

# Clinical Prediction of Deep Venous Thrombosis Using Two Risk Assessment Methods in Combination with Rapid Quantitative D-dimer Testing

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**PURPOSE:** The optimal approach to diagnosing deep venous thrombosis is not entirely clear. In this prospective cohort study, we aimed to evaluate the yield of two methods of assessing the pretest probability of deep venous thrombosis—the treating physician's implicit assessment and the Wells score, a validated prediction rule that incorporates signs, symptoms, and the presence or absence of an alternative diagnosis—used in isolation and in combination with D-dimer measurement.

**SUBJECTS AND METHODS:** We studied 278 patients who were referred for suspicion of deep venous thrombosis. All patients were stratified into groups of low, moderate, or high risk of deep venous thrombosis on the basis of the clinical assessment and Wells score, and underwent rapid quantitative D-dimer testing (with a cutoff of 500  $\mu\text{g}/\text{mL}$ ), ultrasound examination, and follow-up for the occurrence of venous thromboembolism.

**RESULTS:** Eighty-two patients (29%) had a deep venous

thrombosis. The accuracy of both methods was good (area under the receiver operating characteristic curve = 0.72), despite only fair agreement at the level of individual patients (weighted kappa = 0.31; 95% confidence interval [CI]: 0.23 to 0.40). The negative predictive value of D-dimer measurement was 96% (95% CI: 91% to 100%). When restricted to patients with low pretest probability, the negative predictive value of D-dimer measurement was 100% (95% CI: 96% to 100%) with the use of the Wells score and 96% (95% CI: 88% to 100%) with the physician's assessment. Our results were unchanged in analyses restricted to patients with proximal deep venous thrombosis or outpatients.

**CONCLUSION:** Clinical assessment to stratify a patient's likelihood of having deep venous thrombosis should be taught to physicians. *Am J Med.* 2002;112:198–203. ©2002 by Excerpta Medica, Inc.

The clinical diagnosis of deep venous thrombosis, which has been viewed as a clinical challenge for many years (1), has been improved through two innovations—the use of the standardized assessment of the clinical probability of deep venous thrombosis before performing a diagnostic test (i.e., the pretest probability) (2) and the measurement of D-dimer levels, which are products of fibrin degradation that increase with venous thromboembolism (3).

Wells and his colleagues developed and validated clinical criteria that stratify patients into low-, moderate-, and high-risk groups (4). We believed, however, that further evaluation of the Wells criteria was needed in three areas. First, this score was established after excluding patients with previous deep venous thrombosis, which is relatively common (10% to 35%) among patients in

whom a deep venous thrombosis is suspected (2,5,6). Furthermore, recommendations to use the Wells score do not specify that it was developed and validated in patients without previous deep venous thrombosis (7). Second, before encouraging the widespread dissemination and implementation of a newly proposed prediction rule, its performance should be assessed in other settings (8,9). Third, clinical experience suggests that medical educators or clinicians might be reluctant to teach, promote, or use prediction rules, preferring to recommend the clinician's general impression based on implicit clinical reasoning rather than explicit criteria (10). A comparison between the pretest probability of deep venous thrombosis provided by the Wells score and one given by the physician's implicit clinical assessment is warranted.

The measurement of plasma D-dimer levels has been established as a useful tool for the exclusion of deep venous thrombosis. Although many different assays are available, one of the most reliable testing methods is the rapid enzyme-linked immunosorbent assay (ELISA) (11). A negative result, defined as  $\leq 500 \mu\text{g}/\text{mL}$ , has a very high negative predictive value for the exclusion of lower limb deep venous thrombosis (3). Additional research on the clinical utility of D-dimer testing in patients with suspected recurrent deep venous thrombosis and on the

