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Comparison of ventilation/perfusion scintigraphy and helical CT for diagnosis of pulmonary embolism; strategy using clinical data and ancillary findings

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Key words
lung embolism; lung scintigraphy; spiral CT

Abbreviations
CT; helical computed tomography; DVT, deep venous thrombosis at venography; MSPD, multiple segmental and subsegmental mismatched perfusion defects on SCINT; No, number of patients; PE, pulmonary embolism; SCINT, ventilation/perfusion scintigraphy.

Introduction
Ventilation/perfusion scintigraphy (SCINT) is a preferred diagnostic method for pulmonary embolism (PE) because of its non-invasive character, easiness to perform, high sensitivity, low radiation burden and low cost (ACCP, 1998; Burkill et al., 1999; Maki et al., 1999). However, a high incidence of non-diagnostic findings has led to disbelief of its value (Gottschalk et al., 1993; Woodard, 1997) and stimulated the use and development of helical computed tomography (CT). It has been suggested that CT may complement and even replace SCINT (Goodman & Lipchik, 1996; Hansell, 1997; Cross et al., 1998), although also CT has largely unnoticed shortcomings (Fennerty, 1997) in terms of non-diagnostic, false positive and negative results (Maki et al., 1999; Rathbun et al., 2000). Evaluation of non-invasive techniques is hampered by that even the 'golden standard' for diagnoses of PE, angiography, is not absolutely reliable (Baile et al., 2000), and gives high radiation and contrast doses.

Our objective was to find an answer to the question whether SCINT or helical computer tomography (CT) should be the first hand method for diagnosis of (PE).

Material and methods
Among 4426 SCINTs and 422 CTs performed during 3 years, both methods were performed with respect to PE on clinical indication in 128 patients (33 inpatients and 95 outpatients,
aged 15–90 years). Time interval between the methods is shown in Fig. 1. Approval was obtained from the ethical committee.

Lung scintigraphy

The method that allows ventilation and perfusion to be studied in 1 h was recently described (Tagil et al., 2000). Supine patients inhaled 30 MBq of aerosolized $^{99m}$Tc-DTPA (TechneScan DTPA, Mallinckrodt Medical, Petten, Holland). Planar images in posterior, anterior and posterior oblique projections were taken in sitting position. A second posterior image was taken to allow calculation of DTPA clearance from the lungs. Immediately thereafter, perfusion was studied after i.v. injection of 100 MBq $^{99m}$Tc$^{99m}$-MAA (TechneScan LyoMAA, Mallinckrodt Medical) in the same projections.

Interpretation criteria for SCINT

The findings with respect to PE were described as (1) no embolism, (2) embolism and (3) non-diagnostic. Basic criteria were.

No embolism
- Absence of perfusion defects
- Perfusion defects matched by ventilation defects or caused by known pathology

Embolism
- More than one area of mismatch with a pattern suggesting segmental or subsegmental nature, which implies a peripheral location and usually a wedge-shaped form. One clearly delineated segmental perfusion mismatch in a lower lobe is also considered as PE.

Non-diagnostic
- Ventilation/perfusion abnormalities so severe that match and mismatch cannot be evaluated

- A single lobar or pulmonary perfusion defect with mismatch.
  Ancillary findings like patterns of obstructive or parenchymal disease, heart failure or alveolar inflammation as well as clinical data were considered in the interpretation with respect to PE and reported. On the basis of a vast experience our tradition is to avoid intermediate reports and to give the clinician a clear answer as above.

CT method

With a Toshiba Express CT scanner (Toshiba Corporation, Medical System Division, Tokyo, Japan) a contrast-enhanced study was performed from 2 cm above the diaphragm to the upper aspect of the aortic arch, using 3-mm collimation and a table feed of 3 mm s$^{-1}$. The field of view (FOV) was 22–40 cm. A 200 ml of Omnipaque 240 mg I ml$^{-1}$ (Amersham Health, Buckinghamshire, UK) was infused at 5 ml s$^{-1}$ starting 15 s before scanning. Standard scan time was 50–60 s.

Interpretation criteria for CT

PE was diagnosed when central, eccentric or mural filling defects was observed in pulmonary arteries (Rathbun et al., 2000).

Final diagnosis

The final diagnosis was based upon the results from both CT and SCINT, combined with available laboratory records, X-ray and clinical information. It was reached in consensus between the authors. Patients with PE were seen for follow-up for at least 6 months (CGO); or if treated with a thrombolytic drug for up to 24 months. Patients without PE were followed by their medical records.

Results

Both CT and SCINT were studied because of non-diagnostic results from initial test ($n = 19$), physician’s opinion that CT ($n = 48$) or SCINT ($n = 5$) has low sensitivity, continuing symptoms after negative initial test or follow up of treatment ($n = 43$) or unclear ($n = 13$). A final diagnosis was established in 126 of 128 patients as one or both methods failed in two. Thirty-two had PE.

