

Taking the Test: Deep-Vein Thrombosis and Pulmonary Embolism



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There is no single, non-invasive test for accurately diagnosing deep-vein thrombosis (DVT) and pulmonary embolism (PE). Diagnostic pathways have been investigated and reported upon in the literature. Based on the results of clinical trials reported in the literature, firm recommendations can be made for diagnostic testing in patients with suspected venous thrombosis.¹ DVT and PE are common clinical disorders (Figure 1).

DVT

Venous ultrasound

Venous ultrasound is the most accurate noninvasive diagnostic test currently available for diagnosing a first episode of symptomatic proximal DVT.¹ Venous ultrasound is less accurate for the diagnosis of symptomatic isolated calf DVT. Withholding anticoagulant therapy in symptomatic patients with suspected DVT who have normal results on serial venous ultrasonography is safe.¹ Serial testing requires a second test using ultrasonography on about the seventh day of follow-up, placing the burden of mandatory follow-up on the patient. To reduce this burden, other strategies are required. These include D-dimer and clinical probability estimates.^{2,3}

D-dimer and clinical probability estimates

A negative enzyme-linked immunosorbent assay (ELISA) D-dimer assay and/or low clinical probability estimates, using validated instruments² (e.g., the Wells score) (Table 1) will avoid the need for a second ultrasound test.³ According to Stein, *et al*³ "for excluding PE or DVT, a negative result on quantitative rapid ELISA is as diagnostically useful as a normal lung scan or negative duplex ultrasonography finding."

Clinical probability estimates now play a key role as an adjunct to doppler ultrasonography by categorizing the probability for DVT or PE in patients as low, moderate, or high.

Diagnostic pathways

Diagnostic pursuit using clinical probability estimates, a negative ELISA D-dimer assay and doppler ultrasonography provide a definitive



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diagnosis in the majority of patients with suspected venous thrombosis. Combining a negative rapid ELISA result with a low or moderate clinical probability for DVT or PE rules out these diagnoses (Figure 2). The non-ELISA assays, when combined with a low clinical probability for DVT or PE, also provide a reasonable certainty of ruling out these disorders.³

There is no single, non-invasive test for accurately diagnosing DVT and PE.

Diagnosis of PE

The two types of studies for the diagnosis of PE are accuracy and management.

Accuracy studies are those tests which are compared with angiography and which estimate the sensitivity, specificity and likelihood ratios of the test in question.

Management studies assess clinical outcome and the safety of withholding anticoagulants when results of the test in question are normal.

While the number of patients discharged from short-stay hospitals in the US with a diagnosis of DVT has gradually increased over the past 21 years, the number of patients being discharged with a diagnosis of acute PE has remained stable (Figure 1).⁴ The use of venous ultrasound for the diagnosis of PE has increased since 1979; the use of ventilation perfusion scanning increased from the early 1980s until the late 1980s when its use began to decline.⁴

From 1979 to 2001, the proportion of imaging tests by CT scan, ventilation perfusion lung scan, pulmonary angiography and venous ultrasound was assessed in patients with PE from the National Hospital Discharge Survey. By 2001 there was a higher proportion of imaging tests with CT scans than ventilation perfusion scans (36% vs. 32%). Even so, in the US, a large proportion of patients continued to have ventilation perfusion scans.⁵

Table 1

Clinical module for predicting pretest probability for deep-vein thrombosis (DVT)²

Clinical features	Score
Active cancer (treatment ongoing or within previous 6 months or palliative)	1
Paralysis, paresis, or recent plaster immobilization of the lower extremities	1
Recently bedridden for > 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 > 3 cm when compared with the asymptomatic leg (measured 10 cm below the tibial tuberosity)	1
Pitting oedema (greater in the symptomatic leg)	1
Collateral superficial veins (non-varicose)	1
Alternative diagnosis as likely or greater than that of DVT	-2

0: Low probability

1 to 2: Moderate probability

3: High probability

* In patients with symptoms in both legs, the more symptomatic leg is used.

With the changes in technology, it is important that there be comprehensive recommendation for the diagnostic approach to patients with suspected PE. These recommendations have been incomplete or completely absent from the literature.

