Intermediate Probability Lung Scans (IPLS): Retrospective Review of 82 Cases

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ABSTRACT

Objective: In the light of a reported 30-40% prevalence of pulmonary embolism (PE) in intermediate probability lung scans (IPLS) based on results of the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) study, we examined the frequency of documented PE in 82 patients with IPLS, the management strategy employed in these patients with regards to additional imaging (e.g. further evaluation with venous sonography or spiral computed tomographic angiography (CTA)), anticoagulation therapy, and subsequent follow-up outcomes.

Method: Retrospective review of the medical records of 82 patients with intermediate probability ventilation-perfusion (V/Q) lung scans from January 1998 to July 1999.

Results: 14.1% of V/Q scans were reported as having an intermediate probability of PE. 72% of IPLS were subject to further evaluation with venous Doppler ultrasound and/or CTA, and 39% of these patients had evidence of thrombo-embolic disease. All patients with imaging evidence of thrombo-embolic disease were started on anticoagulation therapy. In addition, 19 patients were treated based on clinical judgement. Amongst the 35 patients who were not treated, 17 (49%) were based on clinical findings without further imaging. There was no mortality on follow-up of 28 cases of untreated IPLS.

Conclusion: The majority of IPLS will have further imaging, out of which over one-third will have thrombo-embolic disease. Approximately half of IPLS cases will receive anticoagulation therapy. No mortality or PE was found on follow-up of patients who were not treated.

Keywords: pulmonary embolism, V/Q scan, intermediate probability, spiral CTA, Doppler ultrasound.

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INTRODUCTION

The clinical diagnosis of PE is often unreliable and difficult to establish, because the symptoms are non-specific and may be present in many other chest diseases, hence the need for imaging studies to confirm or exclude the diagnosis.

Lung scintigraphy has traditionally played a major role in the evaluation of patients with suspected PE. The V/Q lung scan is most useful when it is interpreted as either a low or high probability of PE in conjunction with a corresponding clinical likelihood of PE; i.e. a normal or low probability scan is associated with a 4% prevalence of PE when the clinical suspicion is low, while a high probability scan has a 97% prevalence of PE when the clinical suspicion is high[1]. Unfortunately, IPLS has been reported to represent more than one-third of all lung scans[2], and in such cases the presence or absence of PE remains uncertain. To make matters worse, there exists a 25-30% inter-observer variability in the interpretation of the intermediate and low probability V/Q scan categories[2]. Because 30 - 40% of pulmonary arteriograms in patients with IPLS has been reported to show positive findings[2], additional investigations beyond the radionuclide scan is often recommended. The aims of our study were: (1) to determine the frequency of thrombo-embolic disease in IPLS; (2) to examine the subsequent imaging strategy in the work-up of patients who had a IPLS result; and (3) to identify any significant mortality or PE on follow-up, especially in the group that had not received anticoagulation.

METHODS

Over a 19-month period between 1 January 1998 and 31 July 1999, 1,147 patients with suspected PE were referred to our centre for V/Q lung scan. Their scan reports were reviewed, out of which 162 (14.1%) patients had their lung scans interpreted as having an intermediate/moderate probability of PE. Fifty-seven of these patients were referred from other institutions and were not included in the analysis. Nine patients whose medical records were unavailable were excluded.

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Table I. Patients who received treatment

Basis for treatment	No of patients (n=47)
Positive findings for PE on CTA	4
Positive findings for DVT on Doppler ultrasound	19
Clinical judgement, negative Doppler ultrasound	8
Clinical judgement, negative Doppler ultrasound and CTA	6
Clinical judgement, no ultrasound or CTA	5
Already on anticoagulation	5

PE: pulmonary embolism, CTA: computed tomographic angiography, DVT: deep vein thrombosis.

Table II. Patients who were not treated

Reason for withholding treatment	No of patients (n=35)
Negative CTA and negative Doppler ultrasound	7
Negative Doppler ultrasound	7
Negative CTA	4
Clinical judgement, no Doppler ultrasound or CTA	16
Anticoagulation contraindicated, no Doppler ultrasound or CTA	1

CTA: computed tomographic angiography.

