Computerized Tomographic Pulmonary Angiography Versus Ventilation Perfusion Lung Scanning for the Diagnosis of Pulmonary Embolism

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Abstract and Introduction

Abstract

Purpose of Review: The purpose of this review is to focus on recent research that has addressed the relative merits of computed tomographic pulmonary angiography (CTPA) and ventilation perfusion (V/Q) scanning for the diagnosis of pulmonary embolism.

Recent Findings: Computed tomographic pulmonary angiography is the most sensitive test for the diagnosis of pulmonary embolism and its use has been associated with a rising incidence of the condition. Diagnostic algorithms using either CTPA or V/Q scanning have proven to be comparably safe to exclude the diagnosis of pulmonary embolism. Negative multidetector CTPA study results essentially ruled out the diagnosis of pulmonary embolism without the need to routinely exclude the presence of deep vein thrombosis. Use of multidetector CTPA was associated with significant radiation exposure that potentially increases risk of secondary malignancies. This is particularly a concern for young women given the risk of breast cancer. Single photon emission tomography (SPECT) V/Q and modified diagnostic criteria for V/Q scan interpretation increased their diagnostic accuracy compared with V/Q scanning and offer nuclear medicine modalities that are alternatives to CTPA in at least some patients with suspected pulmonary embolism at a fraction of the risk of radiation exposure. Excluding low risk patients for pulmonary embolism as defined by clinical scoring systems and D-dimer testing would enhance the yield of diagnostic testing.

Summary: Computed tomographic pulmonary angiography is the most reliable test for diagnosis of pulmonary embolism. However, diagnostic algorithms using V/Q scanning are safe and may be preferred in some patient populations.

Introduction

Pulmonary embolism is a common and serious medical condition leading to the hospitalization or death of more than 250 000 people in the United States each year.[1] Given the high mortality of untreated pulmonary embolism, timely accurate diagnostic tests are essential to enable the initiation of antithrombotic therapy for patients proven to have the condition while avoiding its risks to patients in whom the diagnosis is excluded.[2] For 30 years ventilation perfusion (V/Q) lung scanning has been the noninvasive imaging procedure of choice in patients with suspected pulmonary embolism. However, a complex probability scoring system and frequent nondiagnostic scans have dampened enthusiasm about this procedure. In the past decade computed tomographic pulmonary angiography (CTPA) has proven to be a more accurate test with relatively few inadequate studies, which has been embraced by many clinicians.[3] However, concerns about radiation exposure and the side effects of contrast administration with CTPA dictate that there remains a role for V/Q scanning in the evaluation of patients with suspected pulmonary embolism.[4] The purpose of this review is to focus on recent research that has addressed the relative merits of CTPA and V/Q scanning for the diagnosis of pulmonary embolism.

Clinical Probability Assessment and D-dimer Testing

Patients with suspected pulmonary embolism should undergo a careful clinical examination for pretest probability and usually D-dimer testing before consideration is given to the performance of diagnostic imaging.[5] If a clinical scoring system identifies that the diagnosis of pulmonary embolism is unlikely and D-dimer testing is negative, then no further diagnostic imaging is required.[6,7] For patients in whom a clinical scoring system indicates that pulmonary embolism is likely and/or a D-dimer test result is positive, then diagnostic imaging with either CTPA or V/Q scanning is required. Recent studies have identified in some major centres that fewer than 10% of patients referred for diagnostic imaging are confirmed to have pulmonary embolism.[8-10] Failure to exclude low risk patients using a clinical probability assessment and D-dimer was felt to account, at least in part, for the low yield of diagnostic testing.

Accuracy of Computed Tomographic Pulmonary Angiography Versus V/Q Scanning for Excluding Pulmonary Embolism

With the advent of CTPA, the historical gold standard test for the diagnosis of pulmonary embolism, namely pulmonary angiography, is rarely performed. A sub-study of the PIOPED II trial determined that when discordant results were observed between CTPA and pulmonary angiography, blinded expert reviewers found that the pulmonary angiogram was more likely to be falsely abnormal than the CTPA.[11] With its increased accuracy CTPA has also eclipsed V/Q scanning in many centres for the diagnosis of pulmonary embolism. Attractive features of CTPA include that it provides direct visualization of the thrombus and a simple positive or negative result.[12,13] The test may be able to determine an alternative explanation for symptoms if pulmonary embolism is excluded and it may also offer clues to the aetiology for patients with pulmonary embolism such as the presence of...
The comparative safety of excluding the diagnosis of pulmonary embolism with either CTPA or V/Q scanning was recently evaluated in a head-to-head trial. Over 1400 patients at high likelihood of pulmonary embolism were randomized to either undergo CTPA or V/Q scanning as their initial diagnostic test. Those with negative CTPA or nondiagnostic V/Q scans underwent bilateral ultrasonography of the proximal venous system to evaluate for deep vein thrombosis (DVT). Patients in whom pulmonary embolism was considered excluded were then followed without receiving anticoagulants for a 3-month period for the identification of failures in the diagnostic approach.