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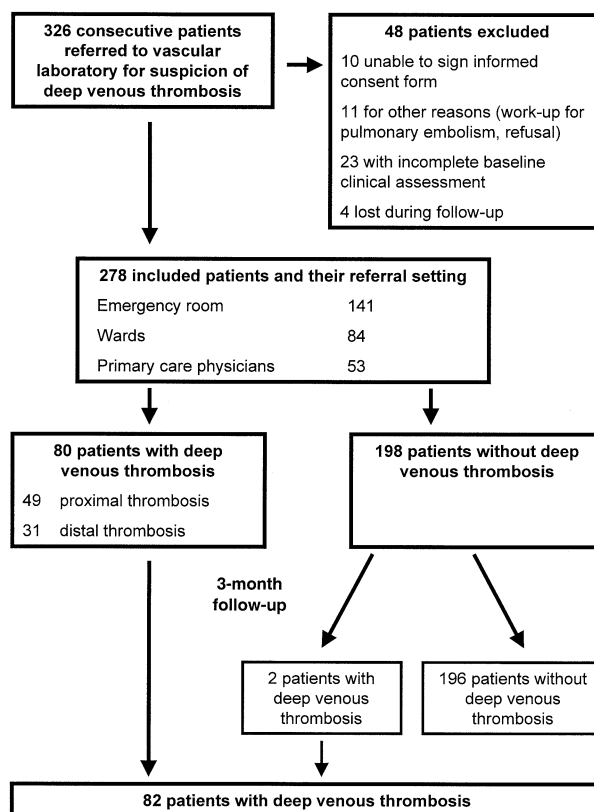
safety of avoiding venous ultrasound examination in patients who have low clinical probability and a negative D-dimer result has been recommended (12). We therefore performed a prospective cohort study comparing implicit clinical assessment and the Wells score, in isolation and in combination with rapid quantitative D-dimer measurements.

## POPULATION AND METHODS

Three hundred twenty-six consecutive adult patients were referred to the vascular laboratory of Lausanne University Hospital, Switzerland, because of a suspicion of a deep venous thrombosis. A patient was eligible if he or she had symptoms or signs of a deep venous thrombosis and was sufficiently fluent in French to understand and sign the informed consent form. Pregnant women were not eligible. We excluded 10 patients who were unable to sign the informed consent form, 3 who were admitted for pulmonary embolism work-up, 4 who were sent by their primary care physicians with information already available on D-dimer levels, 4 who refused to participate, and 4 who were lost during follow-up. We also excluded 23 patients for whom we did not have both a Wells score and a physician's assessment. The final cohort included 278 patients (Figure 1).

Study patients were assessed by a trained clinical nurse who used the Wells score. She was taught how to derive it during a pilot phase involving 20 patients. This score gives 1 point for each of these features: active cancer; paralysis, paresis, or recent immobilization; recently bedridden (for at least 3 days) or major surgery; tenderness localized in the deep venous system; entire leg swollen; calf swelling of more than 3 cm; pitting edema; and dilated superficial veins. An alternative diagnosis that is at least as likely as deep venous thrombosis counts for minus 2 points. A final score was then calculated: 3 or more points indicated a high probability of deep venous thrombosis, 1 or 2 points indicated a moderate probability, and less than 1 point indicated a low probability. The question about an alternative diagnosis was posed by the nurse to the physicians caring for the patient.

Patients were also classified as having a low (<20%), moderate (21% to 80%), or high probability (>80%) of deep venous thrombosis according to the physician's assessment. Physicians who were either third-year residents or chief residents were asked to base their clinical probability on the presence or absence of common clinical features for deep venous thrombosis. To encourage a uniform frame of mind for the physician's estimate, a list of such clinical features was made available in our intranet hospital network and published in a regional medical review (13).



**Figure 1.** Flow diagram for patients with suspected deep venous thrombosis in the study.

We asked the physicians and the research nurse to return their assessment form before the venous ultrasound result was made available. To ensure that the clinical nurse and the physicians were blinded to each other's assessment, we asked them to return their assessment sheets to two different locations. All physicians and the research nurse were blinded to the aim of the study; they were only informed that we were studying the assessment of the probability of deep venous thrombosis and outcomes of venous examination.

