

Comparison of Four Clinical Prediction Scores for the Diagnosis of Lower Limb Deep Venous Thrombosis in Outpatients

Joël Constans, MD, Catherine Boutinet, MD, L. Rachid Salmi, MD, Jean-Claude Saby, MD, Marie-Line Nelzy, MD, Patrice Baudouin, MD, Françoise Sampoux, MD, Jean-Marie Marchand, MD, Caroline Boutami, MD, Véronique Dehant, MD, Stéphane Pulci, MD, Jean-Paul Gauthier, MD, Véronique Cacareigt-Bourdenx, MD, Damien Barcat, MD, Claude Conri, MD

PURPOSE: We compared three scores for the prediction of deep venous thrombosis with a new score designed specifically for outpatients.

METHODS: Patients referred for evaluation because of suspected deep venous thrombosis were examined by ultrasonography. Sensitivity and specificity were calculated for three clinical scores (Wells [nine components], Kahn [four components], and St. André [six components]). We developed a new score by multivariate analysis, and then compared this score with the others in a new sample.

RESULTS: Four hundred and forty-four outpatients were included in the first sample, of whom 126 (28%) had deep venous thrombosis. The Wells score was a better predictor of deep venous thrombosis than the Kahn and St. André scores. According to the Wells score, 73 patients had a high probability of deep venous thrombosis (of whom 51 [70%] actually had a throm-

bosis) and 178 had a low probability of deep venous thrombosis (of whom 19 [11%] had a thrombosis). A new score was developed as follows: male sex (+1), lower limb palsy or immobilization (+1), confinement to bed >3 days (+1), lower limb enlargement (+1), unilateral lower limb pain (+1), and other plausible diagnosis (-1). In a validation sample of 282 outpatients, this score identified 31 patients who had a high probability of deep venous thrombosis (score ≥ 3), of whom 18 (58%) had a thrombosis, and 70 patients who had a low probability (score ≤ 0), of whom 3 (4%) had a thrombosis. The Wells score and this ambulatory score had similar test operating characteristics in the validation sample.

CONCLUSION: Our new six-component score had similar diagnostic utility as the nine-component Wells score among outpatients being evaluated for deep venous thrombosis. *Am J Med.* 2003;115:436-440. ©2003 by Excerpta Medica Inc.

Clinical diagnosis of deep venous thrombosis is difficult, in part because the individual clinical signs and symptoms lack sensitivity and specificity (1-5). Nevertheless, treatment must be undertaken rapidly to avoid potentially fatal pulmonary embolism (6). Measurement of D-dimers may improve diagnostic strategies, but the test has many false-positive results (7,8). Some investigators have developed clinical scores based on history and physical examination for predicting the probability of deep venous thrombosis before confirmation by objective testing (9-12). Scores including nine (Wells) (10,13-15), six (St. André hospital) (12), or four (Kahn) (3,11) items can improve the efficiency of early detection. However, the Kahn score, which is simple to compute,

was not particularly useful in medical inpatients (12). Although the Wells index seems useful in outpatients (16), we developed the St. André score for hospitalized patients, and it requires validation in an ambulatory setting.

METHODS

Patients

Outpatients referred for ultrasound exploration for suspected deep venous thrombosis were included in two prospective samples. In a derivation sample, the Wells, Kahn, and St. André scores were measured. In addition, we developed a new score, specifically for outpatients. A second validation sample was used to assess all four scores prospectively. The following items and weights were used for the Wells score: cancer (+1), lower limb paralysis or immobilization (+1), confinement to bed >3 days (+1), localized tenderness (+1), whole lower limb enlargement (+1), calf enlargement ≥ 3 cm compared with the other side (+1), unilateral pitting edema (+1), superficial venous dilation (+1), and other diagnosis at least as plausible as deep venous thrombosis (-2). For the Kahn score, we used the following: male sex (+1), orthopedic surgery

From the Service de Médecine Interne et Pathologie Vasculaire (JC, CB, DB, CC), Hôpital Saint-André, Bordeaux, France; Société Régionale de Médecine Vasculaire Aquitaine (JC, JCS, MLN, PB, FS, JMM, CB, VD, SP, JPG, VCB), France; and Institut de Santé Publique (LRS), Epidémiologie et Développement, Université Victor Segalen-Bordeaux II, Bordeaux, France.

