Diagnosis of Lower Limb Deep Venous Thrombosis in Emergency Department Patients: Performance of Hamilton and Modified Wells Scores

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Study objective: We validate and compare the Hamilton score for assessment of lower limb deep venous thrombosis with the modified Wells score.

Methods: Consecutive patients presenting to the emergency department of a tertiary center for suspected lower limb deep venous thrombosis were prospectively recruited. Hamilton score and modified Wells score calculations, D-dimer, and complete (calf veins included), single lower limb ultrasonographic examination were performed for all patients. All patients with a negative ultrasonographic examination result for deep venous thrombosis were followed up for 3 months.

Results: The study population consisted of 116 men and 193 women, with an average age of 55.6 years (SD 20.1). A total of 67 (21.7%) patients were diagnosed with deep venous thrombosis. Forty (59.7%) of these patients had isolated calf deep venous thrombosis, and the other 27 (40.3%) patients had proximal deep venous thrombosis. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+), and negative likelihood ratio (LR–) for an unlikely Hamilton score (score ≤2) and D-dimer were 99% (95% confidence interval [CI] 92% to 99.96%), 42 % (95% CI 36% to 49%), 32% (95% CI 26% to 39%), 99% (95% CI 95% to 99.98%), 1.7 (95% CI 1.52% to 1.9%), and 0.04 (95% CI 0.01 to 0.25), respectively. The sensitivity, specificity, PPV, NPV, LR+ and LR– for an unlikely modified Wells score (score ≤1) and D-dimer were 99% (95% CI 92% to 99.96%), 33 % (95% CI 27% to 39%), 29% (95% CI 23% to 35%), 99% (95% CI 93% to 99.97%), 1.47 (95% CI 1.34 to 1.62), and 0.05 (95% CI 0.01 to 0.32), respectively.

Conclusion: An unlikely probability of Hamilton score and a negative D-dimer may effectively exclude a lower limb deep venous thrombosis. Hamilton and modified Wells scores have similar performance characteristics. [Ann Emerg Med. 2006;48:678-685.]

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INTRODUCTION

Background

Objective testing for deep venous thrombosis is essential because clinical assessment alone is unreliable.[1-5] Untreated deep venous thrombosis is associated with a high risk of pulmonary embolism,[6] and false diagnosis of deep venous thrombosis results in unnecessary anticoagulant therapy, which is associated with risk for bleeding.[6-8] Accurate diagnosis of deep venous thrombosis and prompt therapy[9] are essential to reduce the risk of thromboembolic complications.

Importance

The Wells score for diagnosis of deep venous thrombosis is the most often tested scoring system for determining the pretest probability of disease.[10] However, recently it has been reported that Wells score does not adequately rule out deep venous thrombosis in primary care patients.[11] The original Wells score has been modified.[12] The modified Wells score has overlapping redundant features such as lower limb enlargement, calf enlargement, and pitting edema, which renders the score less accurate in stratification and more

Editor's Capsule Summary

What is already known on this topic

Clinical scoring systems can be used to risk stratify patients with suspected lower extremity deep venous thrombosis in many, but not all, clinical settings. The modified Wells score currently considers 10 factors in assigning a risk score.

What question this study addressed

Whether a clinical scoring system with 7 factors (Hamilton score) plus D-dimer results would perform as well as the Wells score plus D-dimer results, in emergency department (ED) patients with suspected lower extremity deep venous thrombosis.

What this study adds to our knowledge

In this study of 309 adults with suspected deep venous thrombosis, a scoring system with fewer elements (Hamilton score) performs as well as the Wells score when combined with D-dimer testing for ED patients.

How this might change clinical practice

The Hamilton score with D-dimer is an acceptable alternative to risk stratify ED patients with suspected lower extremity deep venous thrombosis.

cumbersome to calculate. Important risk factors such as history of deep venous thrombosis or pulmonary embolism, pregnancy, and oral contraceptives were not considered when the Wells score was developed. The subjective item of the rule—presence of an alternative diagnosis—has never been unambiguously defined and often causes controversy among users of the rule.[13] In addition, above-knee ultrasonographic examinations were used rather than complete examination of the lower limb as the reference standard, which excluded the diagnosis of isolated (nonpropagating) calf vein thrombosis.