Stein, *et al* have formulated diagnostic management recommendations based on the results of the Prospective Investigation Of Pulmonary Embolism Diagnosis II (PIOPED II) and outcome studies.^{6,7} “The PIOPED II investigators recommend stratification of all patients with suspected PE according to an objective clinical probability assessment. D-dimer should be measured by the quantitative rapid ELISA and the combination of a negative D-dimer with a low or moderate clinical probability can safely exclude PE in many patients. If PE is not excluded, contrast-enhanced CT angiography in combination with CT venography is recommended by most PIOPED II investigators, although CT angiography plus clinical assessment is an option. In pregnant women, ventilation/perfusion scans are recommended by many as the first imaging test

following D-dimer and perhaps venous ultrasound. In patients with discordant findings of clinical assessment and CT angiograms or CT angiogram/CT venogram, further evaluation may be necessary.”⁶ “The sequence for diagnostic test in patients with suspected PE depends on the clinical circumstances.”⁶

“Managing patients for suspected PE on the basis of pretest probability and D-dimer result is safe and decreases the need for diagnostic imaging”⁸ (Figure 3).

The diagnostic pathway, according to patients’ clinical probability for PE (Table 2) is shown in Figures 4, 5 and 6.

Optional pathway

Venous ultrasound detects DVT in 13% to 15% of patients with suspected PE and in 29% of patients with proven PE, thereby allowing treatment with no further obligatory testing. A venous ultrasound prior to imaging with CT angiography/CT venography is optional and may guide treatment if positive.⁶

Table 2

Model for determining the clinical probability of pulmonary embolism (PE) according to the Wells Score^{7,8}

Clinical features	Score
Clinical signs and symptoms of DVT (objectively measured leg swelling and pain with palpation in the deep-vein system)	3
Heart rate: > 100 bpm	1.5
Immobilization 3 consecutive days (bed rest except to go to bathroom) or surgery in previous 4 weeks	1.5
Previous objectively diagnosed PE or DVT	1.5
Hemoptysis	1
Cancer (with treatment within past 6 months or palliative treatment)	1
PE likely or more likely than alternative diagnoses (on the basis on history, physical examination, chest radiograph, ECG and blood tests)	3

2: Low probability

2 to 6: Moderate probability

6: High probability

Special patient groups

The reader is referred to Stein, *et al*⁶ for the diagnostic pathways for special patient groups, including:

- women of reproductive age and pregnant women,
- patients with allergies to iodinated contrast material,
- patients with impaired renal function and
- patients in extremis.

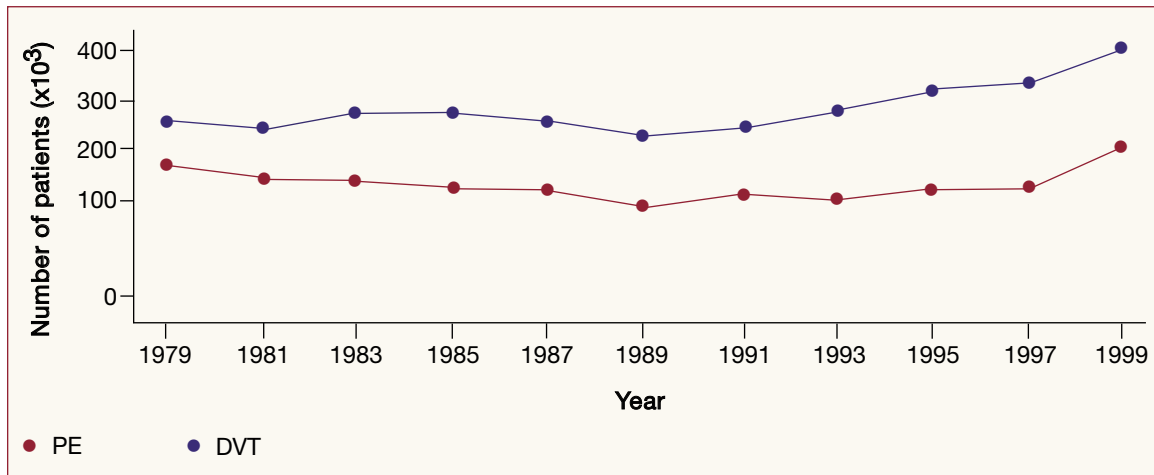


Figure 1. Twenty-one year trends in the number of patients discharged from short-stay hospitals in the US with a diagnosis of DVT or acute PE.⁴

