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Comparison of the diagnostic performance of the original and modified Wells score in inpatients and outpatients with suspected deep vein thrombosis

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ABSTRACT

Introduction: The original and modified Wells score are widely used prediction rules for pre-test probability assessment of deep vein thrombosis (DVT). The objective of this study was to compare the predictive performance of both Wells scores in unselected patients with clinical suspicion of DVT.
Methods: Consecutive inpatients and outpatients with a clinical suspicion of DVT were prospectively enrolled. Pre-test DVT probability (low/intermediate/high) was determined using both scores. Patients with a non-high probability based on the original Wells score underwent D-dimers measurement. Patients with D-dimers <500 μg/L did not undergo further testing, and treatment was withheld. All others underwent complete lower limb compression ultrasound, and those diagnosed with DVT were anticoagulated. The primary study outcome was objectively confirmed symptomatic venous thromboembolism within 3 months of enrollment.
Results: 298 patients with suspected DVT were included. Of these, 82 (27.5%) had DVT, and 46 of them were proximal. Compared to the modified score, the original Wells score classified a higher proportion of patients as low-risk (53 vs 48%; $p<0.01$) and a lower proportion as high-risk (17 vs 15%; $p=0.02$); the prevalence of proximal DVT in each category was similar with both scores (7-8% low, 16-19% intermediate, 36-37% high). The area under the receiver operating characteristic curve regarding proximal DVT detection was similar for both scores, but they both performed poorly in predicting isolated distal DVT and DVT in inpatients.
Conclusion: The study demonstrates that both Wells scores perform equally well in proximal DVT pre-test probability prediction. Neither score appears to be particularly useful in hospitalized patients and those with isolated distal DVT.

1. Introduction

Deep vein thrombosis (DVT) is a common problem in ambulatory and hospitalized patients. Untreated DVT may lead to potentially fatal pulmonary embolism (PE). On the other hand, unjustified anticoagulation therapy poses a risk for bleeding [1]. Correct diagnosis and prompt treatment are therefore crucial. Unfortunately, symptoms and signs of DVT are unspecific. Less than 25% of patients with clinically suspected DVT do actually have the disease [2,3], underscoring the importance of accurate diagnostic strategies. Several clinical prediction rules have been developed and validated in various populations to simplify and improve the diagnostic process of patients with suspected DVT [4–9]. Diagnostic strategies based on combining pretest probability with D-dimers measurements have been shown to be safe and cost-effective [10], leading to a significant reduction of ultrasound examinations [5,11,12].

The best validated prediction rule is the Wells score, consisting of nine clinical items (Table 1) [6]. This score has been developed in ambulatory patients addressed to a tertiary care center for a suspected first episode of proximal and distal lower limb DVT [6,13,14]. It has been subsequently validated in the emergency department, and the hospital setting [4,11,15]. More recently, Wells and colleagues published a modified score, adding an item for previously documented DVT [5]. This modified Wells score has been validated in outpatients [5], and emergency department patients only [8]. The aim of this prospective cohort study was to compare the accuracy of the two scores in predicting proximal and isolated distal DVT in a broad, unselected population of ambulatory and hospitalized patients with suspected DVT.

Abbreviations: DVT, deep vein thrombosis; CCUS, complete compression ultrasound; PE, pulmonary embolism; VTE, venous thromboembolism.

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Table 1
The Original Wells Score [6].

	Score
Clinical Feature	
Active cancer (treatment ongoing or within the previous 6 months or palliative)	+1
Paralysis, paresis, or recent plaster immobilization of the lower extremities	+1
Recently bedridden for more than 3 days or major surgery within 4 weeks	+1
Localized tenderness along the distribution of the deep venous system	+1
Entire leg swollen	+1
Calf swelling by more than 3 cm when compared to the asymptomatic leg (measured below tibial tuberosity)	+1
Pitting edema (greater in the symptomatic leg)	+1
Collateral superficial veins (nonvaricose)	+1
Alternative diagnosis as likely or greater than that of DVT	− 2
Additional feature in the Modified Wells Score	
Previously documented DVT	+1

Note: Risk category: low risk ≤0 points; intermediate risk = 1 or 2 points; high risk ≥3 points.