A blood sample was taken from each patient before the ultrasound examination was ordered and before heparin was administered. We measured ELISA D-dimer levels in citrated plasma. A negative result was defined as  $\leq 500$   $\mu\text{g/mL}$  (14,15). This sample was not available in 51 patients (18%) because of logistical issues (e.g., an ultrasound examination before a D-dimer test was performed).

All patients also underwent a lower limb duplex ultrasound examination within 24 hours by an experienced vascular physician who was blinded to the results of the clinical assessments and D-dimer levels. The assessment of lower limb veins included proximal and calf veins. The diagnosis was based on the presence of a noncompressible venous segment on ultrasound images (16,17). Com-

pressibility of the veins distal to the popliteal vein could be tested in all but 5 patients. If a patient had a high probability of deep venous thrombosis but for whom an ultrasound examination was not immediately available (e.g., admission between midnight and 7 AM), the recommendations were to obtain a blood sample for D-dimer measurement, to give a single dose of low molecular weight heparin, and to perform an ultrasound examination the next morning. After undergoing the venous examination, patients underwent additional tests based on the physician's pretest probability, D-dimer level results, and venous ultrasound examination (4,13).

Patients were followed by their primary care physicians. Three months after the index visit, a questionnaire was either sent by mail (65%) or administered by phone (35%) to all study patients to obtain follow-up information on the occurrence of deep venous thrombosis or pulmonary emboli (Figure 1). This follow-up information was validated by asking physicians to confirm the venous thrombotic event. Diagnosis of venous thromboembolic events was established with usual criteria (deep venous thrombosis with abnormal compression ultrasound, and pulmonary embolism by high probability ventilation-perfusion scan or abnormal angiogram). We used the combination of index visit testing and follow-up information as a gold standard for the final diagnosis. We also checked our hospital's medical record system for readmissions. Cause of death was ascertained by reviewing death certificates. Follow-up information was collected by a research assistant who was blinded to the final goal of the study.

The agreement between physicians' assessments and Wells scores was quantified by the weighted kappa ( $\kappa$ ), a measure of agreement beyond chance (18). This measure captures both complete and partial agreement (ie, disagreement of only one category between measures). Good agreement is usually defined as  $>0.60$  (19). The diagnostic performance of physicians and Wells predictions were assessed by the area under the receiver operating characteristic (ROC) curve. We constructed these curves by choosing two cutoff points: the first between low and moderate probability, and the second between moderate and high probability. We calculated the predictive values and the likelihood ratios (with their 95% confidence interval [CI]) of D-dimer results. We used the SAS statistical package (SAS Institute, Cary, North Carolina) for statistical analyses. The protocol was approved by the Ethics Committee of our institution.

## RESULTS

The mean ( $\pm$ SD) age of the patients was  $60 \pm 19$  years. The distribution of the clinical features, including those that constitute the Wells score, are listed in Table 1.

**Table 1.** Characteristics of the 278 Patients with Suspected Deep Venous Thrombosis

| Characteristic  | Number (%) |
|---|------------|
| Male sex  | 173 (62)   |
| History of previous deep venous thrombosis                            | 50 (18)    |
| Active cancer   | 27 (10)    |
| Paralysis, paresis, or recent immobilization of the lower extremities | 27 (10)    |
| Recently bedridden ( $>3$ days) or major surgery ( $<4$ weeks)        | 77 (28)    |
| Localized tenderness along the distribution of deep venous system     | 195 (70)   |
| Entire leg swollen  | 66 (24)    |
| Calf swelling ( $>3$ cm)  | 21 (8)     |
| Pitting edema   | 167 (60)   |
| Dilated superficial veins   | 51 (18)    |
| Alternative diagnosis   | 169 (61)   |
| Dermatitis/cellulitis   | 34 (20)    |
| Edema (from different origins)  | 30 (17)    |
| Superficial thrombophlebitis  | 26 (15)    |
| Muscular injury   | 18 (11)    |
| Venous insufficiency  | 16 (10)    |
| Baker's cyst  | 15 (9)     |
| Hematoma  | 7 (4)      |
| Other (e.g., sciatica, cramp)   | 23 (14)    |

Eighty-two patients (29%) had a final diagnosis of deep venous thrombosis; 80 of which were diagnosed at the index visit and 2 during the 3-month follow-up. Forty-nine patients (60%) had a proximal deep venous thrombosis. No pulmonary emboli were reported at 3-month follow-up, and venous thromboembolism was not the direct cause of death in the 5 patients who died during the follow-up.