The major results of this study determined that significantly more patients were diagnosed with pulmonary embolism using the CTPA (19.2%) than V/Q scanning (14%). For patients in whom a diagnosis of pulmonary embolism was excluded only 0.4% of patients in the CTPA arm versus 1.0% of patients in the V/Q arm developed venous thromboembolism in a 3 month follow-up period (difference -0.6%, 95% confidence interval -1.6-3%). The findings from the study showed that CTPA clearly diagnosed more patients with pulmonary embolism than V/Q scanning. However, as the event rates in those in whom the diagnosis of pulmonary embolism was considered excluded were comparable in the two groups, it suggested that at least some of the pulmonary emboli diagnosed by CTPA were clinically unimportant.

One limitation of this study is that some crossover occurred in violation of the study protocol. In the CTPA arm, crossover to V/Q scanning tended to occur for technical reasons (unable to cannulate veins, contrast allergy). However, in the V/Q arm, when crossover did occur CTPA was usually performed because there remained a strong clinical suspicion for pulmonary embolism by clinicians, despite the nondiagnostic V/Q scan and negative ultrasonography. Nine of 29 (31%) such patients had pulmonary embolism on CTPA and were treated for this condition. Therefore, consideration should be given to performing CTPA in patients with nondiagnostic V/Q lung scans in whom the clinical suspicion for pulmonary embolism remains high.

Although investigators have acknowledged the greater accuracy of CTPA, a number of recent studies have attempted to better define a potential role for V/Q scanning for the diagnosis of pulmonary embolism. The PIOPED II investigators reanalysed V/Q scan results using only the perfusion images and two distinct sets of diagnostic criteria. Using a modification of the PIOPED II criteria, the sensitivity of lung scanning improved to 85%, the specificity declined to 93% and the nondiagnostic scan rate result was reduced to 21%. Interpreting the perfusion lung scan using the PI-SAPED criteria found the sensitivity for lung scan was 80%, the specificity was 97% and no nondiagnostic results were observed.

The PIOPED II investigators performed an analysis of very low probability lung scans, demonstrating that only about 8% of patients with this test result were proven to have pulmonary embolism. If the patient's clinical probability was also felt to be low, then the predictive value for pulmonary embolism of a very low probability V/Q scan result was further reduced to about 3%. This scan result was found in over 50% of the patients in the PIOPED II study.

One retrospective study evaluated the impact of a policy change of diagnostic testing for pulmonary embolism following the introduction of CTPA. The policy dictated that perfusion lung scanning was only performed in patients that had a normal chest radiograph and no history of lung disease. CTPA was performed in all other patients. This policy change resulted in a significant increase in the proportion of normal V/Q scans from 39 to 60%. There was a modest increase in the number of high probability V/Q scans from 15 to 18%. Overall, the proportion of diagnostic lung scans increased from 54 to 78% with actually 25% fewer lung scans being performed after the policy change took effect.

V/Q scanning and CTPA were directly compared for the diagnosis of chronic pulmonary embolic disease in a retrospective review of patients referred for evaluation of chronic pulmonary hypertension. Seventy-eight patients were confirmed to have chronic pulmonary embolism. Seventy-five of the 78 patients had high probability V/Q scans, one had intermediate probability and two had a low probability studies. However, CTPA was positive in only 40 of the 78 patients. This study demonstrated that V/Q is a much more sensitive test for the diagnosis of chronic thromboembolic disease in potential surgical candidates than CTPA.

### Value of the Detection of Deep Vein Thrombosis in Patients With Suspected Pulmonary Embolism

The role of bilateral ultrasonography for the diagnosis of DVT in patients with suspected pulmonary embolism has been more clearly defined by a recent clinical trial by Rigini et al. Over 1800 patients at high clinical probability were randomized to either undergo bilateral ultrasonography of the proximal leg veins and if negative, CTPA; or CTPA alone. Patients in whom pulmonary embolism was considered excluded were not started on anticoagulants and were then followed up for a 3-month period for the development of DVT or pulmonary embolism (failure rates).

Both arms of this study reported similar rates of pulmonary embolism (approximately 20%) in the initial evaluation period. The thromboembolic failure rates in follow-up in whom pulmonary embolism was considered excluded were identical (0.3%) in the two groups. Approximately, 9% in the ultrasound group of patients were confirmed to have DVT. Ultrasound was positive in 21% of the
patients with symptoms of DVT but only 7% of patients who lacked symptoms. The authors concluded that the routine performance of bilateral lower limb venous ultrasonography was not required and that the diagnosis of pulmonary embolism could be reliably excluded with CTPA.