2. Methods

2.1. Patients

Consecutive patients, ≥18 years of age, with clinically suspected lower limbs DVT addressed to the thrombosis consultation of the vascular medicine service of a teaching hospital were potentially eligible for the present study. Outpatients presenting to the emergency department or directly referred by their general practitioner and inpatients referred by their physician in charge were eligible.

Exclusion criteria were as follows: clinical suspicion of PE, treatment with therapeutic anticoagulation for more than 48 hours before presentation, planned long-term anticoagulation for a diagnosis other than venous thromboembolism (VTE), pregnancy, an estimated life expectancy of less than 3 months, and unwillingness or inability to give informed consent. The study was approved by the local ethics committee.

2.2. Clinical evaluation and diagnostic tests

All patients were examined by one of eleven vascular medicine specialists who, using standardized data collection forms, prospectively recorded the patient's demographic characteristics (age, gender), VTE risk factors (active cancer, recent major surgery, trauma or immobilization, post-partum, hormone therapy, known thrombophilia, varicose veins, post-thrombosis syndrome, obesity, and prior personal history of VTE), and leg symptoms/signs of DVT (localized tenderness, entire leg or calf swelling, pitting edema, and collateral superficial veins). The vascular physician then determined the patient's pre-test DVT probability using the original Wells scores [6] (Table 1). The modified Wells score was calculated retrospectively. The latter uses the same features as the original one except for adding 1 point for previously documented DVT [5]. Patients were stratified into three categories: low (≤0 point), intermediate (1–2 points), and high (≥3 points) pre-test probability of having DVT. In patients with low or intermediate pre-test probability according to the original Wells score, D-dimer testing was performed. A highly sensitive D-dimer test was used (rapid ELISA; Vidas DD, bioMérieux, France) [16,17]. In patients with D-dimer levels <500 μg/L, no further diagnostic testing was performed and anticoagulation treatment was withheld [18]. Patients with D-dimer levels ≥500 μg/L, and all patients with a high pre-test probability underwent a complete compression ultrasound (CCUS). CCUS was performed by a trained vascular medicine specialist following a standardized protocol using real-time B mode compression ultrasonography with a linear probe of 5–10 MHz [19]. Patients were first examined in the supine position. Common femoral vein, proximal deep femoral vein, and the entire superficial femoral vein were examined. With the patient in the sitting position the following veins were examined: popliteal, muscular, peroneal, posterior, and anterior tibial. Incompressibility was the sole diagnostic criteria for proximal (down to the trifurcation of the popliteal vein) and distal DVT. All patients with a normal initial diagnostic workup (D-dimer levels <500 μg/L or negative CCUS) received no therapeutic anticoagulant treatment, and were followed for 3 months. Patients with confirmed DVT received parenteral treatment with low-molecular-weight heparin, unfractionated heparin, or fondaparinux, followed by oral vitamin K antagonists for at least 3 months.

2.3. Follow-up

Three months after the index visit, a study nurse contacted all enrolled patients by telephone to obtain follow-up informations on the occurrence of symptomatic DVT or non-fatal or fatal PE. If necessary, these informations were complemented by proxy interview, interview of the patient's primary care physician, and/or hospital chart review. Diagnosis of VTE was established with usual criteria (positive CCUS, venography, spiral computer tomography, pulmonary angiography, or a high-probability ventilation-perfusion scan). Cause of death was reviewed by 2 independent clinical experts and adjudicated as definitely due to PE, possibly due to PE (sudden death without any other obvious cause), or due to another cause. We used the combination of index visit testing and the occurrence of symptomatic DVT during follow-up as a reference standard for the final diagnosis of DVT.