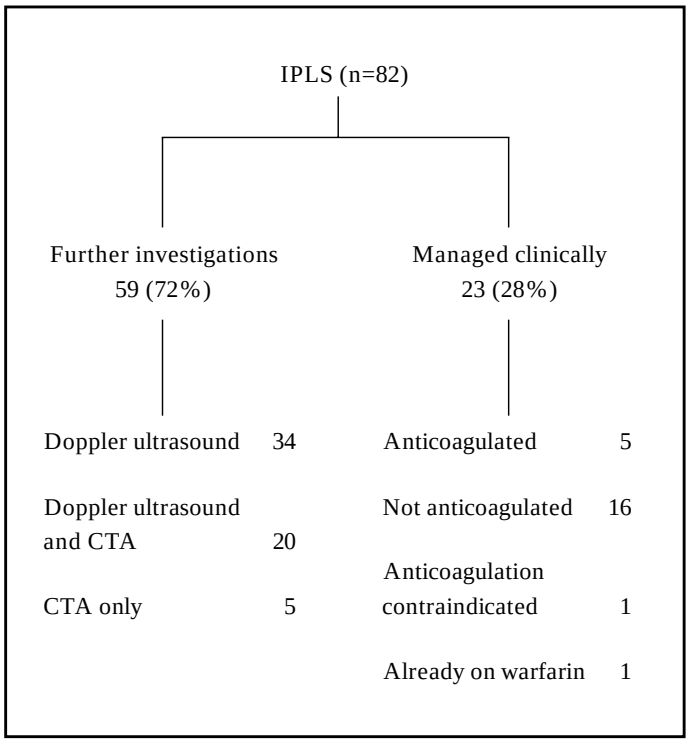

Fig. 1 Management strategy of all IPLS (intermediate probability lung scan) patients investigated for suspected pulmonary embolism. CTA: computed tomographic angiography.

There were six patients who already had a history of PE and two patients with a history of deep vein thrombosis (DVT), and these were also excluded from the study. For those patients who had several lung scans during this period, only the initial scan was analysed. Our final study population consisted of the remaining 82 patients.

From the medical records, we extracted results of imaging studies (CTA, Doppler ultrasound, echocardiogram, pulmonary angiography), whether treatment (ie anti-coagulation, inferior vena cava filter placement or both) was initiated, the basis for treatment, diagnosis at discharge and clinical outcomes on follow-up. If patients were already on anticoagulation therapy for pre-existing atrial fibrillation or valvular heart disease, this was also recorded. Lung scans consisted of ventilation images obtained with 740 - 1,110 MBq (20 - 30 mCi) 99mTechnetium-pentetate (DTPA) using an aerosol delivery system, followed by perfusion images using 185 - 222 MBq (5 - 6 mCi) of intravenous 99mTechnetium-macroaggregated albumin (MAA). The scan images were interpreted according to the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) criteria[1], and within the intermediate probability category, several scans were further classified into "low-to-intermediate" or "intermediate-to-high" probabilities.

RESULTS

A total of 82 patients with suspected PE and IPLS were studied. These comprised 37 (45%) males and 45 females (55%). Patients ranged in age from 14 to 86 years (mean, 56 years). The majority of patients presented with shortness of breath, chest pain, or reduced arterial oxygen saturation. A summary of the subsequent management of the patients is shown in Fig. 1.

Out of the 82 patients, 59 (72%) were evaluated with further imaging. Thirty-four (58%) patients had lower limb Doppler ultrasound only, 5 (8%) had spiral CTA only, and 20 (34%) had both Doppler ultrasound and CTA. A total of 23 patients were found to have thrombo-embolic disease – ultrasound demonstrated DVT in 21 patients, while CTA was positive for PE in four cases. Two patients had concomitant leg vein thrombosis and PE. Of the 23 (28%) patients who were managed on clinical grounds, 5 (22%) were empirically anticoagulated, 16 (70%) were not treated, and anticoagulation was contraindicated in one. One patient was already on warfarin for chronic rheumatic heart disease.