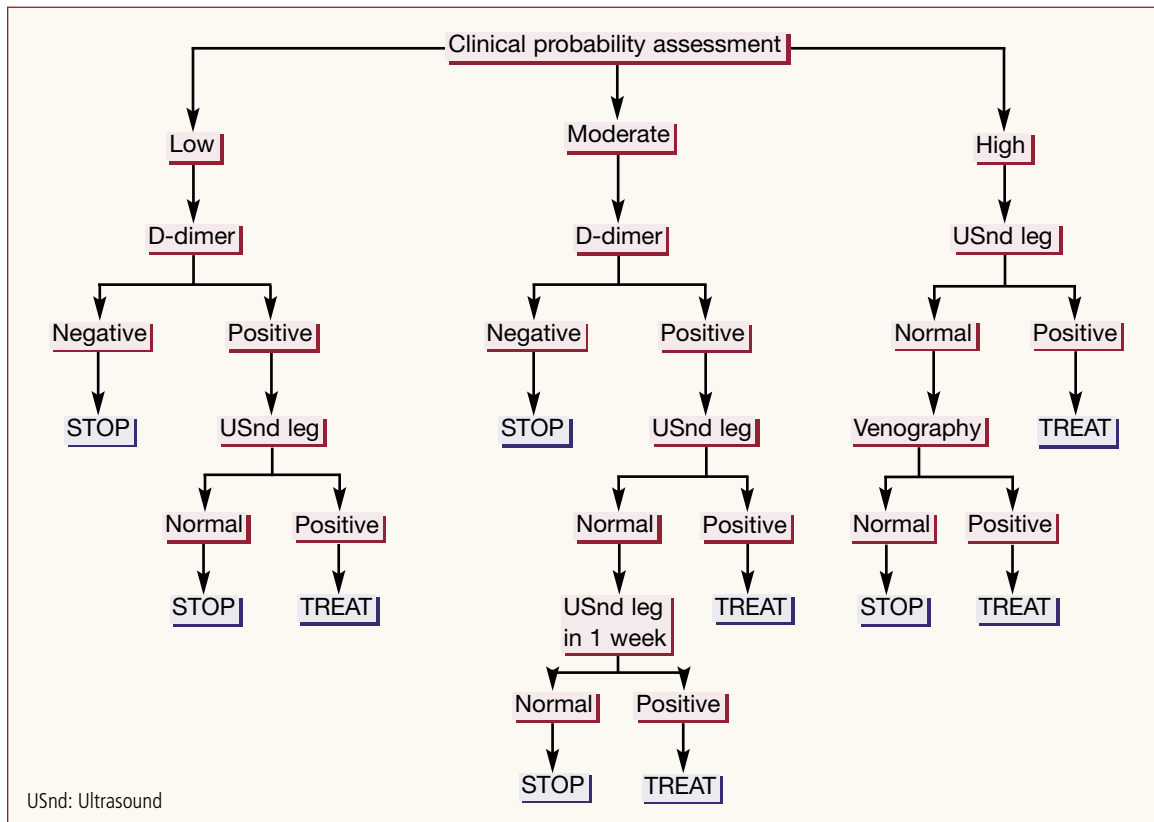


Figure 2. Diagnostic pathway for patients with suspected DVT.