2.4. Statistical analysis

Categorical variables were compared using the chi-squared statistic or the Fisher's exact test if appropriate. The proportion of patients per category (low, intermediate and high) and the percentage of DVT (proximal or isolated distal DVT) per category for each score were compared using the McNemar test. P-values of <0.05 were considered statistically significant. To compare the discriminatory power of the two scores, we calculated the area under the receiver operating characteristic (ROC) curve for each score for proximal and isolated distal DVT. Subgroup analyses of the ROC curves for ambulatory versus hospitalized, and for patients with or without prior history of VTE were performed. All statistical analyses were performed using STATA version 9.1 (StataCorp, College Station, Texas, USA).

3. Results

Between May 4, 2007 and May 31, 2009, 447 consecutive patients with clinically suspected DVT of the lower limbs were screened. 149 patients were excluded because at least 1 of the predefined exclusion criteria was present (clinical suspicion of PE: 39; treatment with therapeutic anticoagulation for more than 48 hours prior to inclusion: 31; planned long-term anticoagulation for a diagnosis other than VTE: 22; pregnancy: 17; life expectancy less than 3 months: 5; unwillingness or inability to give informed consent: 59). Thus, the final study sample comprised 298 patients with suspected lower limb DVT (Table 2). Patients in whom DVT was confirmed were younger, more likely to be men, and to have active cancer. Furthermore, in patients with DVT, the presence of localized tenderness along the distribution of the deep venous system, and calf swelling of more than 3 cm compared to the asymptomatic leg was significantly more frequent than in patients without DVT. On the other hand, fewer patients with DVT were initially thought to have an alternative diagnosis than patients without DVT. The percentage of inpatients considered to have an alternative diagnosis at least as likely as DVT was 54%, compared to 45% in the outpatient group ($p = 0.5$).

Most of the patients came from the outpatient setting (69%). Among the inpatients, 31% were hospitalized in a medical (including geriatrics and oncology), and 69% in a surgical ward (including orthopedic surgery). Compared to outpatients, inpatients were older

Table 2
Patient Baseline Characteristics.

Characteristic	Total (n = 298)	DVT (n = 82)	no DVT (n = 216)	*p* value
	Number (%) or Mean (SD)			
Demographic characteristics				
Age, mean (SD), y	57.5 (17)	54.1 (16)	58.8 (17)	*0.02*
Male gender	137 (46)	47 (57)	90 (42)	*0.02*
Setting				
Outpatients	205 (69)	60 (73)	145 (67)	*0.32*
Inpatients	93 (31)	22 (27)	71 (33)	
Clinical characteristics				
Risk factors for thrombosis				
History of venous thromboembolism	57 (19)	21 (26)	36 (17)	*0.08*
Active cancer	46 (15)	20 (24)	26 (12)	*0.01*
Recent major surgery (<4 weeks)	46 (15)	8 (10)	38 (18)	*0.11*
Recent trauma (< 4wk)	35 (12)	10 (12)	25 (12)	*0.88*
Recent immobilization (<4 weeks)	78 (26)	20 (24)	58 (27)	*0.67*
Bed ridden (>72 hours)	55 (18)	10 (12)	45 (21)	*0.09*
Plaster cast	14 (5)	5 (6)	9 (4)	*0.54*
Long-distance travel (>6 hours)	14 (5)	7 (9)	7 (3)	*0.07*
Postpartum	5 (2)	0 (0)	5 (2)	*0.33*
Hormone therapy*	24 (8)	9 (11)	15 (7)	*0.25*
Known thrombophilia	3 (1)	1 (1)	2 (1)	*>0.99*
Varicose veins	77 (26)	20 (24)	57 (26)	*0.73*
Post-thrombosis syndrome	9 (3)	3 (4)	6 (3)	*0.71*
Obesity (BMI ≥ 30 kg/m^2)	62 (21)	11 (13)	51 (24)	*0.05*
Clinical presentation				
Localized tenderness along distribution of deep venous system	120 (41)	48 (59)	72 (33)	*<0.01*
Entire leg swelling	75 (25)	27 (33)	48 (22)	*0.06*
Calf swelling by >3 cm when compared to the asymptomatic leg	53 (18)	22 (27)	31 (14)	*0.01*
Pitting edema (greater in symptomatic leg)	143 (48)	46 (56)	97 (45)	*0.08*
Collateral superficial veins (non-varicose)	9 (3)	3 (4)	6 (3)	*0.71*
Alternative diagnosis as likely or greater than that of DVT	202 (68)	40 (49)	162 (75)	*<0.01*

Note: DVT = deep vein thrombosis.
* Defined as oral contraception and hormone replacement therapy.

