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EDITORIALS

Ruling out DVT using the Wells rule and a D-dimer test

Safety confirmed for first and recurrent events in patients without cancer

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The development of a clinical prediction guide, from inception to use in everyday practice, is often a long and winding journey. In a linked paper, Geersing and colleagues (doi:10.1136/bmj.g1340) re-evaluate the Wells rule,[1] which aids in the assessment of patients with suspected deep vein thrombosis (DVT) and was initially conceived almost 20 years ago.[2]

To understand how this study advances the specialty, consider the case of a 50 year old man presenting with a five day history of calf pain and swelling that began after he felt a sudden "popping" in the calf. Physical examination shows tenderness just below the popliteal fossa. Current diagnostic algorithms recommend determining a pretest probability for DVT, which can be done by clinical acumen or with a quantitative clinical prediction guide, such as the Wells rule. This patient would initially be assigned a Wells score of 2 (calf swelling, localised tenderness) that would be downgraded to zero if an astute clinician believed this patient had plantaris muscle tendon rupture as a "more likely alternative diagnosis." The next step would be D-dimer testing, an index of thrombin generation, which in this patient gives a negative result. A low Wells score (≤1) coupled with a negative D-dimer result indicates a post-test probability for DVT of less than 2%, which is low enough for this diagnosis to be excluded; treatment with rest, ice, and a non-steroidal anti-inflammatory drug would be reasonable and would avoid the inconvenience and cost of additional investigations.

Although this management approach is supported by practice guidelines,[3] many doctors continue to rely on venous ultrasonography to exclude DVT. Doctors are often reluctant to use clinical prediction guides until they are convinced that it is safe to withhold definitive diagnostic tests and that the guide is applicable to a broadly defined patient population. For example, the Wells rule might not be directly applicable if the aforementioned patient has atypical characteristics such as previous DVT or cancer. Should the study by Geersing and colleagues convince doctors to use the Wells rule in atypical patients with suspected DVT too?

The authors provided a robust framework for re-evaluation of the Wells rule in both typical patients and patient subgroups. They assembled a dedicated team of investigators and collected data from 13 studies of patients with suspected DVT in various clinical settings. They pooled individual patient data from 10 000 patients, with a mean DVT rate of 20%.

Traditionally, researchers evaluating clinical prediction guides use a split cohort method that includes a derivation step (usually by logistic regression or by a classification algorithm) then a validation step (usually by simple replication of the classification properties), ideally followed by an implementation study to verify that using the guide or rule has a beneficial effect on patient outcomes.

Geersing and colleagues[1] used a more sophisticated method to test the performance of the Wells rule. Their approach is more powerful than traditional methods, and the authors use it to good effect to explore the performance of the Wells rule combined with a D-dimer test to exclude DVT in atypical patient subgroups. The success of this approach is underpinned by having access to data from a large population to increase precision, and stratification of patients by the "source" study they belong to (as in classic meta-analysis) as a way to avoid bias and confounding. This design can also be used to generate new clinical prediction guides and, given the richness of the pooled cohorts, may even remove the need for a validation step in an independent cohort.

The power of this approach is reflected in the three important messages of this study. Firstly, consistent with previous understanding, the Wells rule cannot rule out DVT safely when used alone. Secondly, the combination of a Wells score of 1 or less (low clinical probability) and a negative D-dimer test result unequivocally excludes DVT, with an overall failure rate of approximately 1.2%. Analysis of the confidence interval shows that the expected failure rate is less than 0.2% when the prevalence of DVT is 5%, and remains less than 2% when the prevalence increases to 40%. If the study's findings are extrapolated to real world practice, additional diagnostic testing such as venous ultrasonography can be avoided in about 1 in 3 patients assessed for suspected DVT. Thirdly, the combination of a D-dimer test and a modified version of the Wells rule (where one point is added for previous thrombosis) allows

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doctors to rule out DVT in patients with a history of the condition. This novel aspect of the study—how to apply a clinical prediction guide to atypical patients—is a benefit of individual patient data but requires asking the right question, selecting eligible patients across different studies, and conducting the appropriate analysis.[4]

In summary, this study should reassure doctors and patients that venous ultrasonography is not necessary when a Wells score is low (that is, ≤1) and a D-dimer test result negative. Moreover, we now have good evidence that will help doctors use this clinical prediction guide safely in patients with suspected recurrent DVT and encourage them to avoid it in patients with active cancer. The journey of a clinical prediction guide from development through to validation and eventually safe and effective practice might have been a long one, but thanks to Geersing and colleagues[1] we can now answer the question "Are we there yet?" with a resounding "Yes."

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