About 80% of patients were classified in the moderate- or low-probability groups by both the Wells score and the physician's estimate, although the Wells score resulted in slightly lower probability assessments (Table 2). As the pretest probability scores went up, the proportion of patients with deep venous thrombosis also rose, from 13% in the low-probability categories to more than 60% in the high-probability categories (Table 2).

Agreement between the physician's assessment and Wells score was fair (weighted  $\kappa$  of 0.31; 95% CI: 0.23 to 0.40), suggesting that physicians drew on clinical features other than those listed in the Wells score to assess their pretest probability. However, the overall accuracy of the two clinical stratification methods, expressed as the area under the ROC curve, was similar for both methods at 0.72 (Figure 2). When we restricted the analysis to patients with proximal deep venous thrombosis, we found higher accuracies (0.78 for the physicians' estimates and 0.77 for the Wells score).

**Table 2.** Distribution of the Clinical Estimates of Deep Venous Thrombosis and the Prevalence of Deep Venous Thrombosis

| Risk Category                                    | Wells Score      | Physicians'                             |
|--|------------------|---|
|  |                  | Estimate                                |
|  |                  | Number<br>(% [95% Confidence Interval]) |
| Proportion of 278 patients in risk category      |                  |   |
| Low  | 109 (39 [33–45]) | 86 (31 [26–36])                         |
| Moderate   | 121 (44 [38–50]) | 127 (46 [40–52])                        |
| High   | 48 (17 [13–21])  | 65 (23 [18–28])                         |
| Deep venous thrombosis by assigned risk category |                  |   |
| Low  | 14 (13 [7–19])   | 11 (13 [6–20])                          |
| Moderate   | 36 (30 [22–38])  | 30 (24 [17–31])                         |
| High   | 32 (67 [54–70])  | 41 (63 [53–73])                         |

Among the 49 patients with D-dimer levels  $\leq 500$   $\mu\text{g}/\text{mL}$ , 2 were diagnosed with deep venous thrombosis (1 distal and 1 proximal). Thus, the overall negative predictive value of D-dimer measurement was 96% (Table 3). The negative predictive value of a D-dimer measurement with the same cutoff among patients with low pretest probability was 100% when this probability was derived from the Wells score, but 96% when it was assessed by the physician ordering the ultrasound. The strategy of not performing an ultrasound examination in patients with both a low pretest probability by Wells score and a D-dimer level  $\leq 500$   $\mu\text{g}/\text{mL}$  would have avoided 28 (10%) of

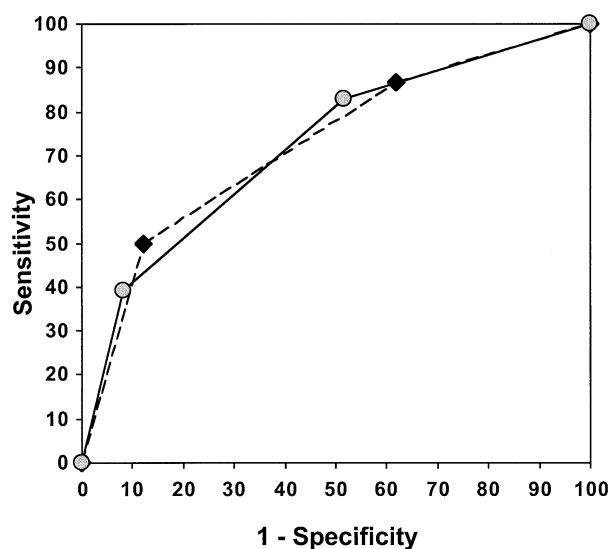
the ultrasound examinations that were performed in these 278 patients. As expressed as a likelihood ratio (Table 3), a negative D-dimer test (ie,  $\leq 500$   $\mu\text{g}/\text{mL}$ ) is very helpful, especially in the circumstance of low clinical probability, whereas a positive test does not add much information to the diagnostic work-up.

