Review: The Wells rule is more useful than individual clinical features for predicting risk for deep venous thrombosis

Clinical impact ratings: Emergency Med ★★★★☆☆ GIM/FP/GP ★★★★★★★ Hospitalists ★★★★☆☆ Hematol/Thrombo ★★★★★☆

QUESTION

In patients with suspected deep venous thrombosis (DVT), how well do individual clinical features, structured risk scores, and physicians' empirical judgments detect the presence or absence of DVT?

METHODS

Data sources: MEDLINE, EMBASE/ Excerpta Medica, CINAHL, Web of Science, Cochrane Database of Systematic Reviews, Cochrane Controlled Trials Register, Database of Reviews of Effectiveness, *ACP Journal Club* (to January 2005), and bibliographies of retrieved articles.

Study selection and assessment: Diagnostic cohort studies (published as full articles or abstracts in English, French, Spanish, or Italian) of patients with suspected DVT that evaluated clinical findings, risk scores, and physicians' empirical judgments compared with diagnosis by a reference standard (ultrasonography or venography). Excluded were case–control studies, studies with < 10 patients, and those that assessed risk for DVT in the future. Evaluation of study quality included whether the reference standard was applied independently of the clinical assessment, and whether the observers of both the clinical assessment and the reference standard were blinded to the results of the other test.

Outcomes: Pooled positive and negative likelihood ratios (LRs).

MAIN RESULTS

54 cohorts from 51 studies were included in the meta-analysis. LRs were pooled using a random-effects model. Clinical features that were useful or moderately useful in ruling in DVT were malignant disease, history of DVT, recent immobilization, recent surgery, and a difference in calf diameter between legs (Table). Clinical features that were moderately useful in ruling out DVT were absence of a difference in calf diameter and absence of calf swelling (Table). Individual features that were not useful for diagnosis of DVT included calf pain, obesity, Homan sign, warmth, tenderness, erythema, and edema. The Wells rule, the only validated structured risk score evaluated, performed better than any of the individual clinical features (Table).

Physicians' empirical assessment performed similarly to the Wells score (Table).

CONCLUSIONS

Individual clinical features have limited usefulness for predicting the presence or absence of deep venous thrombosis (DVT) in patients with symptoms. Structured clinical risk scores (the Wells score) and physicians' empirical assessments provide more useful information for detecting DVT.

Pooled likelihood ratios of individual clinical features, the Wells risk score, and physicians' empirical assessment for detecting the presence or absence of deep venous thrombosis (DVT)*

Diagnostic test	Number of studies	+LR (95% CI)	−LR (CI)
Malignant disease	20	2.7 (2.2 to 3.4)	0.89 (0.85 to 0.93)
History of DVT	11	2.3 (1.6 to 3.2)	0.90 (0.85 to 0.95)
Recent immobilization	17	2.0 (1.7 to 2.3)	0.90 (0.85 to 0.94)
Recent surgery	17	1.8 (1.4 to 2.2)	0.94 (0.91 to 0.97)
Difference in calf diameter	8	1.8 (1.5 to 2.2)	0.57 (0.44 to 0.72)
Calf swelling	16	1.5 (1.3 to 1.7)	0.67 (0.58 to 0.78)
Wells risk score High risk Low risk	22	5.2 (4.0 to 6.0) —	— 0.25 (0.21 to 0.29)
Empirical assessment High risk Low risk	4	5.6 (1.9 to 16.6) —	— 0.20 (0.10 to 0.41)

*Diagnostic terms defined in Glossary.

COMMENTARY

Diagnosis of DVT is challenging because of its nonspecific clinical presentation. Recent research has focused on strategies to exclude the diagnosis of suspected DVT and reduce the use of expensive imaging tests. Many such strategies depend on a sensitive assay for D-dimer, a breakdown product of fibrin. Unfortunately, the D-dimer test has insufficient negative predictive value to safely "rule out" DVT on its own (1). Several studies have evaluated the usefulness of combining clinical pretest probability of disease and a sensitive D-dimer test to assess the safety of a low posttest probability of DVT to exclude the diagnosis.

Both physician empirical assessment (gestalt) and formalized clinical prediction guides (CPGs) have been tested. The best-known CPG, devised by Wells and colleagues, has been tested in many studies and has undergone several modifications. Using Wells' 9-point CPG, 3% of patients with a low score had DVT, corresponding to a −LR of 0.16 (2). Subsequent studies found that a negative D-dimer result in this

group of patients refuted the diagnosis of DVT with a low rate of missed disease. These studies have been done mostly in emergency departments and specialty thrombosis clinics.

Goodacre and colleagues' meta-analysis of 51 such studies found that a low Wells score was associated with a −LR of 0.25, with better performance in patients without previous DVT (−LR 0.17) and when only proximal DVT was sought. The authors concluded that the −LR was low enough that addition of a negative sensitive D-dimer result was likely to safely exclude DVT. Interestingly, the authors also found that physician gestalt was associated with a −LR of 0.20, although this finding was based on only 4 studies and had a wide confidence interval.