We developed a pretest probability score (Hamilton score)[14] that considered the important risk factors in the derivation population and used a complete (calf veins included) lower limb ultrasonographic examination and 3-month follow-up as the reference standard rather than limited proximal serial ultrasonographic examinations.

Goals of This Investigation

In this study, we aimed to validate and compare the performance of the Hamilton score with that of the modified Wells score according to the reference standard of objective diagnosis of deep venous thrombosis from a single, complete (calf veins included) ultrasonographic examination of symptomatic lower limb and 3-month clinical follow-up.

MATERIALS AND METHODS

Study Design

This article is a secondary analysis of data collected during a prospective, observational study at a tertiary care center.[15]

Setting

The setting was the emergency department (ED) of a tertiary care center that is located in the North Island of New Zealand. This is the tertiary referral center for 850,000 people who live in the midland region of North Island and primary referral center for 150,000 people who live in the city of Hamilton. The tertiary center has all medical specialities including oncology and vascular surgery. About 85,000 patients per annum attend the ED.

Selection of Participants

Institutional ethics committee approval was granted and informed consent was obtained from all recruited patients. Three hundred nine consecutive patients presenting to the ED of a tertiary center for a suspected lower limb deep venous thrombosis from August 2002 to May 2003 were prospectively recruited for the study. This recruitment period corresponds to the validation phase of the original study, which was carried out from April 2001 to May 2003.[15] All patients were ambulatory outpatients and included those referred to the tertiary center ED by primary care physicians in the community and those self-referred because of symptoms. Patients were included in the study if the emergency physician suspected a lower limb deep venous thrombosis. The exclusion criteria were failure to do a D-dimer test before ultrasonographic examination and failure to perform a technically adequate complete (calf veins included) ultrasonographic examination. Patients were recruited 24 hours a day for the study period.

Data Collection and Processing

Emergency physicians completed a questionnaire comprising details of the medical history and physical examination. A D-dimer blood test was done for all patients before ultrasonographic examination. Neither the Hamilton score nor the modified Wells score was calculated by emergency physicians to determine a patient's further diagnostic evaluation (ie, progression to D-dimer blood test or lower limb ultrasonograph). Data collected by the emergency physicians was used to calculate the Hamilton score and modified Wells score (Table 1) by the study investigators, who were independent of the emergency physicians. Results of D-dimer and ultrasonography were collated by research nurses who were independent of emergency physicians treating the patients.

Methods of Measurement

A semiquantitative, immunochromatographic D-dimer assay called Simplify (Agen Biochemical, Brisbane, Australia) was performed for all 309 patients. This assay gives a semiquantitative result in 10 minutes.[16,17]

Table 1. Hamilton score[14] and modified Wells score.[12]

Characteristics	Hamilton	Modified Wells
Plaster immobilization of lower limb	2	1
Active malignancy (within 6 months or current)	2	1
Strong clinical suspicion of deep venous thrombosis by the emergency physicians without other diagnostic possibilities	2	–
Bed rest (>3 days) or recent surgery (within 4 weeks)	1	1
Male sex	1	–
Calf circumference >3 cm on affected side (measured 10 cm below tibial tuberosity)	1	1
Erythema	1	–
Localized tenderness along the distribution of the deep venous system	–	1
Entire leg swollen	–	1
Pitting edema confined to the symptomatic leg	–	1
Collateral superficial veins (nonvaricose)	–	1
Previously documented deep vein thrombosis	–	1
Alternative diagnosis at least as likely as deep vein thrombosis	–	−2
Unlikely versus likely cutoff score	2 or less	1 or less

Table 2. Characteristics of patients with and without deep venous thrombosis.