Requests for reprints should be addressed to Joël Constans, MD, Service de Médecine Interne et Pathologie Vasculaire, Hôpital Saint-André, 1 rue Jean Burguet, 33075 Bordeaux, France, or joel.constans@chu-bordeaux.fr.

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Table 1. Characteristics of Patients with or without Deep Venous Thrombosis in the Derivation Sample

Characteristic	Thrombosis	No Thrombosis	P Value
	(n = 126)	(n = 318)	
	Number (%)		
Male sex	55 (44)	95 (30)	0.007
Age >65 years	59 (47)	128 (40)	0.25
Cancer	8 (6)	10 (3)	0.18
Lower limb paralysis, immobilization	9 (7)	7 (2)	0.02
Confinement to bed >3 days	15 (12)	12 (4)	0.003
Orthopedic surgery <6 months	9 (7)	27 (8)	0.7
Surgery <3 months	11 (9)	30 (9)	0.96
Hospitalization <3 months	14 (11)	34 (11)	1.04
Localized tenderness	82 (65)	165 (52)	<0.0001
Lower limb enlargement	71 (56)	80 (25)	<0.0001
Calf enlargement >3 cm	50 (40)	60 (20)	<0.0001
Unilateral pitting edema	43 (34)	55 (17)	0.0002
Superficial venous dilatation	14 (11)	10 (3)	0.002
Local warmth	29 (23)	66 (21)	0.6
Unilateral lower limb pain	106 (84)	175 (55)	<0.0001
Previous deep venous thrombosis	4 (3)	13 (4)	0.87
Other diagnosis	16 (13)	124 (39)	<0.0001

<6 months (+1), superficial venous dilation (+1), and local warmth (+1). Although both the Wells and Kahn scores were developed to detect proximal thrombosis, we developed the St. André score to assess both proximal and distal deep venous thrombosis. The St. André score includes cancer (+1), lower limb paralysis or immobilization (+1), unilateral pitting edema (+1), superficial venous dilation (+1), local warmth (+1), and other diagnosis at least as plausible as deep venous thrombosis (-1).

To standardize clinical observations, all investigators met at the beginning of the study to discuss the interpretation of the items on the clinical form. The lower limb was considered enlarged if enlargement was greater than 3 cm. Localized tenderness was thought by most investigators to be difficult to standardize.

Patients were included in the derivation sample from November 2000 to March 2001, and in the validation sample from December 2001 to March 2002. All patients were referred by their general practitioner to 1 of 10 experienced angiologists during the study period. No patients were hospitalized at the time of referral. Each angiologist examined the patient and completed a form that included all the items used in the Wells, Kahn, and St. André scores. Unilateral calf pain was also recorded. Angiologists had to record this information before performing ultrasonography.

Diagnosis of Deep Venous Thrombosis

The diagnosis of deep venous thrombosis was made by duplex compression (7,8,17,18). The inferior vena cava, and the iliac, femoral, popliteal, and calf veins were ex-

amined. The upper limit of deep venous thrombosis was recorded. Because diagnosing deep venous thrombosis in a patient with a previous history of thrombosis is difficult, the main criterion was taken to be a noncompressible vein. However, interpretation also considered vein dilatation and complete venous obstruction. Some authors recommend serial examination in some patients, especially those with high clinical probability and a negative ultrasound examination (19), but these investigators use techniques that do not explore the calf veins. When the whole venous tree is examined by experienced angiologists using modern ultrasound systems, serial examinations are of little use (12,20-22). Moreover, none of the patients who had a negative ultrasound examination in the present study had deep venous thrombosis diagnosed by the participating angiologists during the following 6 months.