Pulmonary angiography was considered by the clinician in four patients who had negative CTA

and negative Doppler ultrasound. One yielded a negative result (but this was done 21 days after the lung scan and initiation of anti-coagulation), one attempt at angiography was unsuccessful, and two patients did not consent to angiography.

In the 47 patients who received treatment, the basis for treatment is shown in Table I. Forty-two patients were initiated on anticoagulation treatment, while five patients were already anticoagulated for other reasons: atrial fibrillation or valvular heart disease. All patients with documented thrombo-embolic disease were treated. In addition, 19 patients were started on anticoagulation treatment without definite imaging evidence of PE or DVT. Three of these patients were found to have atrial fibrillation and raised pulmonary arterial pressure on echocardiography. One patient was deemed to be at high risk for thrombo-embolism because of disseminated carcinoma. Of the patients who were not treated, the reasons are summarised in Table II. Overall, 24 patients remained untreated without further evaluation of the pulmonary arteries with CTA and out of these, 17 were also not evaluated with venous ultrasound.

Out of the 35 patients who were not treated, the follow-up casenotes were available in 28 patients. Mean follow-up was 7.9 months (range one week to 22 months). None of these patients developed PE or DVT during the period of follow-up and there was no mortality in this group.

There were 13 deaths during admission or on follow-up. All 13 cases had received anticoagulation. For two of these 13 patients, PE was recorded as the primary cause of death. (One patient was 83 years of age with ischaemic heart disease, aortic stenosis and renal failure admitted for breathlessness. He died two weeks after anticoagulation. The other was a 67-year-old lady with history of cerebro-vascular and ischaemic heart disease admitted for lower leg swelling, who died three weeks after anticoagulation. Both cases had positive lower extremity venous sonography and had not been investigated with CTA or pulmonary angiography). In four cases, PE was recorded as a secondary/contributory cause of death. All four were elderly patients who were ill on admission. Two had advanced cancer, and two were diagnosed to have sepsis.

DISCUSSION

Results of the PIOPED study show that IPLS may represent more than one-third of all lung scans[2]. The incidence of IPLS in our institution is less (14.1%), but a similar incidence was reported by Mayo et al[3] (14%), Freitas et al[4] (17.4%) in their prospective studies and also by Murchison et al[5], in their retrospective review. Murchison postulated that this lower incidence is probably due to reluctance of the reporting doctors to issue what is generally considered an "unhelpful" report, which neither establishes nor excludes a diagnosis of PE.

As patients with IPLS have a 30 - 40% likelihood of having PE, further investigations beyond the V/Q scan should be warranted[6]. However, several studies have demonstrated that diagnostic imaging beyond an IPLS result has been underused[5-8]. The reasons are thought to be due to unwillingness on the part of the clinicians to order an invasive test, and their misinterpretation of what is meant by an "indeterminate" lung scan result. For instance, Khorasani[8] recently showed that 49% of their patient cohort with IPLS did not undergo additional imaging with either sonography or pulmonary arteriography to exclude DVT or PE. A corresponding figure of 55% was obtained in Murchison's study. Contrary to their findings, the majority (72%) of IPLS patients in our study had additional tests done (venous ultrasound and/or CTA). Thirty-nine percent (23 out of 59) of these subjects had abnormal results of DVT and/or PE on these additional studies. Only 23 patients (28%) were not subject to further imaging, and were managed based on clinical prior probability of PE. Our higher rate of additional imaging can be explained by readily available spiral CTA service. At the time of their studies, both Khorasani and Murchison did not have ready access to CTA.

