Simplifying the diagnosis of pulmonary embolism

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Combining clinical diagnostic scoring with D-dimer analysis

Venous thromboembolism (VTE) occurs in one to two people per 1000 annually in Caucasian populations.[1] About a third of these patients will have symptomatic pulmonary embolism (PE), which is associated with a mortality rate of about 30% if left untreated.[2] Anticoagulant therapy is highly effective for preventing death in patients with symptomatic PE,[3] but causes major bleeding in 2% of patients during the first 3 months. The mortality rate among patients who suffer major bleeding is about 10%.[4] Accurate diagnosis is thus critical to ensure that patients with PE receive effective treatment and that patients without PE do not receive unnecessary anticoagulant therapy, with its associated risks and inconvenience.

The diagnosis of PE is challenging because of the wide spectrum of symptoms and signs, and because most patients with suggestive clinical features do not have the disease.[5,6] Major risk factors for PE include trauma, surgery, and a diagnosis of cancer, but half of patients with symptomatic PE do not have an identifiable risk factor.[1] Typical symptoms of PE include dyspnoea or acute chest pain and, less commonly, cough or haemoptysis, while typical signs include tachycardia, tachypnoea and, less commonly, right ventricular dysfunction.[5] However, none of the typical clinical symptoms and signs are unique to the disorder or invariably present in patients with confirmed PE. Thus, the clinical diagnosis of PE is unreliable and additional testing is required to confirm or refute the diagnosis.

The accuracy of non-invasive testing, which has almost completely replaced pulmonary angiography in the diagnosis of PE, is substantially improved when combined with an assessment of clinical pre-test probability and the results of a sensitive D-dimer assay.[5] Experienced clinicians can use clinical judgment ("gestalt") to assign a pre-test probability of PE with reasonable accuracy, but simple clinical prediction rules, such as the one developed by Wells and colleagues,[7] perform equally well and can be used by less experienced clinicians.[5] To date, the Wells model has not been evaluated in an Australian setting.

In this issue of the Journal, Yap and colleagues (*page 333*) report the results of a prospective cohort study in which they evaluated the use of Wells' model in 633 consecutive inpatients and outpatients with suspected PE referred for lung scanning at a major Australian teaching hospital.[8] Lung scans and multidetector computed tomography (MDCT) were used as the reference standard to establish the diagnosis of PE (positive lung scan or positive MDCT) or to exclude PE (negative lung scan or non-diagnostic scan with negative MDCT). They found that a low clinical pre-test probability of PE (Wells score < 2) was associated with a 4.3% prevalence of PE; a moderate clinical pre-test probability of PE (Wells score 2–6) was associated with a 13% prevalence of PE; and a high clinical pre-test probability of PE (Wells score > 6) was associated with a 67% prevalence of PE. There was no follow-up of patients once diagnostic imaging was completed, and PE may have remained undiagnosed in some patients. Nonetheless, the prevalence of PE in the low, moderate and high pre-test probability categories reported by Yap and colleagues is almost identical to the prevalence reported in the original study by Wells and colleagues,[7] and confirms the ability of the Wells score to accurately classify patients according to their clinical pre-test probability of PE.

Some investigators[9,10] have suggested that patients with a low pre-test probability of PE do not require further investigation because the prevalence of disease in this group is low. However, the risk of missing a diagnosis of PE in such patients can be further

minimised by combining the clinical assessment of pre-test probability with the results of a D-dimer assay. Depending on the sensitivity of the D-dimer assay, patients with low or moderate pre-test probability for PE may not require diagnostic imaging if they have a negative D-dimer test. Patients with a low pre-test probability and a negative *moderately* sensitive D-dimer assay, or patients with a low or moderate pre-test probability and a negative *highly* sensitive D-dimer assay do not require diagnostic imaging because the prevalence of disease in these patients is very low (less than 2%).[11] By contrast, patients with a positive D-dimer test and/or those with a high pre-test probability require diagnostic imaging.

For the past 20 years, clinicians have used lung scanning as the first-line non-invasive imaging test for patients with suspected PE. A normal or near-normal lung scan reliably excludes PE, while a high-probability lung scan confirms the diagnosis. However, as many as half of patients with suspected PE have a non-diagnostic lung scan result, and a quarter of these have PE.[12] Newer lung scanning techniques may reduce the proportion of non-diagnostic scans, although the number of non-diagnostic scans reported by Yap and colleagues is unexpectedly low. MDCT is more rapid and convenient than lung scanning, but requires intravenous injection of contrast medium that is potentially nephrotoxic. The test can also yield non-diagnostic results.[13] Clinicians must interpret non-diagnostic results of imaging studies in the context of the clinical pre-test probability of PE: patients with a moderate or high pre-test probability of PE and a non-diagnostic scan generally require additional or serial testing to establish or refute the diagnosis.[12,13] Patients for whom there is a marked discrepancy between the pre-test probability of PE and the results of diagnostic imaging should also undergo further testing.[13]

The outcomes for patients with suspected PE can be improved by routine use of written diagnostic algorithms that incorporate a clinical probability scoring system.[14] Yap and colleagues have validated the Wells probability scoring system in the Australian setting, and their data should encourage efforts by clinicians and institutions to implement standardised diagnostic strategies that combine assessment of clinical probability with measurement of a sensitive D-dimer in all patients with suspected PE.

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