Clinical SCINT was true positive in 29 (sensitivity 91%) and non-diagnostic in three of 32 patients with PE. Accordingly,
none was false negative in the sense that a case with PE was reported as ‘No embolism’. Three reports were false positive (specificity 96%). Clinical SCINT was non-diagnostic in 10% (Table 1). Figures 2 and 3 show patients with obstructive lung disease and PE to illustrate how far we go in order to avoid non-diagnostic reports.

Reviewed SCINT was true positive in 31 and non-diagnostic in one of 32 patients with PE (sensitivity 97%). None was false positive or false negative (specificity 100%). Rate of non-diagnostic reports was 9%. Clinical CT was true positive in 26 (sensitivity 81%) and non-diagnostic in three of 32 patients with PE. One was false positive (specificity, 99%). Rate of non-diagnostic reports was 8%.

Reviewed CT was true positive in 25 of 32 patients (sensitivity 78%) and non-diagnostic in one of 32 patients with PE. Specificity was 100%.

Clinical CT and clinical SCINT reports showed concordant positive results for PE in 23 of 32 patients with PE (72%). In Table 2 discordant results from the two methods are explained. All false negative or non-diagnostic clinical CT or SCINT reports in patients with PE were performed on the same day or earlier than the method giving the diagnosis. Both clinical SCINT and clinical CT negated PE in 75 of 94 patients without PE (80%).

Among 94 patients without PE, 52 showed ancillary findings of type obstructive or parenchymal disease, increased clearance as in alveolitis, perfusion redistribution as in heart incompensation or focal perturbation of ventilation and perfusion suspected for tumour. In the same group CT described parenchymal and interstitial changes, obstruction/emphysema, pleural effusion, atelectasis or tumour in 38 patients.

Clinical and reviewed SCINT differed with respect to PE in 14 of 126 patients (11%). In 13 of these, one of the reports was

<table>
<thead>
<tr>
<th></th>
<th>True positive</th>
<th>False positive</th>
<th>True negative</th>
<th>False negative</th>
<th>Non diagnostic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical SCINT</td>
<td>29</td>
<td>3</td>
<td>81</td>
<td>0</td>
<td>13 (3 PE)</td>
</tr>
<tr>
<td>Reviewed SCINT</td>
<td>31</td>
<td>0</td>
<td>84</td>
<td>0</td>
<td>11 (1 PE)</td>
</tr>
<tr>
<td>Clinical CT</td>
<td>26</td>
<td>1</td>
<td>86</td>
<td>3</td>
<td>10 (3 PE)</td>
</tr>
<tr>
<td>Reviewed CT</td>
<td>25</td>
<td>0</td>
<td>94</td>
<td>6</td>
<td>1 (1 PE)</td>
</tr>
</tbody>
</table>

Table 1 Diagnostic performance of clinical and reviewed SCINT and CT.

Figure 2 Patient with obstructive lung disease and final diagnosis of PE. Ventilation: uneven ventilation and hot spots because of the deposition of the aerosol. Perfusion: apart from matching defects, mismatch is observed in the lower right lobe (arrow). SCINT reported obstructive disease and suspicion of PE, i.e. a non-diagnostic finding.

Figure 3 Patient with obstructive lung disease and final diagnosis of PE. Ventilation: uneven ventilation and hot spots because of the deposition of the aerosol. Perfusion is dominated by multiple mismatches typical for PE (arrows). SCINT reported PE and obstructive lung disease.
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Table 2

<table>
<thead>
<tr>
<th>Clinical SCINT</th>
<th>Clinical CT</th>
<th>No.</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>True positive</td>
<td>False negative</td>
<td>1</td>
<td>MSPD. Chronic PE.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td>MSPD. DVT.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3</td>
<td>Leg and chest pain.</td>
</tr>
<tr>
<td>True positive</td>
<td>Non diagnostic</td>
<td>4</td>
<td>MSPD, which were normalized at follow up. CT showed fibrosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5</td>
<td>MSPD. CT reported suspicion of subsegmental PE.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6</td>
<td>MSPD and matched defects. DVT in leg and neck. CT showed pneumonia</td>
</tr>
<tr>
<td>Non diagnostic</td>
<td>True positive</td>
<td>7</td>
<td>SCINT reported suspicion of PE. Reviewed SCINT showed PE.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8</td>
<td>SCINT reported obstructive lung disease and suspicion of PE, Fig. 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>9</td>
<td>MSPD unchanged since previous episode. Obstructive lung disease.</td>
</tr>
<tr>
<td>True negative</td>
<td>False positive</td>
<td>10</td>
<td>Normal SCINT. Reviewed CT was normal.</td>
</tr>
<tr>
<td>False positive</td>
<td>True negative</td>
<td>11</td>
<td>MSPD and high DTPA clearance as in alveolitis. Clinical lung fibrosis.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12</td>
<td>Known asthma; new perfusion defects compared to previous SCINT.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>13</td>
<td>Very high DTPA clearance as in alveolitis. Scleroderma.</td>
</tr>
</tbody>
</table>

Patient number; MSPD, multiple segmental and subsegmental mismatched perfusion defects on SCINT; DVT, deep venous thrombosis at venography.