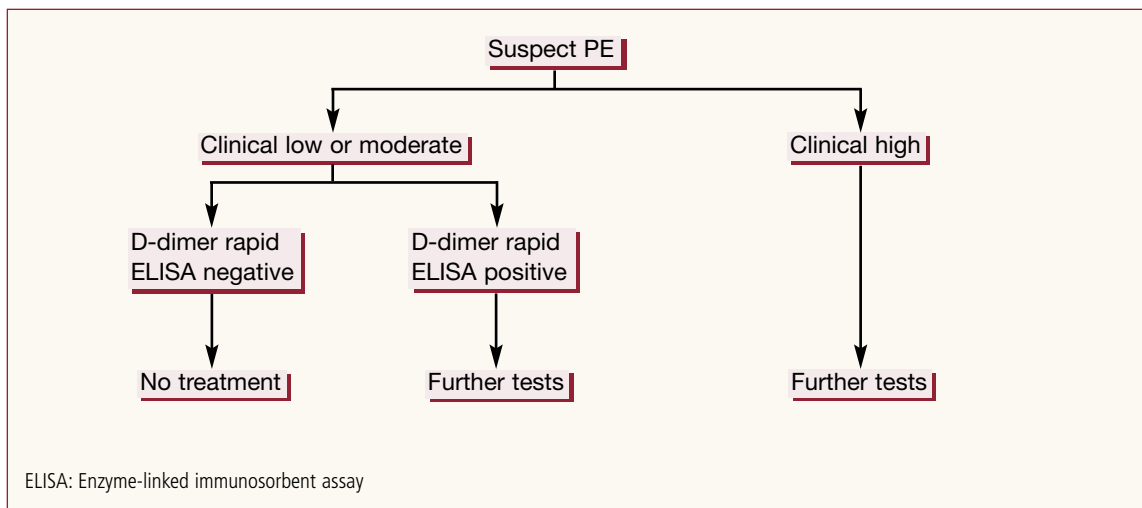


Figure 3. D-dimer rapid ELISA pathway.⁶

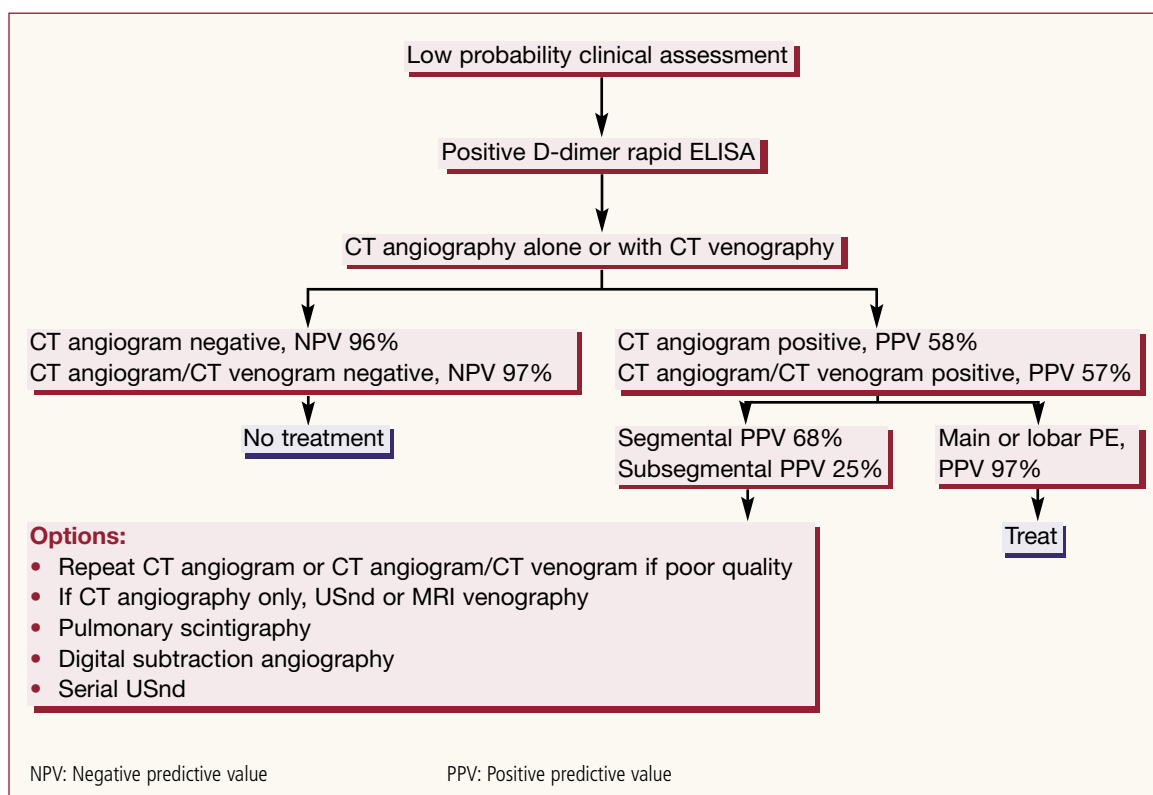


Figure 4. Patients with low probability clinical assessment.⁶

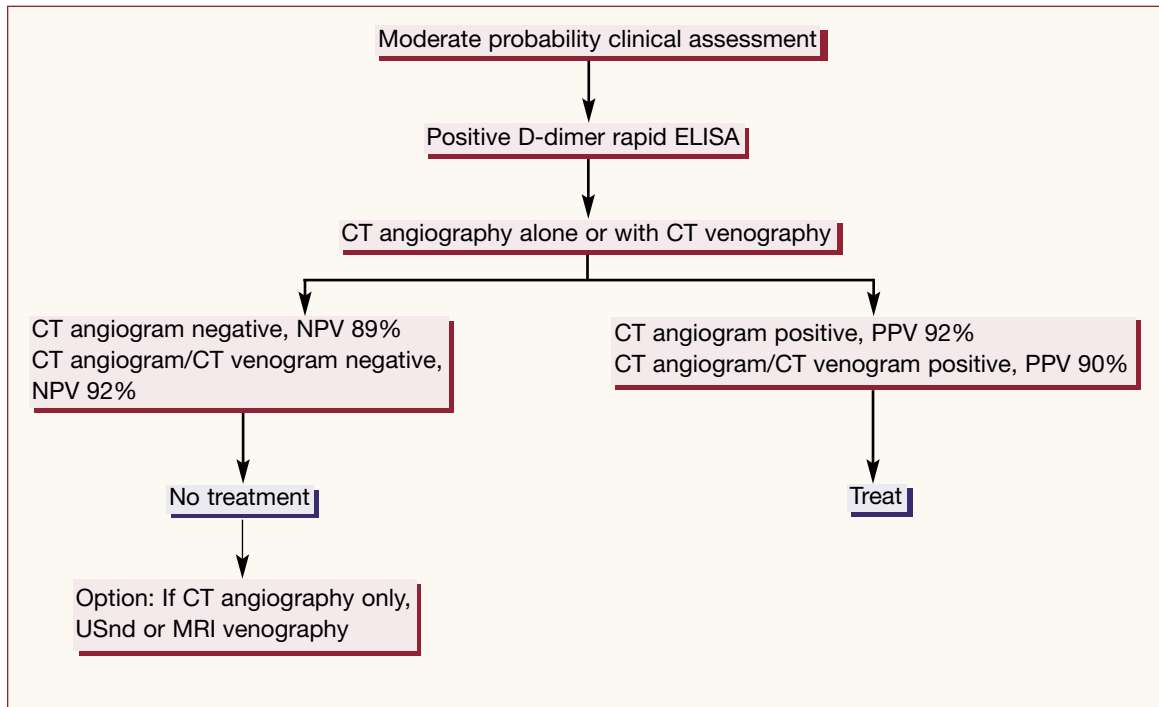