Characteristics	Deep Venous Thrombosis Positive, N=67 (%)	Deep Venous Thrombosis Negative, N=242 (%)
Plaster immobilization of lower limb	17 (25.4)	40 (16.5)
Active malignancy (within 6 months or current)	8 (11.9)	13 (5.4)
Strong clinical suspicion of deep vein thrombosis by the emergency physicians without other diagnostic possibilities	7 (10.4)	12 (5.0)
Bed rest (>3 days) or recent surgery (within 4 weeks)	16 (23.9)	26 (10.7)
Male sex	34 (50.7)	82 (33.9)
Calf circumference >3 cm on affected side (measured 10 cm below tibial tuberosity)	26 (38.8)	43 (17.8)
Erythema	25 (37.3)	64 (26.4)
Localized tenderness along the distribution of the deep venous system	60 (89.6)	186 (76.9)
Entire leg swollen	36 (53.7)	94 (38.8)
Pitting edema confined to the symptomatic leg	32 (47.8)	79 (32.6)
Collateral superficial veins (nonvaricose)	9 (13.4)	79 (32.6)
Previously documented deep vein thrombosis	15 (22.4)	26 (10.7)
Alternative diagnosis at least as likely as deep vein thrombosis	22 (32.8)	117 (48.3)

Diagnosis of deep venous thrombosis was made by duplex compression (Acuson Sequoia 512 ultrasonographic imaging system, Mountain View, CA). The ultrasonography was done by experienced ultrasonographers and radiology residents (third and fourth year) under the supervision of consultant radiologists. The results were interpreted by 7 consultant radiologists who had experience ranging from 2 to10 years in interpreting vascular ultrasonographic studies as consultant radiologists, which reflected the day-to-day clinical practice. The common femoral vein, superficial femoral vein, popliteal vein and trifurcation, and all 3 deep calf vein sets were examined. Noncompressibility of a segment of the veins was the sole criterion for diagnosis of deep venous thrombosis. Doppler examination of these veins was obtained as supplemental information and was used only as a guide, playing no role in determining the reference standard of ultrasonographic examination (whether deep venous thrombosis was present or absent).

Outcome Measures

All patients with a negative result on the complete lower limb ultrasonographic study were followed up for 3 months after the date of the negative result. Patients were contacted by telephone at the end of the 3-month follow-up period. Patients were queried for symptoms of venous thromboembolism or pulmonary embolism (shortness of breath, chest pain, calf swelling, calf tenderness, and new-onset ankle edema), hospitalization, surgical procedures, diagnostic testing, and any new medications. In the instances in which patients were unable to be contacted, their general practitioners were contacted to identify any subsequent venous thromboembolic events. Clinical records, imaging records, and hospital admission records of all patients with a negative ultrasonographic examination result were reviewed by research nurses to identify any evidence for an event of thromboembolism. The minimum follow-up period of 3 months was chosen according to previous studies.[18,19] For each abnormal event, data collected included clinical findings and results of tests and anticoagulation and duration.

Primary Data Analysis

Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+) and negative likelihood ratio (LR−) were calculated for the Hamilton score, the Hamilton score plus D-dimer, the modified Wells score and the modified Wells score plus D-dimer using the cut point of likely versus unlikely pretest probability (defined in Tables 1 and 2). In addition, receiver operator characteristic (ROC) curve analysis for the Hamilton score and the modified Wells score was also performed to evaluate overall accuracy in assessing deep venous thrombosis between the 2 scores. Smooth, fitted curves were obtained using the bivariate binormal ROC model, which correctly accounts for the correlation induced from the paired design of the study.[20] The area under the curve (AUC), along with the corresponding 95% confidence interval (CI), was reported separately for each score.

Table 3. Cross-tabulation of the Hamilton score with ultrasonography and 3-month follow-up (reference standard).*

Reference Standard, Frequency	Hamilton Score 0*	1*	2*	3	4	5	6	7	8	Total, No. (%)
Negative ultrasonographic result, No.	59	66	47	36	21	10	2	0	1	242 (78.3)
Positive ultrasonographic result, No.	4	5	14	17	15	7	2	2	1	67 (21.7)
Total, No. (%)	63 (20.4)	71 (23)	61 (19.8)	53 (17.2)	36 (11.6)	17 (5.5)	4 (1.3)	2 (0.6)	2 (0.6)	309 (100)

*Denotes scores of "unlikely."