Discussion

The main finding is that SCINT performed and interpreted as described is diagnostic at higher rates than previously reported. Among cases with PE observed with only one of the methods the negative study was never performed on a later day than the positive one. Accordingly, thrombolysis was not considered as a reason for the discrepancies.

The study includes a highly selected group of patients in which the second of the two methods CT and SCINT was performed on clinical indication as described. This is a limitation with respect to conclusions valid for the whole population. However, it also strengthens the results as the selection implies a bias towards difficult cases. The observed concordance between methods is from this aspect notable. Likewise, for both methods, clinical and reviewed reports showed good agreement. The low rate of non-diagnostic findings is, particularly for SCINT, in contrast to most previous reports (PIOPED, 1990; Fennerty, 1997). However, a recent study in which ventilation/perfusion scintigraphy was interpreted according to principles similar to ours, the rate of non-diagnostic findings was only marginally higher than the present (Bargouth et al., 2000).

A prerequisite for the high diagnostic power of SCINT, which others and we report, is high quality ventilation and perfusion scintigraphy (Bargouth et al., 2000; Tägil et al., 2000). Ventilation is always studied for reasons discussed by Tagil.
et al. (2000). In the present selected material only 18 patients had normal perfusion. In two of these, alveolar inflammation was indicated by fast clearance of $^{99m}$Tc-DTPA from the lungs. The diagnostic efficiency furthermore reflects daily co-operation and feedback between our departments and a holistic view in diagnostics of PE. Accordingly ‘the assimilation and review of countless cases’ based upon all available information is a prerequisite for optimal diagnostics of PE and alternative pathology as explained by Freeman et al. (2001). Figures 2 and 3 illustrate that optimal diagnostics cannot rely entirely on fixed diagnostic criteria.

CT had a high specificity with respect to PE while sensitivity was lower. This is in line with previous data (Rathbun et al., 2000; Perrier et al., 2001). Beside lower sensitivity, especially on subsegmental level, CT has other limitations. One is radiation exposure. In our setting it is 4.5–5.5 mSv for CT covering 12–15 cm length of field. It is 1.3 mSv for SCINT. (Five mSv corresponds to one year’s natural radiation in Sweden). The importance of the radiation doses associated with CT has been emphasized particularly with respect to studies of women, whose breast receives 20–35 mSv at CT (Remy-Jarden & Remy, 1999). In a woman aged 35, 10 mSv increases the risk for breast cancer by 13%. The difference in radiation dose between CT and SCINT is particularly important when repeated studies are needed. Studies with large numbers of patients with low prevalence of PE imply that ‘indiscriminate use of CT would have dire consequences in terms of radiation dose to the population as a whole’ (Howling & Hansell, 2000).

Another obstacle is that large amounts of iodinated contrast medium restricts or prevents the use of CT at very high age, in patients with renal failure and, of course, in rare cases of known hypersensitivity. The requirement for breath holding is medium restrict or prevents the use of CT at very high age, in patients with renal failure and, of course, in rare cases of known hypersensitivity. The requirement for breath holding is another problem although lessened with the last generation CT machines.

With respect to the limitation related to the selection of the material, this study renders support for SCINT as the first hand modality in circumstances like ours. Even in a material of ‘difficult cases’, SCINT has a superior sensitivity combined with adequate specificity and low rate of non-diagnostic tests. The low radiation dose, the possibility to quantify the degree of embolism and to use the test for follow-up of treatment and its feasibility in very sick patients contribute to the priority of SCINT over CT. The value of CT when SCINT was not available or non-diagnostic was confirmed. Recently, Perrier et al. (2001) considered that CT has too low sensitivity to be used as a single test, but suggests its use within a combined strategy. Important is that SCINT is expeditious and a complete examination is obtained within 1 h (Tagil et al., 2000). However, a limitation in our setting is that SCINT is only available during working hours. In a longer perspective the fast development of CT techniques must be matched by further development of SCINT. Also, tomographic SCINT rendering three-dimensional images of ventilation, perfusion and ventilation/perfusion quotient is feasible in less than 1 h with the same low radiation exposure as our planar method (Palmer et al., 2001). This technique yields even higher sensitivity and specificity with regards to subsegmental emboli than planar SCINT (Bajc et al., 2002).

Acknowledgements

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