By restricting our results to only proximal deep venous thrombosis (49 patients), we found similar results. The overall negative predictive value of D-dimer measurement was 98% (95% CI: 92% to 100%). The negative predictive value was 100% (95% CI: 93% to 100%) among patients with low pretest probability either derived from the Wells score or assessed by the physician ordering the ultrasound examination.

Finally, when we restricted our analyses to outpatients (194 patients), we also found similar results. The overall negative predictive value of a D-dimer measurement  $\leq 500$   $\mu\text{g}/\text{mL}$  was 98% (95% CI: 94% to 100%). Among patients with low pretest probability, the negative predictive value of a D-dimer measurement  $\leq 500$   $\mu\text{g}/\text{mL}$  was 100% (95% CI: 95% to 100%) for Wells-derived probabilities and 95% (95% CI: 86% to 100%) for physician-derived probabilities.

## DISCUSSION

We found that implicit clinical assessment and the Wells score performed similarly for the prediction of deep venous thrombosis in this cohort of unselected patients. This suggests that physicians were able to translate their clinical impression into quantitative predictions that matched the accuracy of a rigorous clinical prediction rule, although the agreement between physicians' estimates and Wells score was only fair. We also found that pretest probabilities, derived either by the Wells prediction rule or by the physician's prediction, had similar accuracy when used in combination with rapid ELISA



**Figure 2.** Deep venous thrombosis diagnostic performance of two risk assessment methods expressed as the area under the receiver operating characteristic (ROC) curve. Diamonds represent physicians' estimates, with an area under the ROC curve of 0.72. Circles represent Wells score estimates, with an area under the ROC curve of 0.72.

**Table 3.** Predictive Values and Likelihood Ratios for D-dimer Testing (cutoff of 500  $\mu\text{g}/\text{mL}$ ) for All Patients, and for Patients with Low, Intermediate, and High Clinical Probability of Deep Venous Thrombosis, From Wells Scores and Physicians' Estimates

| Parameter                 | All Patients<br>(n = 281)           | Low-Risk Patients<br>(n = 88, 69)* | Moderate-Risk<br>Patients<br>(n = 78, 98)* | High-Risk<br>Patients<br>(n = 41, 60)* |
|---------------------------|-------------------------------------|------------------------------------|--|--|
|                           | Parameter (95% Confidence Interval) |                                    |  |  |
| No pretest probability    |                                     |                                    |  |  |
| Positive predictive value | 38% (25%–43%)                       |                                    |  |  |
| Negative predictive value | 96% (91%–100%)                      |                                    |  |  |
| Positive likelihood ratio | 1.39 (1.26–1.52)                    |                                    |  |  |
| Negative likelihood ratio | 0.09 (0.02–0.36)                    |                                    |  |  |
| By Wells score            |                                     |                                    |  |  |
| Positive predictive value |                                     | 16% (7%–25%)                       | 38% (28%–48%)                              | 73% (59%–87%)                          |
| Negative predictive value |                                     | 100% (96%–100%)                    | 90% (77%–100%)                             | 100% (80%–100%)                        |
| Positive likelihood ratio |                                     | 1.56 (1.25–1.93)                   | 1.28 (1.13–1.43)                           | 1.08 (1.01–1.26)                       |
| Negative likelihood ratio |                                     | 0.14 (0.3–0.61)                    | 0.22 (0.06–0.79)                           | 0.23 (0.17–1.0)                        |
| By physician's estimates  |                                     |                                    |  |  |
| Positive predictive value |                                     | 18% (7%–29%)                       | 26% (16%–36%)                              | 72% (60%–84%)                          |
| Negative predictive value |                                     | 96% (88%–100%)                     | 100% (96%–100%)                            | 83% (53%–100%)                         |
| Positive likelihood ratio |                                     | 1.44 (1.05–1.99)                   | 1.32 (1.14–1.52)                           | 1.30 (1.00–1.68)                       |
| Negative likelihood ratio |                                     | 0.28 (0.04–1.00)                   | 0.09 (0.01–0.44)                           | 0.10 (0.02–0.6)                        |

\* The pairs of numbers represent the numbers by Wells score and by physician's estimates.