Table 4. Cross-tabulation of the Wells score with ultrasonography and 3-month follow-up (reference standard).*

Reference Standard, Frequency	Wells Score −2*	−1*	0*	1*	2	3	4	5	6	7	Total, No. (%)
Negative ultrasonographic result, No.	6	30	43	54	51	33	17	4	2	2	242 78.3
Positive ultrasonographic result, No.	0	1	5	11	15	16	11	7	1	0	67 21.7
Total, No. (%)	6 (1.9)	31 (10)	48 (15.5)	65 (21)	66 (21.4)	49 (15.9)	28 (9)	11 (3.6)	3 (1)	2 (0.7)	309 100.00

*Denotes scores of "unlikely."

ROC computations were performed using the ROCKIT software (University of Chicago Department of Radiology, Chicago, IL). Likelihood ratios with CIs were computed using the VassarStats clinical calculator 1 (available at http://faculty.vassar.edu/lowry/clin1.html). All other computations were performed using SAS software (SAS, Version 9.1.2, SAS Institute Inc., Cary, NC).

RESULTS

Characteristics of Study Subjects

A total of 317 patients suspected of having lower limb deep venous thrombosis were enrolled in the study. Eight patients were excluded from the study for failure to do a D-dimer test before ultrasonographic examination (5) and for failure to perform an adequate complete lower limb ultrasonographic study (3). Hence, the study population consisted of 309 patients. Among these, 265 patients (85.8%) were referred by general practitioners, and 44 patients (14.2%) were self-referred. There were 116 men and 193 women, with an average age of 55.6 years (SD ±20.1 years). A total of 67 (21.7%) patients were diagnosed with deep venous thrombosis according to the reference standard, with an average age of 56.4 years (SD ±14.2 years). Forty (59.7%) of these patients had isolated calf deep venous thrombosis, and the other 27 (40.3%) patients had proximal deep venous thrombosis. Thirty-four of these patients were men and 33 were women.

All 242 patients with a negative ultrasonographic result were followed up. Two hundred nineteen patients (90.5%) were contacted by telephone, and research nurses contacted the general practitioners for the other 23 patients (9.5%) who were unable to be contacted by telephone. Medical records of all 242 patients were reviewed. No subsequent thromboembolic event (deep venous thrombosis or pulmonary embolism) or death was noted at the end of the 3-month follow-up period.

Main Results

There were 195 (63.1%) patients in the Hamilton score unlikely category and 114 (36.9%) patients in the Hamilton score likely category (Table 3) compared to 150 (48.5%) patients in the modified Wells score unlikely category and 159 (51.5%) patients in modified Wells score likely category (Table 4). Of those patients determined to be positive for deep venous thrombosis by reference standard, 34.3% (23/67) had a pretest probability from the Hamilton score of unlikely, and 65.7% (44/67) had a pretest probability of likely. Among the same patients, 25.4% (17/67) had a pretest probability from the modified Wells score of unlikely, and 74.6% (50/67) had a pretest probability of likely. Thus, the estimates of sensitivity for the Hamilton score and the modified Wells score using the cut point of likely versus unlikely pretest probability were 0.66 and 0.75, respectively. Likewise, the resulting estimates of specificity for the 2 scores were 0.71 and 0.55, respectively. Table 5 gives the estimates of sensitivity, specificity, NPV, PPV, LR+, and LR− for both the Hamilton score and the modified Wells score.

The resulting ROC curves and associated AUC for the Hamilton score and the modified Wells score are shown in the Figure. The scores performed similarly (Hamilton AUC 0.75 [95% CI 0.68 to 0.81] versus Wells AUC 0.71 [95% CI 0.64 to 0.77]) and demonstrated moderate to good ability to discriminate between cases with and without deep venous thrombosis.

One hundred forty-three patients (46.3%) had a negative D-dimer assay, and 166 patients (53.7%) had a positive D-dimer assay. Of the143 patients with a negative D-dimer assay, 135 (94.4%) patients had negative ultrasonographic examination results; 8 (5.6%) patients had isolated calf deep venous thrombosis. Among the 166 patients with a positive D-dimer assay result, 26 (15.7%) patients had proximal deep venous thrombosis, 33 (19.9%) patients had isolated calf deep

Table 5. Performance characteristics of Hamilton score, modified Wells score, Hamilton score+Simplify D-dimer, and modified Wells score+Simplify D-dimer using the cut point of likely vs unlikely pretest probability, based on complete compression ultrasonography as reference standard.

