

Review: The Wells clinical prediction guide and D-dimer testing predict deep venous thrombosis

Wells PS, Owen C, Doucette S, Fergusson D, Tran H. Does this patient have deep vein thrombosis? JAMA. 2006;295:199-207.

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

QUESTION

Does a clinical prediction guide (CPG) with or without D-dimer testing predict deep venous thrombosis (DVT)?

METHODS

Data sources: MEDLINE (1990 to 1 July 2004) and relevant references in English and French.

Study selection and assessment: Studies were selected if they were prospective trials with ≥ 3 -month follow-up, enrolled consecutive outpatients with symptoms and signs suggestive of DVT, used a validated CPG to estimate the clinical probability (low, moderate, and high) of DVT before D-dimer testing or diagnostic imaging, and evaluated proximal DVT. In studies that included D-dimer testing, testing had to be done before other diagnostic tests. Studies of patients with previous DVT that was not adjusted for by the CPG or the reviewers were excluded. 14 studies ($n = 8239$) met the selection criteria; all evaluated the Wells CPG. 11 studies ($n = 5690$) incorporated D-dimer testing in the CPG. Quality assessment of individual studies was based on independent, blinded comparison of symptoms or signs with a diagnostic reference standard among patients with suspected DVT.

Outcomes: DVT.

MAIN RESULTS

The prevalence of DVT in the low, moderate, and high clinical probability groups was 5.0% (95% CI 4.0 to 8.0), 17% (CI 13 to 23), and 53% (CI 44 to 61), respectively. Meta-analysis showed that the specificity of D-dimer testing (high sensitivity assays, moderate sensitivity assays, and overall) decreased as the clinical probability rose from low to high (overall $P < 0.001$; P value not reported for high-sensitivity and moderate-sensitivity assays, respectively) for predicting DVT, but the sensitivity of D-dimer testing did not differ among the 3 clinical probability groups (Table).

CONCLUSIONS

In patients with suspected deep venous thrombosis (DVT), low clinical probability on the Wells clinical prediction guide combined with negative D-dimer test results rules out DVT. High clinical probability or a positive D-dimer test result requires further ultrasonography testing.

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Diagnostic characteristics of the Wells clinical prediction guide (low, moderate, and high probability) and D-dimer testing for predicting deep venous thrombosis*

Outcomes	Probability	Sensitivity (95% CI)	Specificity (CI)	+LR	-LR
Overall D-dimer testing	Low	88% (81 to 92)	72% (65 to 78)	3.3	0.18
	Moderate	90% (80 to 95)	58% (49 to 67)	2.1	0.19
	High	92% (85 to 96)	45% (37 to 52)	1.6	0.16
Moderate-sensitivity D-dimer testing†	Low	86% (79 to 92)	78% (71 to 83)	4.0	0.20
	Moderate	85% (73 to 93)	66% (58 to 73)	2.4	0.23
	High	90% (80 to 95)	49% (40 to 58)	1.7	0.20
High-sensitivity D-dimer testing‡	Low	95% (82 to 99)	58% (45 to 71)	2.4	0.10
	Moderate	98% (91 to 100)	41% (31 to 52)	1.7	0.05
	High	97% (94 to 99)	36% (29 to 43)	1.5	0.07

*Diagnostic terms defined in Glossary. A random-effects model was used.

†Whole blood assays.

‡Enzyme-linked immunosorbent assays.

COMMENTARY

The systematic review by Wells and colleagues provides important confirmation of the role of clinical assessment in suspected DVT. The Wells rule works, and it is now well-validated.

Prevalence of DVT in the low- and moderate-probability categories is consistent across 14 studies including > 8000 patients. However, although those series included outpatients, this sample was probably not representative of primary care patients since a large proportion had probably already been triaged. However, the prevalence of DVT would be expected to be even lower in primary care patients with a low probability of DVT according to the Wells rule, making it even safer to rule out DVT in combination with a negative D-dimer test result. On the other hand, interobserver variability has not been examined in any of the studies included in this meta-analysis, which might be a concern because the Wells rule contains at least 1 subjective element (i.e., the likelihood of an alternative diagnosis). But this is probably not important because the rule has been validated by a vast number of physicians with varying degrees of experience.

The highly sensitive D-dimer assays have a negative likelihood ratio (–LR) about 0.1, but moderately sensitive assays have a –LR about 0.2. Despite those different characteristics, most experts would probably agree that the combination of a low clinical probability of DVT and a negative result from a D-dimer test of either sort convincingly rules out DVT with a posttest probability < 1%.

But what should we do for patients with moderate clinical probability? In a patient with a negative, moderately sensitive D-dimer assay, the posttest probability of DVT would still be over 4% and lower limb compression ultrasonography should be done. But if a highly sensitive D-dimer assay was negative, the posttest probability would only be about 1%, potentially ruling out DVT without further testing. This strategy is clearly promising but must be tested in other studies on a larger scale before it can be widely advocated.

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