(mean age 62.4 vs. 55.3 years, $p = 0.001$), more likely to have active cancer (24.7 vs. 11.2%, $p = 0.003$), recent major surgery (32.3 vs. 7.8%, $p < 0.001$), and recent immobilization (44.1 vs. 18.1%, $p < 0.001$).

A total of 82 (27.5%; 95% confidence interval [CI], 22.5-33.0%) patients had DVT based on a positive CCUS during the initial work-up. Overall, 46 patients (15.4%; 95% CI, 11.5-20.0%) had proximal DVT and 36 (12.1%; 95% CI, 8.6-16.3%) had isolated distal DVT.

In the outpatient subgroup, 60 patients (29.3%; 95% CI, 23.1-36.0%) had DVT. Overall, 34 (16.6%; 95% CI, 11.8-22.4%) were proximal, and 26 (12.7%; 95% CI, 8.5-18.0%) were isolated distal DVT. In the subgroup of inpatients, 22 (23.7%; 95% CI, 15.5-33.6%) had DVT. Overall, 12 DVTs (12.9%; 95% CI, 6.8-21.5%) were proximal and 10 were (10.8%; 95% CI, 5.3-18.9%) isolated distal DVTs.

During the 3 months follow-up, one inpatient from the low-risk group based on the original Wells score, and with a negative initial CCUS, developed objectively confirmed non-fatal PE. One 72 year-old patient died from generalized cancer without evidence for recurrent VTE. No patient developed symptomatic DVT during follow-up. Four patients (1.9%), with no DVT after initial testing, were lost to follow-up.

3.1. Comparison of original and modified Wells scores

Compared to the original Wells score, the modified score classified significantly less patients in the low probability category (48% vs 53%; $p < 0.001$), and significantly more patients in the high probability group (17% vs 15%; $p = 0.02$) (Table 3). The modified Wells score also classified a significantly smaller proportion of outpatients in the low probability category (53% vs 59%; $p = 0.001$) and a significantly higher proportion of outpatients in the high probability category (13% vs 10%; $p = 0.03$) (Table 4). Six out of 65 (9.2%) outpatients, who were classified in the intermediate probability category according to the original Wells score, were reclassified in the high risk category according to the modified Wells score. These patients all had D-dimers >500 μg/L, and CCUS was positive in five of six patients (83%; 2 proximal and 3 isolated distal DVT). No significant differences in the proportion of patients per probability category were observed among hospitalized patients.

There were no statistically significant differences in the proportion of proximal or isolated distal DVT per risk category between the scores (Table 3). Similarly, no differences in DVT prevalence were observed across risk categories among outpatient and inpatients.

In general, the discriminatory power of both scores, expressed as the area under the ROC curve, was substantially better for proximal than for isolated distal DVT (Table 5). In patients with proximal DVT (but not in those with isolated distal DVT), both scores had much better discriminatory power for predicting DVT among outpatients and those with a prior history of DVT. In terms of discriminatory power, there were no statistically significant differences between the original and modified Wells score, regardless of the type of DVT, treatment setting (outpatient vs inpatient), or prior history of VTE.

4. Discussion

Our results demonstrate that original and modified Wells scores are similarly accurate in determining pre-test probability in patients with clinical suspicion of lower limb DVT. While both scores performed well in patients with proximal DVT, the discriminatory power in patients with isolated distal DVT was much lower. Both scores performed rather poorly in inpatients.