Score/D-dimer	Sensitivity (No.) (95% CI)	Specificity (No.) (95% CI)	PPV (No.) (95% CI)	NPV (No.) (95% CI)	LR+, LR– (95% CI)
Hamilton score	66% (44/67) (53–77)	71% (172/242) (65–77)	39% (44/114) (30–48)	88% (172/195) (83–92)	2.27 (1.75, 2.95), 0.48 (0.35–0.67)
Modified Wells score	75% (50/67) (63–84)	55% (133/242) (48–61)	31% (50/159) (24–39)	89% (133/150) (82–93)	1.66 (1.36, 2.02), 0.46 (0.30–0.70)
Hamilton score and D-dimer*	99% (66/67) (92–99.96)	42% (102/242) (36–49)	32% (66/206) (26–39)	99% (102/103) (95–99.98)	1.70 (1.52, 1.90), 0.04 (0.01–0.25)
Modified Wells score and D-dimer*	99% (66/67) (92–99.96)	33% (80/242) (27–39)	29% (66/228) (23–35)	99% (80/81) (93–99.97)	1.47 (1.34, 1.62), 0.05 (0.01–0.32)

*A positive result was defined as either a positive D-dimer assay result or a likely pretest probability score, whereas a negative result was defined as a negative D-dimer assay result and an unlikely pretest probability score.

