D-dimer is more controversial, because some reports^{44,45} suggest that the sensitivity or specificity is reduced.

Evidence suggests that patients judged to have a moderate or high probability of PDVT, based on the CDR developed by Wells and colleagues,^{29,30} should have a compression ultrasound test.^{37,43} The gold standard test for PDVT is considered to be venography, but because this test is invasive and carries some risk, it is typically not the first-choice test.⁴⁶

Compression ultrasound or duplex ultrasound of the venous system is a diagnostic procedure involving the use of a 3- to 7.5-MHz transducer to produce an image of the tested vein. The patient is typically positioned supine with the tested lower extremity laterally (externally) rotated. Compression is applied with the transducer to the extent that the skin is indented but arterial blood flow is not compromised. Compression is typically applied to the venous system from the inguinal region to the calf. When the vein that is being examined cannot be compressed (collapsed) during the procedure, the test is judged to be positive.¹⁴ Venous compressibility is most easily achieved in the larger veins of the thigh and posterior knee and has been found to be less valid for examining the smaller calf veins.⁴⁷ Compression ultrasonography is almost universally considered to be the first-choice diagnostic test for patients with symptomatic PDVT in the moderate- to high-probability groups.^{14,48} Sensitivity and specificity for compression ultrasonography average approximately 95% for detection of PDVT.⁴⁹ Serial testing is commonly recommended for patients in the moderate- and high-probability groups who have an initial negative diagnostic test, because the false negative rate for compressive ultrasound averages approximately 5%.¹⁴ Serial testing has been found to be

unnecessary for patients in the low-probability group who have a negative D-dimer test or a negative compression ultrasound.^{42,50} The Figure illustrates an algorithm that combines the CDR of Wells and colleagues^{29,30} with the diagnostic test of choice.

If we now return to our hypothetical patient, we can see that the patient would have a score of 1 on the CDR because he had recent major surgery (+1 on the CDR), swelling throughout the lower extremity (+1 on the CDR), and tenderness to palpation in the posterior calf and knee (+1 on the CDR), along with an alternative diagnosis at least as likely as PDVT (postoperative pain and swelling for a score of -2 on the CDR). The probability that this patient has PDVT is approximately 17%.²⁹ Given the potentially serious consequences associated with missing a PDVT, referral to a physician would appear to be appropriate. Because this patient has a moderate probability of PDVT, evidence suggests that the patient should have a compression ultrasound test.

Most experts contend that all patients who are suspected of having PDVT should undergo formal diagnostic testing even if the risk of PDVT is considered to be low.^{14,31,36} For physical therapists, the CDR would appear to have potential to assist them in the examination of outpatients suspected of having PDVT primarily in 2 ways. First, by applying the CDR, physical therapists will raise their awareness of the issue of PDVT and the more important evidence-based variables that increase a patient's risk for PDVT. Because PDVT is a potentially life-threatening disorder, physical therapists should be highly skilled, in our opinion, at identifying outpatients who are at risk for PDVT. Second, by using the CDR, physical therapists can guide the urgency with which a referral should be made to a physician. For example, if a patient is found to have a high probability of PDVT (a score of 3 or higher on the CDR), the physical therapist, in our opinion, should speak to the physician immediately and encourage a diagnostic workup that day. Because the probability for PDVT is approximately 75%, a diagnostic workup should be done immediately to reduce the risk of PE.²³

Clinical data used in isolation do not indicate which outpatients have a PDVT. The CDR recommended by Wells and colleagues^{29,30} appears to provide clinicians with a method for making reasonably accurate estimates of the probability of PDVT in outpatients who are suspected of having PDVT. Application of the CDR in combination with formal diagnostic tests that are matched to PDVT probability appears to be the most credible approach for diagnosing PDVT in outpatients.

