Note: This is a two-article spread with a shared commentary. Please scroll down for the second article.

DIAGNOSIS

A negative D-dimer result and low-risk clinical status effectively ruled out DVT in symptomatic patients

Aschwanden M, Labs KH, Jeanneret C, Gehrig A, Jaeger KA. **The value of rapid D-dimer testing combined with structured clinical evaluation for the diagnosis of deep vein thrombosis.** J Vasc Surg. 1999 Nov;30:929-35.

QUESTION

Can a D-dimer assay, alone or combined with structured clinical risk assessment, be used to rule out deep venous thrombosis (DVT) in symptomatic patients?

DESIGN

A blinded comparison of D-dimer test results plus results from a structured clinical assessment with duplex ultrasonographic scanning (DUS).

SETTING

A university hospital in Basel, Switzerland.

PARTICIPANTS

360 consecutive patients were screened, and 343 participants, who had complete information (median age 61 y, age range 17 to 94 y, 61% women, 52% inpatients, 398 limbs), were investigated for suspected DVT. No exclusion criteria were specified.

DESCRIPTION OF TESTS AND DIAGNOSTIC STANDARD

A D-dimer analysis was done (SimpliRED, Agen Biomedical, Brisbane, Australia) initially. Patients were then divided into groups at low or high risk for DVT based on a previously validated clinical risk assessment score* calculated by using data on the presence of cancer, immobilization, recent surgery, localized tenderness, swelling, pitting edema, and collateral superficial veins. Data were compiled by an examiner who was blinded to the D-dimer test results. DUS (diagnostic standard) was done in a blinded fashion to identify all (proximal and calf) DVT. All scans were conclusive.

MAIN OUTCOME MEASURES

Sensitivity and specificity for the diagnosis of DVT for patients and limbs using D-dimer test results alone and combined with a clinical risk assessment.

MAIN RESULTS

Of the 343 patients, 71% were at low risk for DVT. 16% had proximal DVT, and 5% had isolated calf DVT. The sensitivity of D-dimer assay was 89% in detecting proximal DVT and 87% for all DVT; when combined with a clinical assessment, sensitivity was 98% for proximal DVT and 96% for all DVT (Table).

CONCLUSION

A screening procedure based on negative D-dimer assay results combined with low-risk clinical status effectively ruled out deep venous thrombosis (high sensitivity) in symptomatic patients.

Source of funding: None stated.

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■

*Wells PS, Anderson DR, Bormanis J, et al. Lancet. 1997;350:1795-8.

D-dimer assay and clinical assessment to diagnose deep venous thrombosis (DVT) in symptomatic limbs†

Test strategy	DVT	Sensitivity	Specificity	+LR	–LR
D-dimer alone	All	87%	57%	2.0	0.3
	Proximal	89%	55%	2.0	0.02
	Calf	81%	50%	2.0	0.4
D-dimer plus clinical assessment	All	96%	46%	1.8	0.09
	Proximal	98%	43%	1.7	0.05
	Calf	91%	38%	1.5	0.2

†LRs defined in Glossary and calculated from data in article.

COMMENTARY

In patients who present with a first episode of suspected DVT, DUS of the proximal (thigh) veins is usually done as a screening test. In patients with an abnormal scan, proximal DVT is confirmed, and in those with a normal scan, DUS is repeated within 7 days to exclude a distal (calf) DVT that may extend proximally. Recent studies have established that the combination of a negative D-dimer test result with an abnormal DUS or abnormal impedance plethysmographic measurement obviates the need for repeated noninvasive testing (1–3).

Aschwanden and Lennox and their associates attempt to further simplify the diagnostic assessment of suspected DVT by investigating whether a negative D-dimer test result combined with a low clinical likelihood for DVT obviates the need for DUS. This research is clinically important because approximately 50% of patients with suspected DVT have a low clinical likelihood of DVT (2, 3). Thus, the potential exists for substantial cost savings. In addition, because DUS may not be available on weekends or evenings, many patients with suspected DVT will receive empiric anticoagulant therapy unnecessarily until DUS is done, unless it is possible to rule out DVT with venography.

The D-dimer test investigated in these studies is a whole-blood agglutination assay that is specific for degradation products of thrombus-specific, cross-linked fibrin. A result, based on a subjective assessment, is obtained within 5 minutes. As with other D-dimer tests, the SimpliRED assay is used as a "rule-out" test, with a negative result used to exclude DVT. A positive result is nonspecific and can be caused by DVT or such other conditions as soft-tissue injury, infection, hematoma, malignancy, or pregnancy, all of which can result in elevated plasma D-dimer levels.