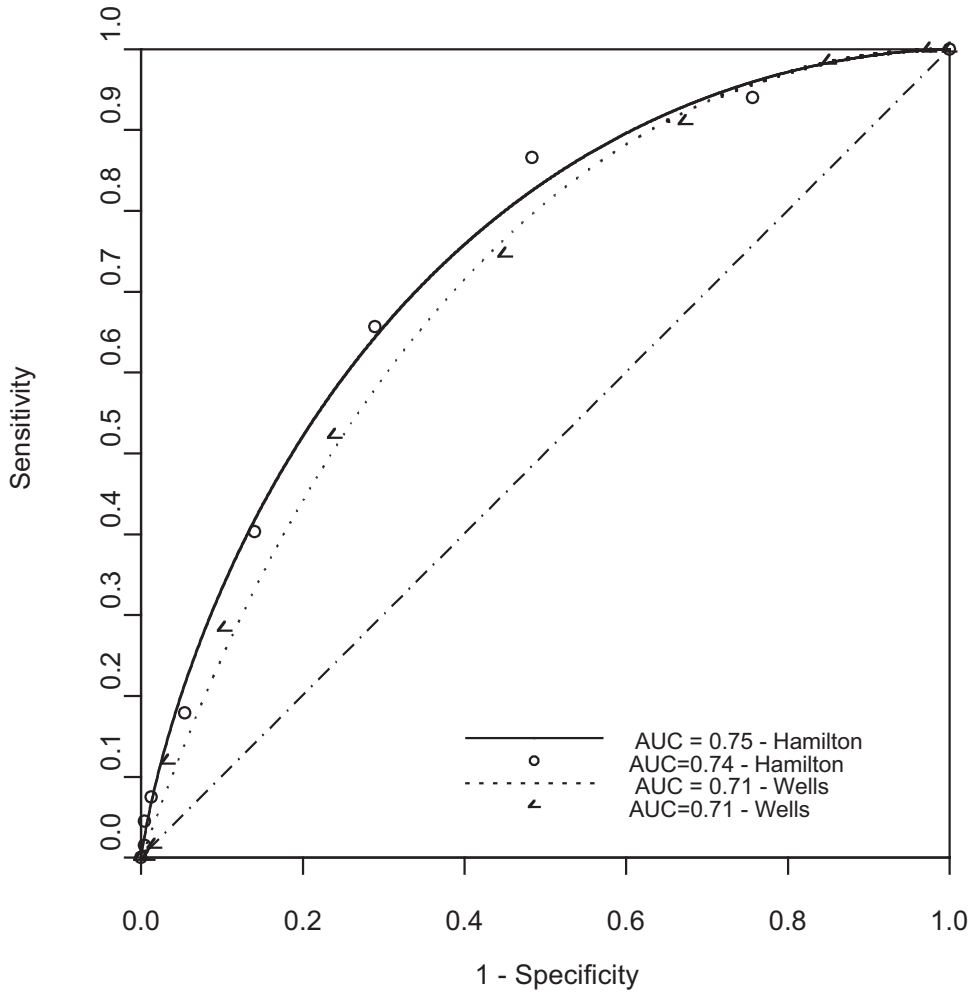

Figure. Bivariate binormal ROC curves for the Hamilton and modified Wells scores. Empirical operating points are overlaid on the smooth fitted curves for the Hamilton (circles) and modified Wells (triangles) scores. Empirical and fitted AUC estimates are reported.

venous thrombosis, and 107 (64.5%) patients had negative ultrasonographic examination results.

Of the 103 patients with an unlikely pretest probability by Hamilton score and a negative D-dimer assay result, 1 patient had isolated calf deep venous thrombosis. Of the 81 patients with an unlikely pretest probability by modified Wells score and a negative D-dimer assay result, 1 patient had isolated calf deep venous thrombosis, which leads to an NPV in excess of 99% for

the Hamilton score plus D-dimer assay and 98.8% for the modified Wells score plus D-dimer assay. However, a larger percentage of patients had an unlikely probability Hamilton score and negative D-dimer assay result versus an unlikely modified Wells score and negative D-dimer assay result (33.3% [103/309] versus 26.2% [81/309] (absolute difference 7.1%; 95% CI −0.1 to 14.3%). Table 5 summarizes the sensitivity, specificity, PPV, NPV, LR+, and LR– of the combined measures. Of note is that when combined with the D-dimer assay, both the Hamilton and modified Wells score are extremely sensitive in detecting deep venous thrombosis, with an estimated sensitivity in each case of 0.99.

LIMITATIONS

Our results are applicable to adult ambulatory ED patients for whom a technically adequate complete lower limb ultrasonographic examination could be performed. Our study was performed in a single institution with experienced senior radiology residents (third and fourth year) and qualified sonographers performing the ultrasonographic examinations under the supervision of consultant radiologists, and thus it is applicable in similar institutions.

Because isolated calf deep venous thrombosis is also included in our study, the prevalence of deep venous thrombosis in the study population may vary from that of other studies. Our study may be limited in that an asymptomatic, small, isolated, calf deep venous thrombosis may have remained undetected by the ultrasonographic examination or 3-month clinical follow-up. In addition, we examined the symptomatic leg rather than both legs by ultrasonography, reflecting the local clinical practice. It has been debated whether bilateral ultrasonographic imaging should be performed for patients with suspected unilateral deep venous thrombosis.[21] There are few clinical data to support such a practice.[22] Though we may have missed small silent thrombus in the asymptomatic leg, this is considered less likely, given that our study population was ambulatory outpatients who presented to the ED.

Simplify D-dimer is a new immunochromatographic D-dimer assay, and there are only 2 studies available in literature establishing the accuracy.[16,17] The interobserver variability and training required to interpret the assay are also not well established.

Finally, a statistical power calculation was not done for the original study,[15] whose data the current findings are based on. This makes it difficult to determine the available power for the desired precision. All reported comparisons remain valid; however, lack of significance in some of the findings could be due to low power.

DISCUSSION

Because 70% to 80% of the patients with suspected deep venous thrombosis do not actually have deep venous thrombosis,[23] the main objective of a prediction score is to identify patients at low risk for deep venous thrombosis, for whom diagnostic imaging can be safely avoided or deferred. The Hamilton score has 7 nonoverlapping components. There are 6 objective components and a clearly defined subjective component (clinician's intuitive judgement of strong likelihood of deep venous thrombosis without the possibility of other diagnoses), which is in contrast to the 10-component modified Wells score with overlapping features and a less-well-defined subjective component of alternative diagnosis at least as likely as deep venous thrombosis.