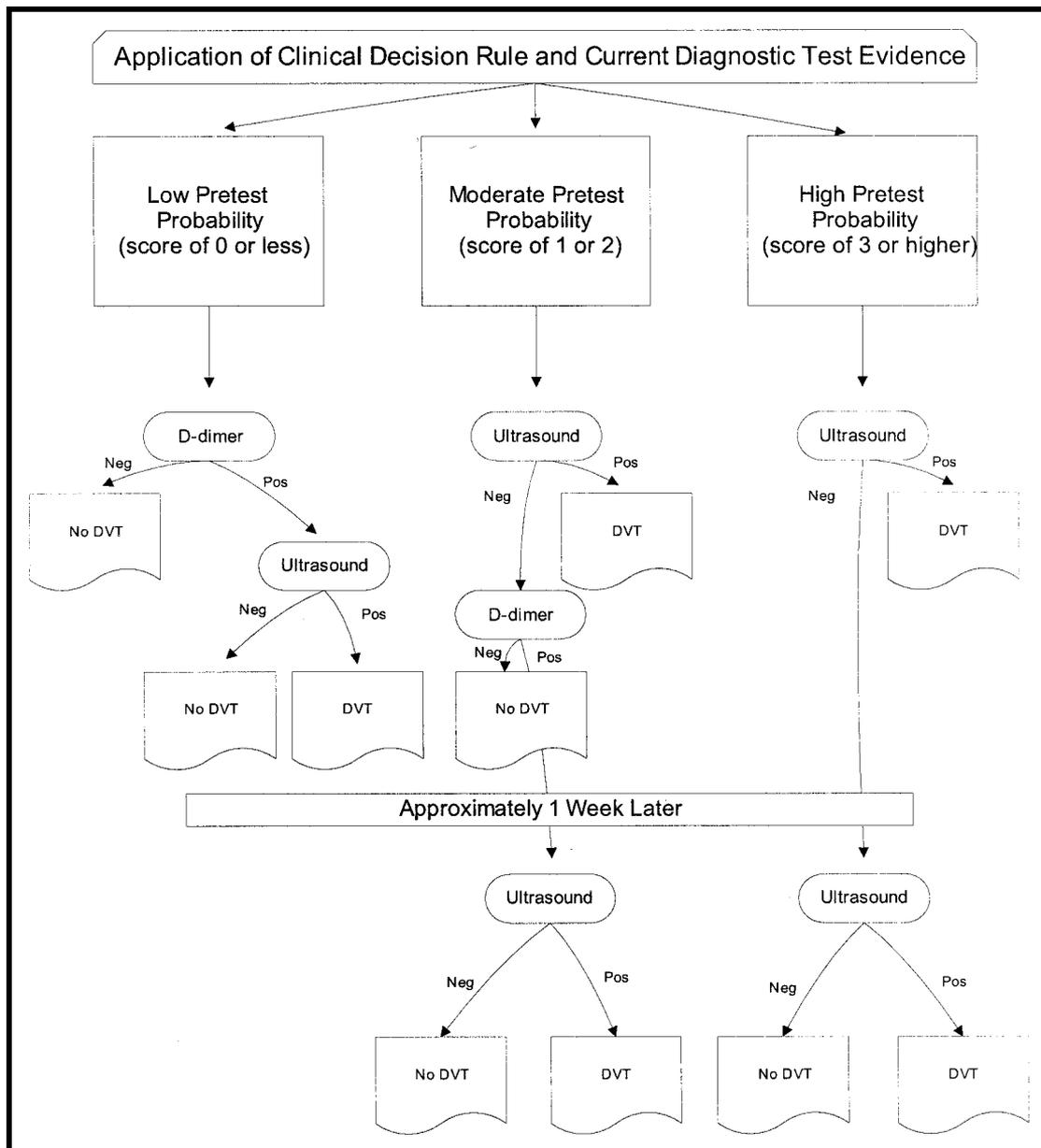


Figure. Algorithm for diagnosing deep vein thrombosis (DVT) in outpatients. Neg=negative, Pos=positive.

References

- 1 Janku GV, Paiement GD, Green HD. Prevention of venous thromboembolism in orthopedics in the United States. *Clin Orthop*. 1996;325:313-321.
- 2 White RH. The epidemiology of venous thromboembolism. *Circulation*. 2003;107(23 suppl 1):I4-I8.
- 3 Colman NC. Pathophysiology of pulmonary embolism. In: Leclerc JR, ed. *Venous Thromboembolic Disorders*. Philadelphia, Pa: Lea & Febiger; 1991:65-73.
- 4 Kearon C. Natural history of venous thromboembolism. *Circulation*. 2003;107(23 suppl 1):I22-I30.
- 5 Douketis JD, Kearon C, Bates S, et al. Risk of fatal pulmonary embolism in patients with treated venous thromboembolism. *JAMA*. 1998;279:458-462.
- 6 Kahn SR, Solymoss S, Lamping DL, et al. Long-term outcomes after deep vein thrombosis: postphlebotic syndrome and quality of life. *J Gen Intern Med*. 2000;15:425-429.
- 7 Hull RD, Raskob GE, Rosenbloom D, et al. Treatment of proximal vein thrombosis with subcutaneous low molecular weight heparin vs intravenous heparin: an economic perspective. *Arch Intern Med*. 1997;157:289-294.
- 8 Anderson FA Jr, Spencer FA. Risk factors for venous thromboembolism. *Circulation*. 2003;107(23 suppl 1):I9-I16.
- 9 Clagett GP, Anderson FA Jr, Heit J, et al. Prevention of venous thromboembolism. *Chest*. 1995;108(suppl):312s-334s.
- 10 Dahl OE, Gudmundsen TE, Haukeland L. Late-occurring clinical deep vein thrombosis in joint operated patients. *Acta Orthop Scand*. 2000;71:47-50.