Table 2. Independent Predictors of Deep Venous Thrombosis in the Derivation Sample (444 Patients)

Predictor	Odds Ratio (95% Confidence Interval)	P Value
Male sex	2.0 (1.2-3.3)	0.006
Lower limb paralysis or immobilization	3.7 (1.1-12)	0.04
Confinement to bed >3 days	2.9 (1.1-7.9)	0.04
Lower limb enlargement	4.0 (2.5-6.6)	<0.001
Unilateral pain	5.1 (2.8-9.3)	<0.001
Other diagnosis	0.2 (0.1-0.4)	<0.001

Table 3. Prediction of Deep Venous Thrombosis from Clinical Scores in the Derivation and Validation Samples

Score Levels	Derivation Sample	Validation Sample
	(n = 444)	(n = 282)
Percentage with Thrombosis (No. with Thrombosis/No. in Level)		
Wells		
≥3	70 (51/73)	69 (37/54)
1–2	29 (56/193)	20 (28/144)
≤0	11 (19/178)	6 (6/84)
Kahn		
≥3	56 (5/9)	0 (0/1)
1–2	31 (69/222)	25 (37/147)
≤0	24 (52/213)	25 (34/134)
St. André		
≥3	71 (5/7)	67 (4/6)
1–2	43 (58/131)	34 (32/93)
≤0	20 (63/306)	15 (35/183)
Ambulatory		
≥3	82 (32/38)	58 (18/31)
1–2	30 (84/278)	27 (50/181)
≤0	7 (10/128)	4 (3/70)

Statistical Analysis

Logistic regression models were used to analyze the associations of variables with deep venous thrombosis. A variable was included in the model if it was associated with deep venous thrombosis at $P \leq 0.25$ in a univariate analysis. For each model, a backward stepwise procedure was applied to remove variables that were not associated with

deep venous thrombosis ($P < 0.05$) (23). Because our aim was to obtain a simple score with no more than six items, we assigned an equal weight to each variable in the final model. For each score, a receiver operating characteristic (ROC) curve was drawn (24); the area under the ROC curve and its 95% confidence interval were estimated (24). We compared the areas under the ROC curves for each of the scores (25). We used the Graphpad PRISM package (San Diego, California) for standard statistical analysis and EGRET 2.0 for Windows for logistic regression (Egret Research Corporation, Seattle, Washington).

RESULTS

Among the 444 patients in the derivation sample (mean [\pm SD] age, 61 ± 18 years), 126 (28%) had deep venous thrombosis diagnosed after duplex echography (Table 1). The upper limit of thrombosis was the popliteal vein or above in 58 of these patients.

Six variables were associated with deep venous thrombosis in a multivariate model (Table 2). We developed the new ambulatory score from these variables, with the following weights: male sex (+1), paralysis or immobilization of lower limb (+1), confinement to bed < 3 days (+1), lower limb enlargement (+1), unilateral lower limb pain (+1), and other diagnosis at least as plausible (–1).

The percentage of patients with deep venous thrombosis, by clinical probability, was determined for each score (Table 3). The area under the ROC curve was 0.76 (95%

Table 4. Characteristics of Patients with or without Deep Venous Thrombosis in the Validation Sample (282 Patients)

Characteristic	Thrombosis	No Thrombosis	P Value
	(n = 71)	(n = 211)	
Number (%)			
Male sex	21 (30)	65 (31)	0.88
Age > 65 years	41 (58)	110 (52)	0.50
Cancer	5 (7)	6 (3)	0.15
Paralysis or immobilization	7 (10)	7 (3)	0.05
Confinement to bed > 3 days	11 (15)	18 (8)	0.11
Orthopedic surgery < 6 months	8 (11)	12 (6)	0.11
Surgery < 3 months	10 (14)	13 (6)	0.14
Hospitalization < 3 months	10 (14)	14 (7)	0.19
Localized tenderness	54 (76)	137 (65)	< 0.0001
Lower limb enlargement	44 (62)	71 (34)	< 0.0001
Calf enlargement > 3 cm	56 (79)	119 (56)	0.001
Unilateral pitting edema	27 (38)	55 (26)	0.07
Superficial venous dilation	8 (11)	2 (1)	0.0003
Local warmth	10 (14)	56 (27)	0.05
Unilateral lower limb pain	56 (79)	119 (56)	0.0007
Previous venous thrombosis	6 (8)	7 (3)	0.15
Other diagnosis	4 (6)	81 (38)	< 0.0001