Our study demonstrated that a negative immunochromatographic D-dimer assay and an unlikely probability Hamilton score would effectively exclude a lower limb deep venous thrombosis safely without an ultrasonographic examination in patients presenting with suspected deep venous thrombosis to the ED, with the exception of 1 false negative. Several other studies have suggested that high NPV of D-dimer testing can be used as part of a diagnostic algorithm.[24-26] The value of combining the clinical pretest probability and D-dimer tests has been confirmed in other studies.[27,28] In our study, patients with unlikely probability Hamilton score and a negative D-dimer result represented about 33% of the study population, and in this group of patients, ultrasonographic examination could have been avoided to effectively exclude a lower limb deep venous thrombosis based on clinical probability and D-dimer result. Using Hamilton score identified 27% (22/81) more patients in the unlikely probability and negative D-dimer group compared with the modified Wells score. Despite this, there was no appreciable clinically important difference in the performance of modified Wells score or Hamilton score in our small sample. A larger multicenter prospective study is needed to determine whether there is a difference in clinical performance of either score.

The diagnostic strategy of clinically excluding deep venous thrombosis by combining the unlikely probability and a negative D-dimer can lead to potential savings in health expenditure on deep venous thrombosis ultrasonographic examinations and allows timely discharge of patients from EDs and rural hospitals where ultrasonography may not be readily available, especially during on-call hours, without compromising patient safety.

We used a complete (calf veins included), single, lower limb, ultrasonographic examination to diagnose deep venous thrombosis rather than above-knee serial ultrasonographic examinations suggested by other studies.[4,12,24] This is another important difference in derivation and validation of the Hamilton score compared with the modified Wells score, which used serial above-knee ultrasonographic examinations. The ultrasonographic study was repeated only if the patient had progressive or new symptoms despite the initial negative study result and re-presented to the ED. It is safe to withhold anticoagulant therapy in patients with clinically suspected deep venous thrombosis after a single, negative-result, complete (including calf veins) lower limb ultrasonographic examination.[15,29-31] All patients who had an isolated calf deep

venous thrombosis were treated with anticoagulation according to local protocol. Using the complete (calf veins included) lower limb ultrasonographic examinations as the reference standard instead of serial above-knee ultrasonographic examinations has resulted in 59.7% (40/67) of patients diagnosed with deep venous thrombosis having isolated calf deep venous thrombosis. This also may have contributed to the higher observed prevalence of deep venous thrombosis among the unlikely pretest probability Hamilton score (34%) and unlikely pretest probability modified Wells score (25.4%) cohorts of patients compared to the prevalence of deep venous thrombosis among the low-pretest-probability Wells score cohort of patients (3%) in the original Wells study.[4]

IN RETROSPECT

In retrospect, this study could have included hospital inpatients, as well as ED patients, for the validation of Hamilton score and the modified Wells score using single, complete (calf veins included), lower limb ultrasonographic examinations and 3-month follow-up as the reference standard.

In conclusion, an unlikely probability Hamilton score and a negative D-dimer assay may effectively exclude a lower limb deep venous thrombosis in ambulatory ED patients. The Hamilton score and modified Wells score had similar performance characteristics.