- 11 Agnelli G, Sonaglia F. Prevention of venous thromboembolism. *Thromb Res.* 2000;97:V49–V62.
- 12 Perrier A, Desmairais S, Miron MJ, et al. Non-invasive diagnosis of venous thromboembolism in outpatients. *Lancet.* 1999;353:190–195.
- 13 Paiement GD, Mendelsohn C. The risk of venous thromboembolism in the orthopedic patient: epidemiological data. *Orthopedics.* 1997;20:7–9.
- 14 American Thoracic Society. The Diagnostic Approach to Acute Venous Thromboembolism. Clinical Practice Guideline. *Am J Respir Crit Care Med.* 1999;160:1043–1066.
- 15 Kahn SR. The clinical diagnosis of deep vein thrombosis: integrating incidence, risk factors and symptoms and signs. *Arch Intern Med.* 1998;158:2315–2323.
- 16 Heijboer H, Buller HR, Lensing A, et al. A comparison of real-time compression ultrasonography with impedance plethysmography for the diagnosis of deep-vein thrombosis in symptomatic outpatients. *N Engl J Med.* 1993;329:1365–1369.
- 17 Wells PS, Hirsh J, Anderson DR, et al. Accuracy of clinical assessment of deep-vein thrombosis. *Lancet.* 1995;345:1326–1330.
- 18 Prandoni P, Mannucci PM. Deep vein thrombosis of the lower limbs: diagnosis and management. *Baillieres Best Pract Clin Haematol.* 1999;12:533–554.
- 19 Sackett DL, Haynes RB, Guyatt GH, Tugwell P. *Clinical Epidemiology: A Basic Science for Clinical Medicine.* 2nd ed. Boston, Mass: Little, Brown and Co; 1991:70–77.
- 20 Richards KL, Armstrong JD Jr, Tikoff G, et al. Noninvasive diagnosis of deep venous thrombosis. *Arch Intern Med.* 1976;136:1091–1096.
- 21 O'Donnell TF, Abbott WM, Athanasoulis CA, et al. Diagnosis of deep venous thrombosis in the outpatient by venography. *Surg Gynecol Obstet.* 1980;150:69–74.
- 22 Haeger K. Problems of acute deep venous thrombosis, I: the interpretation of signs and symptoms. *Angiology.* 1969;20:219–223.
- 23 Anand SS, Wells PS, Hunt D, et al. Does this patient have deep vein thrombosis? *JAMA.* 1998;279:1094–1099.
- 24 Sackett DL, Strauss SE, Richardson WS, et al. *Evidence Based Medicine: How to Practice and Teach EBM.* 2nd ed. New York, NY: Churchill Livingstone Inc; 2000.
- 25 Laupacis A, Sekar N, Steill I. Clinical prediction rules: a review and suggested modification of the methodological standards. *JAMA.* 1997;277:488–494.
- 26 Guyatt G, Rennie D. *Users' Guides to the Medical Literature: A Manual for Evidence-Based Clinical Practice.* Chicago, Ill: American Medical Association; 2002:474–481.
- 27 Landefeld CS, McGuire E, Cohen AM. Clinical findings associated with acute proximal deep vein thrombosis: a basis for quantifying clinical judgment. *Am J Med.* 1990;88:382–388.
- 28 Nypaver TJ, Shepard AD, Kiell CS, et al. Outpatient duplex scanning for deep vein thrombosis: parameters predictive of a negative study result. *J Vasc Surg.* 1993;18:821–826.
- 29 Wells PS, Anderson DR, Bormanis J, et al. Value of assessment of pretest probability of deep-vein thrombosis in clinical management. *Lancet.* 1997;350:1795–1798.
- 30 Wells PS, Hirsh J, Anderson DR, et al. A simple clinical model for the diagnosis of deep vein thrombosis combined with impedance plethysmography: potential for an improvement in the diagnostic process. *J Intern Med.* 1998;243:15–23.
- 31 Segal JB, Eng J, Jenckes MW, et al. *Diagnosis and Treatment of Deep Venous Thrombosis and Pulmonary Embolism.* Evidence Report/Technology Assessment No. 68. Rockville, Md: Agency for Healthcare Research and Quality. March 2003. AHRQ publication 03-E016.
