Diagnosing Pulmonary Embolus:

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Background
Pulmonary embolus (PE) has always been an anathema for clinical diagnosis. PE cannot be reliably diagnosed at the bedside. Regardless of any particular physician's clinical skill, PE will often be misdiagnosed without the aid of imaging investigations. Basic tests such as chest x-ray, arterial blood gases and electrocardiography are also of limited diagnostic use in this setting other than helping to establish an alternative diagnosis to PE. For many years pulmonary angiography was regarded as the "gold standard" for the diagnosis of PE, despite a glaring lack of outcome data to support this claim. This invasive test has been progressively replaced over the past 35 years with ventilation/perfusion scintigraphy (V/Q scan). The V/Q scan relies on demonstrating a difference in radiotracer distribution in the lungs of the ventilation (V) and perfusion (Q) phases. So-called V/Q mismatch is where perfusion is significantly less than ventilation. This is diagnostic of PE. Controversy has, however, been associated with the optimal diagnostic criterion to determine what represents significant V/Q mismatch. Controversy has also existed with regard to the best ventilation agent, as several are readily available for widespread use, but some may be cost prohibitive and others have physical limitations potentially reducing diagnostic utility. More recently, technical advances in computed tomography (CT) have allowed this modality to be used for the diagnosis of PE with some success. Non-imaging techniques measuring activation of thrombolytic pathways in blood specimens have also been refined over the past 10 years and have been used to help exclude the diagnosis of PE.

Commonly Used Diagnostic Modalities

1. Pulmonary angiography.

This fluoroscopic guided test is usually available only in larger hospitals and in some settings is not available after hours for emergency diagnosis. It requires a skilled specialist to both administer radio-contrast via a percutaneous catheter into the pulmonary arteries, and to interpret the radiographic images. This test has a 1% major complication rate due to its invasive nature and use of high dose radio-contrast (1). Its true diagnostic accuracy is unknown due to a paucity of non-negative angiogram outcome study data. However, it is purported to have a diagnostic accuracy of >95% (2).

2. Computed tomography pulmonary angiography (CTPA).

This test has evolved following use of continuous rotating CT x-ray tubes and more recently, improved multi-detector technology that allow rapid imaging of the lungs during breath hold. The test requires a well-timed bolus of intravenous radio-contrast, and an experienced reporter to distinguish what represents true "defect" from partial-volume artefact. The test is limited for use in those patients who can comply with the breath hold and are cooperative within a CT tunnel. Those patients with known radio-contrast allergy, known iodine allergy and those with moderately-severe to severe renal impairment are excluded from testing. This test, like pulmonary angiography delivers a relatively high radiation dose to critical regions such as breast tissue. Although published outcome data indicates that when performed at the highest standards, this test has a high negative predictive value that is the equivalent to that of pulmonary angiography, its true diagnostic sensitivity has not been adequately established (3).

3. D-Dimer Test.

This test has been available for many years but the use of more advanced bedside latex agglutination tests have resulted in a rapid test of high sensitivity, similar to that of the enzyme-linked immunosorbent assays (ELISA). Like the more time consuming ELISA test, these tests have a high false positive rate and relatively low false negative rate. Consequently, the most modern rapid latex agglutination tests are of most use in excluding activation of the thrombolytic biochemical pathways in patients regarded as being of low pre-test risk of PE (4). These tests do not, however, have a 100% negative predictive value. Consequently, when used in isolation, the test is of relatively limited clinical utility. Its role is in combination with a clinical scoring test or other imaging.

4. Simplified Wells Scoring System.

This system is designed for risk stratification in order to assign pre-test probability (low, intermediate or high) for PE (5). It incorporates the use of the D-dimer test, bedside investigations, clinical features and risk factor assessment. The basis of this scoring system in itself is sound enough, but its use is based upon a premise that V/Q scanning is a markedly imperfect test. The authors did not specify how V/Q imaging was per

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formed but it is likely that less than optimal ventilation agents were used in some, if not all of the 4 participating Canadian centres. They used a positive diagnostic criterion of >1-1.5 segment of V/Q mismatch and found more than 47% of scans were classified indeterminate. Had they used the more appropriate diagnostic cut-off point (>0.5 segment V/Q mismatch) the V/Q scan's true diagnostic utility would have been apparent. Although this scoring system was originally intended to reduce the use of investigations for PE, the true value of this method, and other similar scoring systems, lies in the assessment of likelihood ratios following a diagnostic imaging test such as V/Q lung scintigraphy. The role of this scoring system, and its heavy reliance on the rapid D-dimer test in excluding PE at the bedside, remains unproven.

5. V/Q lung scintigraphy.

As a consequence of 2 important factors, this test has been undervalued as the imaging diagnostic test of choice for PE: (i) a major source of published medical data pertaining to V/Q imaging has come from the USA, or been unduly influenced by other data derived from the USA, (ii) V/Q imaging quality in the USA is largely inferior to that in Australia, Europe, other regions of North America and an increasing number of Asian countries due to the widespread use of inferior ventilation imaging agents. With the use of good quality ventilation agents such as Technegas, Krypton-81m or, in selected patients, appropriately administered nebulized Tc-99m diethylene tri-amine penta-acetic acid (DTPA) aerosol, V/Q lung scintigraphy has a very high diagnostic accuracy for PE. SPECT imaging using Technegas ventilation/perfusion has also been shown to enhance the diagnostic ability of this test (6). However, with a diagnostic accuracy of 97% for standard planar imaging, there is little room for improved accuracy (7). The key to understanding the true diagnostic accuracy of this test lies in the use of an appropriate diagnostic criterion. A simple and proven criterion uses ≥0.5 segments or total equivalents of V/Q mismatch as diagnostic for PE and <0.5 segments as negative (7). Using this criterion <5%, and more likely, only about 1% of studies are indeterminate.

Recommendations.

Many very elaborate diagnostic algorithms have been proposed for the diagnosis of PE. Generally, the more complicated the algorithm, the greater the uncertainty expressed in all the currently available diagnostic tools. Although no one test is always correct, on occasion a test is falsely vilified due to either the test being incorrectly performed or incorrectly interpreted. Both of these have occurred in the case of V/Q lung scintigraphy. V/Q lung scintigraphy has been around a long time, and has not been replaced because of an inherent understanding of the value of the test, despite widespread use of inappropriate ventilation agents and inappropriate diagnostic criterion. Used correctly it has the potential to offer a diagnostic accuracy of around 97% in more than 95% of cases.

For a systematic and reliable approach for the diagnosis of PE the clinician should use the simplified Wells score system, or its equivalent, to determine the pre-test risk/probability for PE. Those patients in a low probability group should also have a negative d-dimer test and can then be investigated for another diagnosis. Those in the intermediate and high probability groups should undergo V/Q lung scintigraphy using a reliable ventilation agent such as Technegas. Where using a criterion of ≥ 0.5 segment of V/Q mismatch as diagnostic, a definite diagnosis will be established in all but the small minority of cases. In the rare case of a non-diagnostic V/Q scan, where appropriate, the patient can undergo CTPA to help exclude PE or seek another diagnosis. It should be remembered that a false positive diagnosis for PE is just as life-threatening as a false negative test result. Outcome data confirms a high risk of bleeding complication in patients receiving anticoagulation therapy (8).

References

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