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REFERENCES

1. McLachlin J, Richards T, Paterson J. An evaluation of clinical signs in the diagnosis of venous thrombosis. *Arch Surg.* 1962;85: 738-744.
2. Nicolaides A, Kakkar V, Field E, et al. The origin of deep vein thrombosis: a venographic study. *Br J Radiol.* 1971;44:653-663.
3. Sandler D, Martin J, Duncan J, et al. Diagnosis of deep venous thrombosis: comparison of clinical evaluation, ultrasound, plethysmography, and venoscan with X ray venogram. *Lancet* 1984;2:716-719.
4. Wells P, Hirsh J, Anderson D, et al. Accuracy of clinical assessment of deep venous thrombosis. *Lancet* 1995;345:1326-1330.
5. Hull RD. Re-visiting the past strengthens the present: an evidence-based medicine approach for the diagnosis of deep venous thrombosis. *Ann Intern Med.* 2005;142:583-585.
6. Ginsberg J. Management of venous thromboembolism. *N Engl J Med.* 1996;335:1816-1828.
7. Caranasos G, Stewart R, Cluff L. Drug-induced illness leading to hospitalization. *JAMA.* 1974;228:713-717.
8. Hull R, Hirsh J, Jay R, et al. Different intensities of oral anticoagulation therapy in the treatment of proximal vein thrombosis. *N Engl J Med.* 1982;307:1676-1681.
9. Bates SM, Ginsberg JS. Clinical practice: treatment of deep-vein thrombosis. *N Engl J Med.* 2004;351:268-277.
10. Tamariz LJ, Eng J, Segal JB, et al. Usefulness of clinical prediction rules for the diagnosis of venous thromboembolism: a systematic review. *Am J Med.* 2004;117:676-684.
11. Oudega R, Hoes A, Moons K. The wells rule does not adequately rule out deep venous thrombosis in primary care patients. *Ann Intern Med.* 2005;143:100-107.
12. Wells PS, Anderson DR, Rodger M, et al. Evaluation of D-dimer in the diagnosis of suspected deep-vein thrombosis. *N Engl J Med.* 2003;349:1227-1235.
13. 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.
14. Subramaniam R, Chou T, Heath R, et al. Importance of pretest probability score and D-dimer assay before sonography for lower limb deep venous thrombosis. *AJR Am J Roentgenol.* 2006;186: 206-212.
15. Subramaniam RM, Heath R, Chou T, et al. Deep venous thrombosis: withholding anticoagulation therapy after negative complete lower limb US findings. *Radiology.* 2005;237:348-352.
16. Cini M, Legnani C, Cavallaroni K, et al. A new rapid bedside assay for D-dimer measurement (Simplify D-dimer) in the diagnostic work-up for deep vein thrombosis. *J Thromb Haemost.* 2003;1:2681-2683.
17. Neale D, Tovey C, Vali A, et al. Evaluation of the Simplify D-dimer assay as a screening test for the diagnosis of deep vein thrombosis in an emergency department. *Emerg Med J.* 2004;21: 663-666.
18. Birdwell BG, Raskob GE, Whitsett TL, et al. The clinical validity of normal compression ultrasonography in outpatients suspected of having deep venous thrombosis. *Ann Intern Med.* 1998;128:1-7.
19. Hull R, Raskob GE, Hirsch DR, et al. Continuous intravenous heparin compared with intermittent subcutaneous heparin in the initial treatment of proximal vein thrombosis. *N Engl J Med.* 1986;315:1109-1114.
20. Leisenring W, Alonzo T, Pepe M. Comparisons of predictive values of binary medical diagnostic tests for paired designs. *Biometrics.* 2000;56:345-351.
21. Cronan J. Deep venous thrombosis: one leg or both legs? *Radiology.* 1996;200:323-324.
22. Sheiman R, McArdle C. Bilateral lower extremity US in the patient with unilateral symptoms of deep venous thrombosis: assessment of need. *Radiology.* 1995;194:171-173.
23. Kyrle PA, Eichinger S. Deep vein thrombosis. *Lancet.* 2005;365: 1163-1174.

24. Perrier A, Desmarais S, Miron M, et al. Non-invasive diagnosis of venous thromboembolism in outpatients. *Lancet.* 1999;353:190-195.
25. Bates SM, Grand'Maison A, Johnston M, et al. A latex D-dimer reliably excludes venous thromboembolism. *Arch Intern Med.* 2001;161:447-453.
26. 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.
27. Anderson DR, Wells PS, Stiell I, et al. Management of patients with suspected deep vein thrombosis in the emergency department: combining use of a clinical diagnosis model with D-dimer testing. *J Emerg Med.* 2000;19:225-230.
28. 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.
29. Elias A, Mallard L, Elias M, et al. A single complete ultrasound investigation of the venous network for the diagnostic management of patients with a clinically suspected first episode of deep venous thrombosis of the lower limbs. *Thromb Haemost.* 2003;89:221-227.
30. Stevens SM, Elliott CG, Chan KJ, et al. Withholding anticoagulation after a negative result on duplex ultrasonography for suspected symptomatic deep venous thrombosis. *Ann Intern Med.* 2004;140:985-991.
31. Schellong SM, Schwarz T, Halbritter K, et al. Complete compression ultrasonography of the leg veins as a single test for the diagnosis of deep vein thrombosis. *Thromb Haemost.* 2003; 89:228-234.