Because the modified Wells score comprises an additional variable (previously documented DVT), it classified significantly more patients as high-risk, whereas the original Wells score classified a significantly higher proportion of patients as low-risk. However, the absolute differences in risk classification between the original and modified Wells scores were modest (≤6%) and therefore not clinically relevant. Prevalence of DVT across risk categories based on the modified and original Wells score was similar. Our results are consistent with a prior prospective study finding a similar diagnostic performance for the original and modified Wells score in 297 inpatients and outpatients with clinical DVT suspicion [20]. The authors concluded

Table 3
Patient Classification and Prevalence of DVT by Clinical Probability Category.

	Original Wells Score (n = 298)	Modified Wells Score (n = 298)	*p* value
	% (95% Confidence Interval)		
Proportion of patients classified as			
Low-risk	53 (47-58)	48 (42-53)	*<0.01*
Intermediate-risk	33 (27-38)	35 (30-41)	*0.13*
High-risk	15 (11-19)	17 (13-22)	*0.02*
Prevalence of DVT per category			
Proximal DVT			
Low-risk	8 (4-13)	7 (3-13)	*0.50*
Intermediate risk	19 (11-28)	16 (10-25)	*>0.99*
High-risk	36 (22-52)	37 (24-52)	*0.25*
Isolated distal DVT			
Low-risk	8 (4-14)	8 (4-14)	*>0.99*
Intermediate-risk	20 (12-29)	16 (10-25)	*0.63*
High-risk	9 (3-22)	14 (6-26)	*0.25*

Note: DVT = deep vein thrombosis.

Table 4
Patient Classification and Prevalence of DVT Among Outpatients and Inpatients.

	Outpatients (n = 205)		*p* value	Inpatients (n = 93)		*p* value
	Original Wells Score	Modified Wells Score		Original Wells Score	Modified Wells Score	
	% (95% Confidence Interval)			% (95% Confidence Interval)		
Proportion of patients classified as						
Low-risk	59 (51-65)	53 (46-60)	*<0.01*	40 (30-50)	35 (26-46)	*0.13*
Intermediate-risk	32 (25-39)	34 (28-41)	*0.33*	34 (25 -45)	38 (28-48)	*0.38*
High-risk	10 (6-15)	13 (8-18)	*0.03*	26 (17-36)	27 (18-37)	*>0.99*
Prevalence of DVT per category						
Proximal DVT						
Low-risk	6 (2-12)	6 (2-12)	*>0.99*	14 (5-29)	12 (3-28)	*>0.99*
Intermediate-risk	23 (14-35)	20 (11-31)	*>0.99*	9 (2-25)	9 (2-23)	*>0.99*
High-risk	60 (36-81)	54 (33-73)	*0.50*	17 (5-37)	20 (7-41)	*>0.99*
Isolated distal DVT						
Low-risk	10 (5-17)	10 (5-17)	*>0.99*	3 (0-14)	3 (0-16)	*>0.99*
Intermediate-risk	18 (10-30)	14 (7-25)	*0.63*	22 (9-40)	20 (8-37)	*>0.99*
High-risk	10 (1-32)	19 (7-39)	*0.25*	8 (1-27)	8 (1-26)	*>0.99*

Note: DVT = deep vein thrombosis.

that the use of the somewhat more complex modified Wells score does not add any benefit.

In our study, both Wells scores poorly predicted isolated distal DVT (area under the ROC curve: 0.57). Our results are consistent with prior evidence suggesting that the original Wells score does not accurately predict the probability of isolated distal DVT [2,21], despite the fact that the initial clinical model by Wells and colleagues was derived including distal DVT diagnosed by venography [13,14]. However, most subsequent validation studies using proximal compression ultrasonography only did not look systematically for distal DVT [5,11,15] and therefore, both Wells scores are generally only considered for predicting pre-test probability of proximal DVT [3]. Nevertheless, in daily practice it is sometimes difficult to distinguish a priori an isolated distal from a proximal DVT and most clinicians apply these scores also for distal DVT. The clinical benefit of diagnosing and treating isolated distal DVT is still a matter of controversy [22,23] and is currently being examined in an ongoing randomized clinical trial (ClinicalTrials.gov NCT00539058).