D-dimer measurement for all types of deep venous thrombosis or when only applied to proximal deep venous thrombosis.

Our study has several strengths. First, we included all types of patients with a suspicion of deep venous thrombosis in the lower extremities, including those who reported a history of previous deep venous thrombosis. Our results suggest that the Wells score can be used in patients with a history of previous deep venous thrombosis, a relatively common situation. Second, we used a rapid and quantitative D-dimer test, one of the two tests with the highest sensitivity for the detection of deep venous thrombosis (11). Third, we used this test in a large sample of patients with suspected deep venous thrombosis, including older patients who have a greater probability of false positive D-dimer results because they often have nonthrombotic disorders that increase D-dimer levels. A fourth strength of this study is that we followed patients for subsequent clinical events.

Previous studies have either used a nonvalidated scoring system (6) or a nonquantitative D-dimer assay (6,20), did not apply a gold standard (6,20), or did not use a prospective design to validate their clinical approach (20,21). In a study performed in 165 patients with a suspected first episode of deep venous thrombosis, the comparison of the resident's empirical estimate of clinical probability with the score computed by a senior specialist also revealed only fair agreement ( $\kappa = 0.29$ ) (22).

Our study has some limitations. First, we did not obtain D-dimer measurements in 51 patients. Second, one of the 2 patients with a deep venous thrombosis and a

D-dimer level  $\leq 500 \mu\text{g}/\text{mL}$  had a deep venous thrombosis in the calf diagnosed on ultrasound examination, which is not yet recognized as the gold standard for that diagnosis. However, outcome studies have been reassuring on the yield of such examinations (13,23–25). The low D-dimer levels in patients with distal deep venous thrombosis might have been due to the small thrombi. Third, contamination of physicians' assessment by the use of the Wells score or by talking with the clinical nurse may have been possible, although we tried to minimize this bias by asking the nurse to avoid any discussion of the likelihood of deep venous thrombosis with physicians. Finally, the question related to the alternative diagnosis—a critical item with an important weight in the final probability—was asked by the clinical nurse of the physician caring for the patient after that physician had given his own empirical assessment.

Management of patients with suspected deep venous thrombosis based on clinical probability (assessed either by the Wells score or physician's implicit assessment) and D-dimer measurement, with only targeted use of venous ultrasound, appears to be safe and feasible. Assessing the pretest probability of deep venous thrombosis should be taught to physicians and implemented formally in the care of patients. We favor the Wells score because of its explicit nature and potential to be useful for less experienced clinicians. However, physicians' estimates in our hospital were quite accurate. Further studies are needed to assess the success of implementing clinical probabilities and D-dimer testing in clinical care.