Figure 5. Patients with moderate probability clinical assessment.⁶

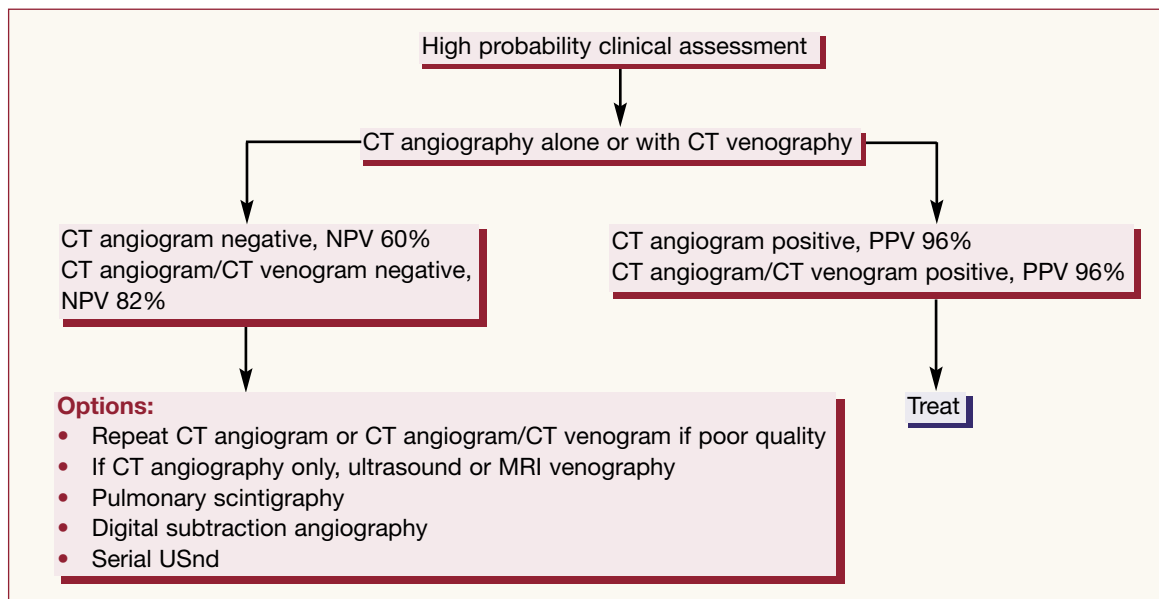


Figure 6. Patients with high probability clinical assessment.⁶



For references, please contact diagnosis@sta.ca.