The study by Oudega and colleagues offered contrasting results when the 9-point Wells score was used by primary care physicians, who received limited training in its application. The incidence of proximal DVT in the group with a low Wells score was 12%, compared with 3%

The Wells rule was not useful in ruling out deep venous thrombosis in a primary care setting

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.

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QUESTION

In primary care patients with symptoms of deep venous thrombosis (DVT), how well does the Wells rule predict the presence or absence of DVT?

METHODS

Design: A diagnostic rule developed by Wells and colleagues in a secondary care setting was evaluated in primary care patients.

Setting: Primary care practices of 110 physicians in the Netherlands.

Patients: 1295 patients > 18 years of age (mean age 60 y, 64% women), who visited their primary care physician with symptoms of swelling, redness, or pain in the legs ≤ 30 days and were suspected to have DVT. Patients with suspected pulmonary embolism were excluded.

Description of prediction guide: The Wells rule consisted of a score of 0 to 8, obtained by summing the presence of 8 characteristics identified from patient history (active cancer, immobilization of the leg, and recently bedridden) and physical examination (localized tenderness, whole leg or calf swelling, pitting edema, and collateral superficial veins), adjusted by −2 if another diagnosis was as or more likely than DVT. A score ≤ 0 indicated low risk, 1 to 2 indicated medium

risk, and ≥ 3 indicated high risk. A normal result on D-dimer testing (< 500 ng/mL), combined with a low risk score on the Wells rule, indicated very low risk.

Outcomes: Sensitivity, specificity, negative predictive value, and negative likelihood ratio.

MAIN RESULTS

By the Wells rule, 39% of patients were categorized as being at low risk, 25% at medium risk, and 36% at high risk. Of patients in the low-risk group, 44% had a normal D-dimer test and were categorized as very low risk (17% of all patients). DVT was diagnosed by B-mode compression ultrasonography in 289 patients (22%): 12% of the low-risk group, 17% of the medium-risk group, and 37% of the high-risk group.

2.3% of patients in the very low-risk group had DVT. The diagnostic test properties, except specificity, improved when the D-dimer test was added to the Wells rule (Table).

CONCLUSIONS

In a primary care setting, the Wells rule was not useful for ruling out deep venous thrombosis in patients with symptoms. With the addition of the D-dimer test, sensitivity and negative predictive value increased, but specificity was poor.

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Operating characteristics of the Wells rule, with and without the D-dimer test, for identifying primary care patients with deep venous thrombosis*

Definition of a negative test	Sensitivity (95% CI)	Specificity (CI)	Negative predictive value (CI)	−LR (CI)
Wells score ≤ 0	79% (74 to 84)	44% (41 to 47)	88% (85 to 91)	0.48 (0.38 to 0.60)
Wells score ≤ 0 and normal D-dimer test	98% (97 to 100)	22% (19 to 24)	98% (96 to 100)	0.08 (0.03 to 0.19)

*Diagnostic terms defined in Glossary.

COMMENTARY

in the Wells study (2) and 7% in the Goodacre meta-analysis, and the −LR was 0.48. When combined with a normal sensitive D-dimer result, the −LR fell to 0.08 (95% CI 0.03 to 0.19). In the population studied, this would correspond to a rate of missed DVT of up to 5.1%. If the data were reanalyzed to allow a Wells score ≤ 1 (corresponding to the more recent 2-category version of the CPG), the rate of missed disease could be as high as 5.6%.

A key challenge for the clinician in the interpretation of medical research is assessing external validity—how well do the results of a study apply to the patient at hand (3)? Oudega and colleagues suggested that the clinical setting accounts for the difference in outcome they observed, because of differences in patient population. Indeed, the population in the Oudega study was slightly older (mean age 60 y, compared with 57 y in the Wells study) and the results of the Goodacre meta-analysis suggested that the Wells score performed worse when the mean patient age was > 60 years (−LR 0.30 vs 0.24 in younger patients). However, it seems unlikely that this small age difference could account for so large a difference in outcome. Another explanation for the conflicting outcomes is that the Wells score is applied differently by different groups of physicians. Some features of the structured risk score, mostly related to physical examination, are prone to greater interindividual variation. It is likely that the specific training in the application of the Wells score received by the physicians participating in the Oudega study, who were

outside of an emergency department or specialty thrombosis setting, was not sufficient to develop adequate skills.

Because of the preponderance of evidence, the Wells score plus D-dimer test still serves as a good platform on which to base the workup of suspected DVT, especially in emergency departments and secondary care settings. Further research is needed, however, to evaluate the Wells score or an alternate CPG in primary care settings. A CPG-based strategy reduces the use of ultrasonography and other expensive tests and makes clinical decisions more objective. However, the algorithm alone cannot replace clinical judgment, as it might fail when applied to certain patients and in certain settings. The astute clinician who still suspects DVT in a patient with a low Wells score (especially a score of 1) and a negative D-dimer result will pursue further testing.

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