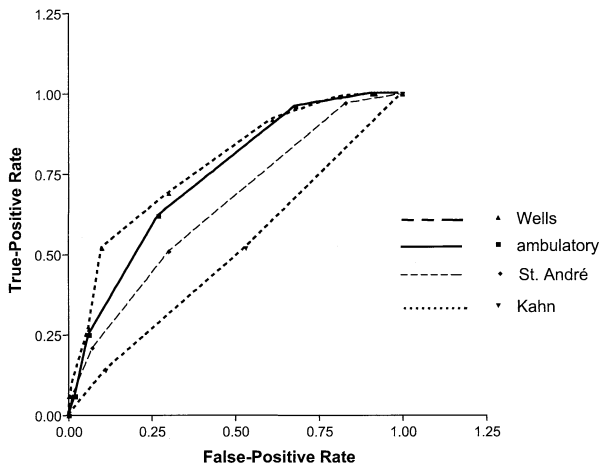


Figure. Receiving operating characteristic curves for the four scores in the validation sample.

confidence interval [CI]: 0.70 to 0.81) for the Wells score, 0.57 (95% CI: 0.50 to 0.63) for the Kahn score, 0.67 (95% CI: 0.61 to 0.73) for the St. André score, and 0.79 (95% CI: 0.74 to 0.84) for the new score.

Of the 282 patients in the validation sample, 71 (25%) had deep venous thrombosis (Table 4). The upper limit of thrombosis was the popliteal vein or above in 36 patients. ROC curves are given for each score in the validation sample in the Figure. The new score had better discriminatory ability than the Kahn and St. André scores, and was similar to the nine-item Wells score (Table 5).

DISCUSSION

We observed differences in the characteristics of outpatients with suspected deep venous thrombosis as compared with previously reported hospitalized patients (12). For example, the prevalence of cancer was very different: 17% of hospitalized patients had cancer compared

with only 4% of outpatients. This may explain why cancer was pertinent in our previous hospital-based (St. André) score and not in the new score. Similarly, confinement to bed was much more frequent in hospitalized than ambulatory patients, which may explain why this item was not useful in the hospital-based score. Although there were similar proportions of men in the hospital and community samples, male sex was included only in the ambulatory score. Kahn et al also found that male sex was associated with deep venous thrombosis (11). They hypothesized that this might be explained by self-referral bias, if women consulted angiologists more frequently than men because of diagnoses other than deep venous thrombosis, such as chronic venous insufficiency. In our validation sample, male sex was not associated with deep venous thrombosis; thus, the relevance of sex needs to be verified further.

It is difficult to separate lower limb enlargement, calf enlargement, and unilateral pitting edema, because these conditions overlap. Nevertheless, they were independent predictors in the multivariate analysis from which the Wells score was developed. Although unilateral pitting edema was included in our hospital-based St. André score, lower limb enlargement was more discriminant in the ambulatory one. On the other hand, superficial venous dilatation is included in the Wells, Kahn, and St. André scores, but not the ambulatory score.

Unilateral lower limb pain was included in our ambulatory index but not in the hospital-based scores. Localized tenderness is part of the Wells score, but this clinical sign is difficult to assess in clinical practice. An alternative diagnosis that is at least as plausible as deep venous thrombosis, is part of the Wells, St. André, and ambulatory scores, emphasizing that deep venous thrombosis is less plausible when erysipelas or a calf hematoma is present.

A remaining issue is the reproducibility of all these items. Although historical data, such as cancer or immobilization, are likely to be reproducible, clinical examination may be less reliable. Therefore, it will be essential to

Table 5. Comparison of the Areas Under the Receiver Operating Characteristic Curves for the Four Scores in the Validation Sample

Pairwise comparisons	Wells	Kahn	St. André	Ambulatory
	Area (95% Confidence Interval)			
	0.78 (0.72–0.84)	0.51 (0.43–0.59)*	0.66 (0.59–0.73)	0.74 (0.67–0.80)
	P Value			
With Wells score	NA	<0.0001	0.99	0.92
With Kahn score	<0.0001	NA	<0.0001	<0.0001
With St. André score	0.99	<0.0001	NA	0.02
With ambulatory score	0.92	<0.0001	0.02	NA

* Not significantly different from chance.
NA = not applicable.

validate the reproducibility of all of these scores in routine clinical settings.

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