Since its introduction in the early 1990s, spiral CTA has emerged as a useful diagnostic imaging modality for the assessment of the pulmonary arteries in the detection or exclusion of PE, and with further improvements in scanner technology, the subsegmental pulmonary arteries are now more reliably analysed. In fact, it has been suggested that routine V/Q scanning should be discontinued in favour of CTA[9], while others have suggested that spiral CTA should be the initial investigation in place of V/Q scanning in those patients who are expected to have non-diagnostic lung scans (e.g. in-patients and patients with chronic obstructive pulmonary disease)[3,10]. Although conventional pulmonary angiography remains the gold standard for diagnosing pulmonary embolism, there has been increasing acceptance of the use of spiral CTA in place of conventional angiography in the search for intravascular clots. Out of our study population of 82 patients, only four were considered for pulmonary angiography, following negative CTA findings. Sonography of the leg veins, from where over 90% of emboli originate, is an important adjunct in the work-up of PE. Not surprisingly, this non-invasive

examination turned out to be the most frequently performed further investigation in our IPLS cohort. Fifty-four out of 59 (92%) patients who had additional imaging were subject to lower extremity venous ultrasound. Results of a cost-effective analysis suggest that patients with IPLS should have ultrasound examination of the leg veins, and that detection of DVT in the legs would render the search for an embolus in the pulmonary vasculature unnecessary, since the treatment of both conditions is similar[11]. In our study, out of the 21 patients with positive findings on sonography, 15 were treated without imaging of the pulmonary vessels.

A total of 23 patients were initiated on treatment based on definite imaging evidence of thrombo-embolic disease. This indicates that at least 28% (23 out of 82) of all IPLS will require anticoagulation treatment. Another 19 patients were treated based on clinical assessment. Therefore, approximately half (51%) Of our study population was treated, either based on clinical findings alone, or together with other imaging diagnosis of thrombo-embolism.

Out of the 35 patients who were not treated, 17 (49%) were managed based on clinical assessment, and did not undergo further imaging tests to exclude thrombo-embolic disease. Although this could well have resulted in under-treatment of patients who do in fact have PE, none of these patients developed clinically evident PE during the follow-up. Seven patients remained untreated based on negative findings on lower limb Doppler studies, without assessment of the pulmonary arteries. Omission of treatment may be acceptable in these patients, as Hull et al[12] have shown that patients with non-diagnostic lung scans had excellent outcomes without anticoagulation therapy if serial lower extremity tests for thrombosis were negative, provided they had adequate cardio-pulmonary reserve.

Our study has several limitations inherent to retrospective reviews. The decision to investigate beyond an IPLS result is initiated by the referring clinicians according to their clinical assessment of the patient. However, we were unable to factor in the pre-test clinical probability (history, physical examination, arterial blood gas, electrocardiogram, chest radiography) for PE in our analysis, as the information could not be reliably determined from the casenotes retrospectively. Also, in an effort to provide a report which would be of greater clinical usefulness, some scans were reported as having a "low to-intermediate" or "intermediate-to-high" probability of PE, having taken into account the number and extent of perfusion defects. These reports may have biased the clinician's decision whether to proceed with further investigations or to treat empirically. Of the 19 patients treated without imaging evidence of PE, 12 were reported as having an intermediate-to-high probability of PE. Of the 17 cases that were left untreated without further investigations, 12 were reported as having a low-to-intermediate probability of PE.

The prevalence of documented thrombo-embolic disease in 28% out of all IPLS cases can only be an under-estimate, since over a quarter of our patients were assessed clinically on follow-up without having had additional imaging. Only 25 out of all 82 patients had CTA of the pulmonary vessels, out of which four were positive. This falls short of the 30 - 40% occurrence of PE in IPLS reported in various studies, but our study size is small. A larger, prospective study would be more accurate in determining the actual prevalence of PE in our IPLS cases.

CONCLUSION

Over two-thirds of patients with an IPLS result on V/Q scanning are referred for further radiological imaging, either with spiral CTA, venous sonography, or both. Our study suggests that at least 28% of all IPLS will have additional thrombo-embolic disease detected by another radiological modality. Approximately half of all IPLS cases will be treated with anti-coagulation, based on clinical assessment with or without other radiological findings. Those patients with no other radiological evidence of thrombo-embolic disease, low clinical probability of PE and who remain untreated are without any mortality on follow-up till two years.

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