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## REFERENCES

- Anand SS, Wells PS, Hunt D, et al. Does this patient have deep vein thrombosis? *JAMA*. 1998;279:1094–1099.
- Wells PH, Hirsh J, Anderson D, et al. Accuracy of clinical assessment of deep-vein thrombosis. *Lancet*. 1995;345:1326–1330.
- Bounameaux H, de Moerloose PH, Perrier A, Reber G. Plasma measurement of plasma D-dimer as diagnostic aid in suspected deep venous thromboembolism: an overview. *Thromb Haemost*. 1994;7:1–6.
- Wells PH, Anderson D, Bormanis J, et al. Value of assessment of pretest probability of deep-vein thrombosis in clinical management. *Lancet*. 1997;350:1795–1799.
- Cornuz J, Pearson SD, Creager MA, et al. Importance of findings on the initial evaluation for cancer in patients with symptomatic idiopathic deep-vein thrombosis. *Ann Intern Med*. 1996;125:785–793.
- 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;30:794–804.
- Grant BJ. Diagnosis of suspected deep vein thrombosis of the lower extremity. In: Rose BD, ed. UpToDate. Wellesley, Massachusetts: UpToDate; 2001. Available at: <http://www.uptodate.com>.
- Rose CC, Murphy JG, Schwartz JS. Performance of an index predicting the response of patients with acute bronchial asthma to intensive emergency department treatment. *N Engl J Med*. 1984;310:573–577.
- McGinn TG, Guyatt GH, Wyer PC, et al. Users' guides to the medical literature: XXII. How to use articles about clinical decision rules. Evidence-Based Medicine Working Group. *JAMA*. 2000;284:79–84.
- Devereaux PJ, Ghali WA, Gibson NE, et al. Physician estimates of perioperative cardiac risk in patients undergoing noncardiac surgery. *Arch Intern Med*. 1999;159:713–717.
- Van der Graaf F, van den Borne H, van der Kolk M, et al. Exclusion of deep venous thrombosis with D-dimer testing: comparison of 13 D-dimer methods in 99 outpatients suspected of deep venous thrombosis using venography as reference standard. *Thromb Haemost*. 2000;83:191–198.
- Douketis J. Commentary. *Evidence-Based Medicine*. 2000;5:92–93.
- Cornuz J, Lamy O, Hayoz D, Schapira M. Diagnostic et traitement de la thrombose veineuse profonde: recommandations pour la pratique clinique. *Rev Med Suisse Romande*. 1999;119:517–529.
- D'Angelo, d'Alessandro G, Tomassini L, et al. Evaluation of a new rapid quantitative D-dimer assay in patients with clinically suspected deep vein thrombosis. *Thromb Haemost*. 1996;75:412–416.
- Perrier A, Desmarais S, Miron MJ, et al. Non-invasive diagnosis of venous thromboembolism in outpatients. *Lancet*. 1999;353:190–195.
- Becker DM, Philbrick JT, Abbitt PL. Real-time ultrasonography for the diagnosis of lower extremity deep venous thrombosis: the wave of the future? *Arch Intern Med*. 1989;149:1731–1734.
- Polak JF. Doppler ultrasound of the deep leg veins: a revolution in the diagnosis of deep vein thrombosis and monitoring of thrombolysis. *Chest*. 1991;99(suppl 4):165S–172S.
- Sackett DL. A primer on the precision and accuracy of the clinical examination. *JAMA*. 1992;267:2638–2644.
- Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics*. 1977;33:159–174.
- Aschwanden M, Labs KH, Jeanneret C, et al. The value of rapid D-dimer testing combined with structured clinical evaluation for the diagnosis of deep vein thrombosis. *J Vasc Surg*. 1999;30:29–34.
- Miron MJ, Perrier A, Bounameaux H. Clinical assessment of suspected deep vein thrombosis: comparison between a score and empirical assessment. *J Intern Med*. 2000;247:249–254.
- Bigaroni A, Perrier A, Bounameaux H. Is clinical probability assessment of deep vein thrombosis by a score really standardized? [letter]. *Thromb Haemost*. 2000;83:788–789.
- Heijboer H, Buller HP, Lensing AWA, et al. A comparison of real-time compression ultrasonography with impedance plethysmography for the diagnosis of deep venous thrombosis in symptomatic outpatients. *N Engl J Med*. 1993;329:1365–1369.
- Vaccaro JP, Cronan JJ, Dorfman GS. Outcome analysis of patients with normal compression US examinations. *Radiology*. 1990;175:645–649.
- Birdwell BG, Raskob GE, Whitsett TL. The clinical validity of normal compression ultrasonography in outpatients suspected of having deep venous thrombosis. *Ann Intern Med*. 1998;128:1–7.