Our results show that the original and modified Wells scores do not accurately predict the presence of DVT in hospitalized patients. Areas under the ROC curve varied between 0.52 and 0.60 in this patient subgroup. The original Wells score was derived in a sample of outpatients with clinical DVT suspicion only, potentially explaining the lower diagnostic performance among inpatients. In hospitalized patients, the differential diagnosis of leg pain or swelling may be broader than in outpatients, leading to a decrease in specificity of the Wells scores. This phenomenon is indirectly confirmed by the higher proportion of inpatients in whom an alternative diagnosis was at least as likely as DVT compared to outpatients (54% vs 45%). In contrast to our findings, a study by Ambid-Lacombe, et al. found areas under the ROC curve of 0.92 to 0.96 for the diagnosis of DVT among 217 inpatients with suspected DVT [20]. The excellent discriminatory power in the study by Ambid-Lacombe may be explained by the fact that determination of pretest probability was performed by a single vascular physician rather than by a pool of several vascular physicians as in our work. Two prior studies that prospectively examined the diagnostic performance of the original Wells score in surgical and medical inpatients with suspected DVT did not report any area under the ROC curve values, making a comparison difficult [7,15]. However, prevalence of DVT appropriately increased from 9-10% among low-risk to 51-76% among high-risk patients in these studies [7,15] while in our study prevalence of proximal DVT among low- and high-risk patients, based on the original Wells score, was 14% and 17%, respectively.

Table 5
Comparison of the Areas Under the Receiver Operating Characteristic Curves.

	Original Wells Score	Modified Wells Score	*p* value
	Area of ROC curve (95% Confidence Interval)		
Proximal DVT			
All patients (n = 298)	0.69 (0.61-0.77)	0.70 (0.62-0.78)	*0.46*
Outpatients (n = 205)	0.77 (0.68-0.85)	0.77 (0.68-0.85)	*0.87*
Inpatients (n = 93)	0.52* (0.34-0.70)	0.56 (0.38-0.75)	*0.24*
No history of VTE (n = 241)	0.66 (0.56-0.77)	0.66 (0.56-0.77)	*>0.99*
History of VTE (n = 57)	0.79 (0.67-0.92)	0.75 (0.62-0.87)	*0.34*
Isolated distal DVT			
All patients (n = 298)	0.57 (0.49-0.66)	0.57 (0.49-0.66)	*0.82*
Outpatients (n = 205)	0.56 (0.46-0.66)	0.57 (0.46-0.68)	*0.57*
Inpatients (n = 93)	0.60 (0.47-0.74)	0.58 (0.44-0.72)	*0.08*
No history of VTE (n = 241)	0.57 (0.48-0.66)	0.57 (0.48-0.66)	*>0.99*
History of VTE (n = 57)	0.56 (0.34-0.78)	0.68 (0.39-0.96)	*0.10*

Note: DVT = deep vein thrombosis, VTE = venous thromboembolism,* vs Outpatients: p = 0.02.

Since the only difference between the original and the modified Wells score is history of previously documented DVT, as an additional predictor variable in the modified Wells score, we also analyzed the performance of the two scores in patients with and without previous diagnosis of DVT. While we found no difference in predictive performance between the two scores, both scores somewhat better predicted DVT among patients with a prior history of DVT compared to patients without this condition. Because the derivation sample of the original Wells score excluded patients with previous diagnosis of DVT [6,13], this finding is somewhat paradoxical and is in contrast with results of a meta-analysis which found that the original Wells score had a worse performance in patients with previous VTE [2]. Nevertheless, our results and those of another study suggest that the original Wells score can also be used in persons with previous DVT [24].

