Clinical Probability Tools for Deep Venous Thrombosis, Pulmonary Embolism, and Bleeding

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KEYWORDS

• Pulmonary embolus • Diagnosis • Pretest probability • Clinical decision tools
• Deep vein thrombosis • Bleeding • Venous thromboembolism

KEY POINTS

- Several validated clinical tools exist to estimate pretest probability for venous thromboembolism and bleeding.
- Pretest probability tools for venous thromboembolism can be combined with the D-dimer to further improve venous thromboembolism probability assessment.
- There are drawbacks to overevaluation and overdiagnosis for pulmonary embolism.
- The clinical probability tools for venous thromboembolism are only validated in certain populations.
- Clinical probability tools for bleeding risk cannot reliably predict major bleeding events but can place patients in a low-risk bleeding category.

INTRODUCTION

Venous thromboembolism (VTE), which includes both deep venous thrombosis (DVT) and pulmonary embolism (PE), is the third most common cardiovascular disease after acute coronary syndrome and stroke. VTE affects up to 900,000 Americans annually.[1,2] It is a significant contributor to mortality—studies suggest that it causes up to 300,000 fatalities, and it is often cited as the most common cause of in-hospital preventable death.[2–4]

VTE can present a diagnostic challenge to clinicians. Despite its high incidence and potential severity, presenting symptoms are often nonspecific or even absent, and this creates a low threshold for evaluation. As the availability and sensitivity of noninvasive diagnostic methods has increased, this has culminated in a phenomenon of overdiagnosis.[5]

Although there are multiple clinical tools to estimate VTE pretest probability, they are underused—in 1 study, only 45.5% of 3500 computed tomography pulmonary angiography scans followed Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) II recommendations to commence evaluation with a clinical score and D-dimer.[6] Given the risks of imaging and overdiagnosis, the thoughtful workup of VTE is essential, beginning with clinical tools to estimate probability and guide management.

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CLINICAL PROBABILITY TOOLS FOR DEEP VENOUS THROMBOSIS

A DVT usually forms in the lower legs. Given its multiple risk factors, nonspecific presentation, and potentially significant risk (up to 40% may cause PEs), it is a commonly suspected diagnosis.[7] To decrease the use of ultrasound examination and false-positive results, guidelines recommend assessment of clinical pretest probability before imaging.[8,9]

The Wells Scores for Deep Venous Thrombosis

The Wells Score is the best known and most widely used DVT pretest probability tool. The original model incorporated 9 predictors with 1 point given to each: active cancer; lower extremity immobility, paralysis, or paresis; recent immobility for more than 3 days or major surgery within 4 weeks; entire leg edema; localized tenderness along deep venous system; calf circumference difference of greater than 3 cm (measured 10 cm below the tibial tuberosity); unilateral pitting edema; and collateral nonvaricose superficial veins.[10] Two points were subtracted for the last factor, alternative diagnosis as likely or greater than DVT. Three risk groups were defined—low ($\leq$0 points), moderate (1–2), high ($\geq$3)—and in their 2006 metaanalysis, Wells and colleagues[11] observed DVT rates of 5%, 17%, and 53%, respectively.

In 2003, this model was revised into the modified Wells. Three changes were made: a tenth predictor for previous documented DVT was added and assigned 1 point, the length of time from major surgery was increased from 4 to 12 weeks, and probability was grouped into DVT unlikely (<2 points) or likely ($\geq$2).[12] In their unlikely populations, DVT rates were 0.4% (with normal D-dimer testing) and 1.4% (controls; underwent ultrasound examination alone without D-dimer testing). This rule was validated in a metaanalysis of 13 studies; an unlikely score with negative D-dimer testing was associated with a 1.2% failure rate.[13]

Management after Clinical Deep Venous Thrombosis Probability Assessment

Pretest probability guides subsequent evaluation. In the unlikely or low-risk groups, most guidelines suggest D-dimer testing—if negative, no further testing is required; if positive, leg ultrasound examination should be performed.[2,9] Multiple studies have validated this approach.[14] In the intermediate group, either high sensitivity D-dimer or leg ultrasound examination (complete venous vs proximal) should be done. High-probability patients should proceed immediately to imaging.

Limitations of the Wells Score for Deep Venous Thrombosis

Notably, the individual Wells elements are not useful in diagnosing DVT, nor does the score work as well in those who had distal DVT, were older, and had prior DVT.[13,15] Importantly, the Wells Scores have mixed accuracy in the hospital, with Silveira and colleagues[16] noting a 5.9% failure rate in 1135 inpatients.

Alternate Deep Venous Thrombosis Probability Scores

The Oudega rule was created after a high failure rate was noted in low-risk Wells patients with normal D-dimer.[17] This score assigns 6 points to elevated D-dimer, 2 to calf circumference difference of greater than 3 cm, and 1 each to male gender, oral contraceptive use, cancer, recent surgery, absence of leg trauma, and vein distension.[18] With a cutoff of less than 4 as low risk, the failure rate was less than 1.5%. The Hamilton index is another alternative—although its criteria are similar to the Wells Score, it includes gender and weights immobility, cancer, and DVT suspicion more highly.[19] Notably, although studies show similar failure rates between the Wells, Oudega, and Hamilton, these latter 2 systems have not been as widely validated.[20,21]

CLINICAL PROBABILITY TOOLS FOR PULMONARY EMBOLISM

PEs can present with a wide variety of symptoms, ranging from dyspnea, tachypnea, and pleuritic chest pain to circulatory collapse or death in a small number of patients.[22] Given the nonspecificity of presenting symptoms and the potential severity of a missed PE, it is often at the top of a differential list. As such, overdiagnosis is particularly evident in PE—incidence has increased but severity and mortality have improved. Furthermore, treatment of less severe disease has caused higher admission rates, charges, and anticoagulation complications.[23–27]

To prevent overdiagnosis, guidelines outline diagnostic algorithms for PE evaluation. Before any laboratory testing or imaging in hemodynamically stable patients, pretest probability of PE should be assessed with clinical scores.[28–31]

The Wells Scores

The original and modified Wells Scores

The Wells Scores are perhaps the most widely used PE probability tools. Originally developed in 1998 from literature review, the first model predicted PE well but was fairly complex with multiple