These studies suggest that in patients with suspected DVT, the combination of a negative D-dimer test result and a low clinical likelihood reliably excludes DVT, thereby obviating the need for DUS. Both studies were well-designed, blinded, and compared a D-dimer test plus a structured clinical assessment with a diagnostic reference standard, DUS. These studies differ from other diagnostic studies because both inpatients and outpatients were assessed, thereby increasing the generalizability of the results. Furthermore, DUS, not venography, was used as the diagnostic standard to assess proximal and calf DVT. DUS is essentially as accurate as venography for the diagnosis of symptomatic proximal DVT, but DUS for calf DVT has not been adequately evaluated and may not be as accurate in settings outside the institutions involved in these and similar studies. Thus, the study results that pertain to calf DVT should be interpreted with caution.

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A negative D-dimer test result alone or combined with low-risk clinical status effectively ruled out symptomatic DVT

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 Nov;30:794-804.

QUESTION

Can a D-dimer assay, alone or combined with clinical examination results, rule out all, proximal, and calf deep venous thrombosis (DVT) in symptomatic patients?

DESIGN

A blinded comparison of D-dimer test results, either alone or combined with a clinical risk assessment score, with duplex ultrasonographic scanning (DUS).

SETTING

A university hospital in London, England, United Kingdom.

PATIENTS

200 consecutive inpatients and outpatients (mean age 58 y, age range 18 to 91 y, 63% women, 59% inpatients) with suspected DVT. Exclusion criteria were previous or chronic DVT, symptom duration > 1 month, anticoagulant therapy > 48 hours before assessment, or suspected or confirmed pulmonary embolism.

DESCRIPTION OF TESTS AND DIAGNOSTIC STANDARD

Patients were classified as being at low, moderate, or high risk for DVT based on a clinical assessment score that included data on the presence of cancer, immobilization, localized tenderness or leg swelling, family history, history of leg trauma, unilateral pitting edema or erythema, dilated superficial veins, hospitalization within 6 months, and erythema of symptomatic leg only. D-dimer levels were assessed by using a rapid whole-blood assay (SimpliRED, Agen Biomedical, Brisbane, Australia) by an examiner who was blinded to the clinical findings. DUS (diagnostic standard) was done in a blinded manner to identify all, proximal, and calf DVT. Patients with inconclusive scan results had repeated scans done until the diagnosis was conclusive.

MAIN OUTCOME MEASURES

Sensitivity and specificity for the diagnosis of DVT for patients with varying risk based on clinical assessment.

MAIN RESULTS

Of the 200 patients assessed, 44% were at low risk for DVT. 14% of patients had proximal DVT, and 9% had isolated calf DVT. The sensitivity of D-dimer assay was 100% in detecting proximal DVT and 91% for all DVT (Table).

CONCLUSION

A negative D-dimer test result, alone or combined with low-risk status, effectively ruled out (high sensitivity) all and proximal DVT in symptomatic persons.

Source of funding: None stated.

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D-dimer assay in the diagnosis of symptomatic deep venous thrombosis (DVT)

Patients	DVT	Sensitivity	Specificity	+LR	–LR
All	Proximal	100%	76%	4.2	0.0
All	Isolated calf	82%	69%	2.7	0.3
All	All	91%	82%	5.1	0.1
High risk	All	100%	47%	1.9	0.0
Moderate risk	All	75%	78%	3.4	0.3
Low risk	All	75%	90%	7.5	0.3

*LRs defined in Glossary and calculated from data in article.

COMMENTARY *(continued from page 108)*

When the study results were limited to proximal DVT, the combination of a negative D-dimer test result and a low clinical likelihood effectively excluded proximal DVT in about 99% of patients. Another noteworthy finding is that the D-dimer test is not sufficiently accurate to be used as a "stand-alone" test in patients with suspected DVT. Although Lennox and colleagues reported a sensitivity of 100% with D-dimer alone for proximal DVT, this finding is based on relatively few patients. In the study by Aschwanden and colleagues, the sensitivity of D-dimer for proximal DVT, 89%, was lower than that reported in other studies (4) and may reflect a higher proportion of patients with less extensive DVT and the inclusion of patients with previous DVT. Patients with previous DVT may have a persistently abnormal DUS in the absence of acute DVT.

Clinicians should be aware that D-dimer tests may show false-negative results in patients with small popliteal DVT or calf DVT and in patients with biochemically inactive DVT who undergo testing > 14 days after the onset of symptoms (5) and in patients with cancer (6). Furthermore, the accuracy of D-dimer testing varies depending on the assay used (4). Thus, a structured history and clinical examination is an integral component in the evaluation of patients with suspected DVT.

Are the results of these studies sufficient to change current clinical practice? Not yet. Before DUS can be rendered unnecessary in patients with suspected DVT who have a low clinical likelihood and a negative D-dimer test result, prospective studies with important clinical outcomes are needed to validate the safety of this management approach. Additional research questions include the clinical utility of D-dimer testing in patients with suspected recurrent DVT and in patients who are receiving anticoagulant therapy.

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