Our study has several limitations. First, 15% of enrolled patients with a low or intermediate probability of DVT had negative D-dimers and did not undergo CCUS. However, given the excellent negative predictive value of a negative highly sensitive D-dimer test in patients with a non-high clinical DVT probability (99%, 95% CI of 96 to 100% [3,17]) and the fact that no patient had symptomatic DVT during follow-up, it is very unlikely that we missed any clinically significant DVTs in these patients. Second, one inpatient in whom DVT was ruled out at the initial work-up (low clinical probability, negative CCUS) developed non-fatal PE without DVT during follow-up. Thus, we cannot exclude that DVT may have already been present at time of enrollment despite a negative initial CCUS. Third, DVT pretest probability based on original and modified Wells scores was estimated by trained vascular physicians. Therefore, it is possible that the two scores would not have performed

equally well when calculated by less specialized emergency department or primary care physicians [25]. However, a recent study showed a good interobserver agreement between consultant and nurse practitioner in the emergency department setting [26]. Fourth, our study sample is rather small, especially the subgroup of patients with a history of previously documented DVT. Nevertheless, in the latter subgroup the areas under ROC curve for the diagnosis of proximal DVT are highly significant suggesting that the application of both scores is suitable for patients with previously documented DVT. For the subgroup of inpatients, further studies with larger patient numbers are needed to confirm or infirm the usefulness of the Wells scores in these patients. Finally, although the modified Wells score was originally used in a dichotomous fashion ($\leq$1 point: DVT unlikely; $\geq$2 points: DVT likely) [5], subsequent investigators used the three-category version (low, intermediate, or high probability of DVT) of the modified Wells score [11]. To facilitate the direct comparison with the original Wells score, we chose the three-category version of the modified Wells score. Furthermore, the three-category version seems to be more appropriate than the dichotomous one when highly sensitive D-dimer tests are used [27].

In conclusion, our results demonstrate that the original and modified Wells scores perform equally well in predicting pre-test DVT probability, especially in patients with proximal DVT and outpatients. Neither score appears to be particularly useful in inpatients and patients with isolated distal DVT. Scores that accurately predict DVT pre-test probability among inpatients with suspected DVT are therefore needed.

Conflict of interest statement

No conflict of interest to declare.