- 32 Finnish Medical Society Duodecim. Deep venous thrombosis. Helsinki, Finland: Duodecim Medical Publications Ltd; 2002. Available at: <http://www.ebm-guidelines.com>.
- 33 American College of Emergency Physicians–Medical Specialty Society. Clinical policy: critical issues in the evaluation and management of adult patients presenting with suspected lower-extremity deep venous thrombosis. *Ann Emerg Med.* 2003;42:124–135.
- 34 Scheibel NE, Spooner CH, Sukhrani N, et al. The validity of a clinical model to predict the presence or absence of deep vein thrombosis in the emergency department. *Acad Emerg Med.* 2001;8:560.
- 35 Kraaijenhagen RA, Piovella F, Bernardi E, et al. Simplification of the diagnostic management of suspected deep vein thrombosis. *Arch Intern Med.* 2002;162:907–911.
- 36 Kelly J, Rudd A, Lewis RR, Hunt BJ. Plasma D-dimers in the diagnosis of venous thromboembolism. *Arch Intern Med.* 2002;162:747–756.
- 37 Lennox AF, Delis KT, Serunkuma S, et al. Combination of a clinical risk assessment score and rapid whole blood D-dimer testing in the diagnosis of deep vein thrombosis in symptomatic patients. *J Vasc Surg.* 1999;30:794–803.
- 38 Wells PS, Anderson DR, Ginsberg J. Assessment of deep vein thrombosis or pulmonary embolism by the combined use of clinical model and noninvasive diagnostic tests. *Semin Thromb Hemost.* 2000;26:643–656.
- 39 Bates SM, Grand'Maison A, Johnston M, et al. A latex D-dimer reliably excludes venous thromboembolism. *Arch Intern Med.* 2001;161:447–453.
- 40 Hansson PO, Eriksson H, Eriksson E, et al. Can laboratory testing improve screening strategies for deep vein thrombosis at an emergency unit? *J Intern Med.* 1994;235:143–151.
- 41 Kearon C, Ginsberg JS, Douketis J, et al. Management of suspected deep vein thrombosis in outpatients by using clinical assessment and D-dimer testing. *Ann Intern Med.* 2001;135:108–111.
- 42 Kearon C, Ginsberg JS, Douketis J, et al. Diagnosis of a first DVT in outpatients: interim analysis of a management study based on clinical evaluation and D-dimer results. *Thromb Haemost.* 1997;78:588.
- 43 Michiels JJ, Freyburger G, Van Der Graaf F, et al. Strategies for the safe and effective exclusion and diagnosis of deep vein thrombosis by the sequential use of clinical score, D-dimer testing and compression ultrasonography. *Semin Thromb Hemost.* 2000;26:657–667.
- 44 Couturaud F, Kearon C, Bates SM, Ginsberg JS. Decrease in sensitivity of D-dimer for acute venous thromboembolism after starting anticoagulant therapy. *Blood Coagul Fibrinolysis.* 2002;13:241–246.
- 45 Siragusa S. Plasma D-dimer test accuracy can be affected by heparin administration [letter to the editor]. *Arch Intern Med.* 2003;163:246.
- 46 Chumilal SD, Ginsberg JS. Strategies for the diagnosis of deep vein thrombosis and pulmonary embolism. *Thromb Res.* 2000;97:V33–V48.
- 47 Pedersen OM, Aslaksen H, Vik-Mo H, Bassoe AM. Compression ultrasonography in hospitalized patients with suspected deep venous thrombosis. *Arch Intern Med.* 1991;151:2217–2220.
- 48 Ginsberg JS. Management of venous thromboembolism. *N Engl J Med.* 1996;335:1816–1828.
- 49 Baker WF. Diagnosis of deep vein thrombosis and pulmonary embolism. *Med Clin North Am.* 1998;82:459–476.
- 50 Anderson DR, Kovacs MJ, Kovacs G, et al. Combined use of clinical assessment and D-dimer to improve the management of patients presenting to the emergency department with suspected deep vein thrombosis (the EDITED Study). *J Thromb Haemost.* 2003;1:645–651.