In a subgroup of patients, Righini et al. [23•] assessed whether the diagnostic utility of ultrasound in the evaluation of patients with suspected pulmonary embolism could be increased by performing full leg length ultrasounds to diagnose calf DVT. Most studies evaluating ultrasonography for the diagnosis of DVT only involved an evaluation of the proximal venous system above the level of the popliteal vein. A subgroup of 541 patients in the Righini study underwent bilateral ultrasonography of both the proximal venous systems and the calf venous systems and DVT isolated to the calf veins was found in 59 (11%). Twenty-one of these patients did not have pulmonary embolism on CTPA. One patient was treated with anticoagulation outside the study protocol. The remaining 20 patients did not receive anticoagulant therapy and none subsequently experienced thromboembolic complications. This study concluded that full leg ultrasonography did not increase the diagnostic utility of the test for the evaluation of patients with suspected pulmonary embolism. [23•]

Two studies compared the accuracy of bilateral ultrasonography with CT-venography for the diagnosis of deep vein thrombosis in patients with suspected pulmonary embolism. [24,25] One study of 235 patients reported ultrasonography was the more accurate technique. [24] In contrast, in 711 patients in the PIOPED II trial there was a 95% concordance rate in diagnostic findings between the two studies. [25] Given the findings of Righini et al. [22•] there would seem little justification for the routine performance of imaging of the proximal venous system with CT-venography or ultrasonography for patients with pulmonary embolism excluded by multidetector CTPA. Bilateral ultrasonography would still be recommended in the evaluation of patients with suspected pulmonary embolism who have nondiagnostic V/Q scan results.

Safety of Computed Tomographic Pulmonary Angiography

The American College of Radiology has come out with a position paper outlining concern and consideration to minimize inappropriate radiation exposure. [26] They stated ‘the rapid growth of CT and certain nuclear medicine studies may result in increased incidences of radiation cancers in the not too distant future’. They advocate that although the benefits of radiology development are profound, consideration of radiation exposure should be a factor in selection of testing procedures for individual patients. [26] Concerns of high radiation exposure have been raised as an issue for CTPA.

A recent study examined the radiation dose of CTPA for women undergoing a single 64-slice multidetector CTPA procedure. [27] The estimated exposure was 12.4-31.8 mSv. This was estimated to increase the risk of breast cancer by 1.004 to 1.042 and lung cancer from 1.005 to 1.076. The excess risk of cancer for individuals over 55 would be less than 1%; however, for a young 20-year-old woman this would be estimated to increase the relative lifetime risk of breast or lung cancer by 1.7 to 5.5%.

Several recent studies have evaluated the impact of lowering the radiation exposure to patients on the diagnostic accuracy and quality of CTPA. [28-30] Results were generally positive that modestly reducing the kilo-voltage of CTPA and/or providing shields maintained good quality images and reduced organ radiation exposure to patients. [28-30]

Single Photon Emission Tomography Imaging

Single photon emission tomography (SPECT) provides three-dimensional volumetric images and has the potential to improve the diagnostic accuracy of the nuclear medicine imaging for pulmonary embolism. A direct comparison has been performed between SPECT V/Q, V/Q planar scanning and four-slice CTPA in 83 patients. [31] In this study the sensitivity and specificity of SPECT were superior to planar V/Q and comparable to CTPA (sensitivity of SPECT was 97% versus 86% for CTPA, specificity of SPECT was 91% compared with 98% for CTPA, with a diagnostic accuracy of 94 versus 93%, respectively).

A prospective cohort study followed 405 patients classified as negative for pulmonary embolism by SPECT V/Q who did not receive anticoagulant therapy. Six patients (1.5%) subsequently developed venous thromboembolic complications in follow-up. [32] Only 3% of patients had indeterminate SPECT V/Q scan findings. A larger retrospective evaluation of SPECT V/Q reported similar findings. [33] SPECT V/Q is a promising modality, but large prospective multicentre accuracy and outcome studies are required to determine the utility of this test.

Change in the Epidemiology of Pulmonary Embolism in the CTPA Era

Two studies using state based administrative databases have reported the incidence of pulmonary embolism has risen over the past decade although mortality did not appear to be changing. [34,35] One study reported the increased rate of pulmonary embolism paralleled a rise in use of CTPA. [34] A number of single institution studies have been performed demonstrating an increased incidence of pulmonary embolism in the era of CTPA. [36,37] Centres again have reported the rise in incidence of pulmonary embolism occurred coincidentally with the rise in the use of CTPA and the decline in V/Q scanning but did not appear to be associated with changes in the mortality rates of pulmonary embolism. [37] Authors of these reports have speculated CTPA has resulted in the early diagnosis of pulmonary embolism. The clinical implications of the incremental incidence of pulmonary embolism in the CTPA era are uncertain.
Conclusion

Computed tomographic pulmonary angiography is the most accurate modality for the diagnosis of pulmonary embolism. However, diagnostic algorithms using either CTPA or V/Q scanning have proven to be comparably safe to exclude the diagnosis of pulmonary embolism. Recent studies have demonstrated a negative CTPA study result essentially rules out a diagnosis of pulmonary embolism without the need to routinely exclude the presence of DVT. Concerns about radiation exposure and side effects of CTPA provide impetus to improve nuclear medicine imaging modalities including SPECT V/Q for the diagnosis of pulmonary embolism. Further research is required to determine the implications of the apparent rising incidence of pulmonary embolism observed with increased use of CTPA.

References


Papers of particular interest, published within the annual period of review, have been highlighted as:
• of special interest
•• of outstanding interest