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References

[1] Hirsh J, Hoak J. Management of deep vein thrombosis and pulmonary embolism. A statement for healthcare professionals. Council on Thrombosis (in consultation with the Council on Cardiovascular Radiology), American Heart Association. Circulation 1996;93:2212–45.
[2] Goodacre S, Sutton AJ, Sampson FC. Meta-analysis: The value of clinical assessment in the diagnosis of deep venous thrombosis. Ann Intern Med 2005;143:129–39.
[3] Wells PS, Owen C, Doucette S, Fergusson D, Tran H. Does this patient have deep vein thrombosis? JAMA 2006;295:199–207.
[4] Constans J, Nelzy ML, Salmi LR, Skopinski S, Saby JC, Le Metayer P, et al. Clinical prediction of lower limb deep vein thrombosis in symptomatic hospitalized patients. Thromb Haemost 2001;86:985–90.
[5] Wells PS, Anderson DR, Rodger M, Forgie M, Kearon C, Dreyer J, et al. Evaluation of D-dimer in the diagnosis of suspected deep-vein thrombosis. N Engl J Med 2003;349:1227–35.
[6] Wells PS, Anderson DR, Bormanis J, Guy F, Mitchell M, Gray L, et al. Value of assessment of pretest probability of deep-vein thrombosis in clinical management. Lancet 1997;350:1795–8.
[7] Constans J, Boutinet C, Salmi LR, Saby JC, Nelzy ML, Baudouin P, et al. Comparison of four clinical prediction scores for the diagnosis of lower limb deep venous thrombosis in outpatients. Am J Med 2003;115:436–40.
[8] Subramaniam RM, Snyder B, Heath R, Tawse F, Sleigh J. Diagnosis of lower limb deep venous thrombosis in emergency department patients: performance of Hamilton and modified Wells scores. Ann Emerg Med 2006;48:678–85.
[9] Kahn SR, Joseph L, Abenhaim L, Leclerc JR. Clinical prediction of deep vein thrombosis in patients with leg symptoms. Thromb Haemost 1999;81:353–7.
[10] Perone N, Bounameaux H, Perrier A. Comparison of four strategies for diagnosing deep vein thrombosis: a cost-effectiveness analysis. Am J Med 2001;110:33–40.
[11] Anderson DR, Kovacs MJ, Kovacs G, Stiell I, Mitchell M, Khoury V, 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;1:645–51.
[12] Schutgens RE, Ackermark P, Haas FJ, Nieuwenhuis HK, Peltenburg HG, Pijlman AH, et al. Combination of a normal D-dimer concentration and a non-high pretest clinical probability score is a safe strategy to exclude deep venous thrombosis. Circulation 2003;107:593–7.
[13] Wells PS, Hirsh J, Anderson DR, Lensing AW, Foster G, Kearon C, et al. Accuracy of clinical assessment of deep-vein thrombosis. Lancet 1995;345:1326–30.
[14] Wells PS, Hirsh J, Anderson DR, Lensing AW, Foster G, Kearon C, 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.
[15] Wells PS, Anderson DR, Bormanis J, Guy F, Mitchell M, Gray L, et al. Application of a diagnostic clinical model for the management of hospitalized patients with suspected deep-vein thrombosis. Thromb Haemost 1999;81:493–7.
[16] de Moerloose P, Desmarais S, Bounameaux H, Reber G, Perrier A, Dupuy G, et al. Contribution of a new, rapid, individual and quantitative automated D-dimer ELISA to exclude pulmonary embolism. Thromb Haemost 1996;75:11–3.
[17] Stein PD, Hull RD, Patel KC, Olson RE, Ghali WA, Brant R, et al. D-dimer for the exclusion of acute venous thrombosis and pulmonary embolism: a systematic review. Ann Intern Med 2004;140:589–602.
[18] Bates SM, Kearon C, Crowther M, Linkins L, O'Donnell M, Douketis J, et al. A diagnostic strategy involving a quantitative latex D-dimer assay reliably excludes deep venous thrombosis. Ann Intern Med 2003;138:787–94.
[19] Schellong SM, Schwarz T, Halbritter K, Beyer J, Siegert G, Oettler W, et al. Complete compression ultrasonography of the leg veins as a single test for the diagnosis of deep vein thrombosis. Thromb Haemost 2003;89:228–34.
[20] Ambid-Lacombe C, Cambou JP, Bataille V, Baudoin D, Vassal-Hebrard B, Boccalon H, et al. Excellent performances of Wells' score and of the modified Wells' score for the diagnosis of proximal or distal deep venous thrombosis in outpatients or inpatients at Toulouse University Hospital: TVP-PREDICT study. J Mal Vasc 2009;34:211–7.
[21] Blattler W, Martinez I, Blattler IK. Diagnosis of deep venous thrombosis and alternative diseases in symptomatic outpatients. Eur J Intern Med 2004;15:305–11.
[22] Schellong SM. Distal DVT: worth diagnosing? Yes. J Thromb Haemost 2007;5 (Suppl 1):51–4.
[23] Righini M, Paris S, Le Gal G, Laroche JP, Perrier A, Bounameaux H. Clinical relevance of distal deep vein thrombosis. Review of literature data. Thromb Haemost 2006;95:56–64.
[24] Cornuz J, Ghali WA, Hayoz D, Stoianov R, Depairon M, Yersin B. Clinical prediction of deep venous thrombosis using two risk assessment methods in combination with rapid quantitative D-dimer testing. Am J Med 2002;112:198–203.
[25] Oudega R, Hoes AW, Moons KG. The Wells rule does not adequately rule out deep venous thrombosis in primary care patients. Ann Intern Med 2005;143:100–7.
[26] Dewar C, Corretge M. Interrater reliability of the Wells score as part of the assessment of DVT in the emergency department: agreement between consultant and nurse practitioner. Emerg Med J 2008;25:407–10.
[27] Bounameaux H, Perrier A, Righini M. Diagnosis of venous thromboembolism: an update. Vasc Med 2010;15:399–406.