Detection of pulmonary embolism with combined ventilation/perfusion SPECT and low-dose CT: Head-to-head comparison with CT-angiography

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Incidence of PE

Mortality in untreated patients

Pulmonary Embolism

PE is a blockage of the main pulmonary artery or one of its branches by a dislodged thrombus
Pulmonary embolus?

ECG

Blood gas test

Chest X-ray

Echocardiography

Biomarkers

Pulmonary Angiography

Pulmonary MDCT angiography?

V/Q-SPECT?
Pulmonary MDCT vs. V/Q-scintigraphy (planar) in PE diagnostic

Pulmonary MDCT: Higher sensitivity and specificity

V/Q-SPECT vs. V/Q-planar in PE diagnostic

V/Q-SPECT: Higher sensitivity and specificity

V/Q-SPECT vs. MDCT in PE diagnostic

V/Q-SPECT: Higher sensitivity

Pulmonary MDCT: Higher specificity

• Addition of low-dose CT?
• Prospective?
• Simultaneously acquired MDCT and V/Q-SPECT?
• 16 slice CT?
• Krypton$^{81m}$
Aim

- Compare MDCT angiography and V/Q-SPECT alone and in combination with low-dose CT using state-of-the-art methods on a hybrid MDCT-SPECT scanner in the diagnosis of PE.
Material & Methods

• Inclusion criteria
  
  • Consecutive patients suspected of pulmonary embolism
  
  • Well’s score over 2 or a positive D-dimer test
Material & Methods

- Hybrid SPECT-CT scanner

  - MDCT (16 slice) scanner

  - Two head SPECT camera
    - Kr-81m
    - TC-99m-MAA
V/Q SPECT

- Scan time 14 min.
- Matrix 128 x 128
- Angles 72
- 360° (180° pr. camera head)
- Sec./angle 20
- Colimator LEGP
- Astonish reconstruction - 3 iterations and 16 subsets
Low dose CT

- No contrast enhancement
- Tidal breath (no breath hold)

- Fusion with V/Q SPECT
- Attenuation correction
Detection of Pulmonary Embolism with Combined Ventilation–Perfusion SPECT and Low-Dose CT: Head-to-Head Comparison with Multidetector CT Angiography

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The diagnosis of pulmonary embolism (PE) is usually established by a combination of clinical assessment, D-dimer testing, and imaging with either pulmonary ventilation-perfusion (V/Q) scintigraphy or pulmonary multidetector CT (MDCT) angiography. Both V/Q SPECT and MDCT angiography seem to have high diagnostic accuracy. However, only limited data directly comparing these 2 modalities are available. Hybrid V/Camera/MDCT systems have been introduced and allow simultaneous 3-dimensional lung V/Q SPECT and MDCT angiography, suitable for diagnosing PE. The aim of our study was to compare, in a prospective design, the diagnostic ability of V/Q SPECT, V/Q SPECT combined with low-dose CT, and pulmonary MDCT angiography obtained simultaneously using a combined SPECT/MDCT scanner in patients suspected of having PE. Methods: Consecutive patients from June 2006 to February 2008 suspected of having acute PE were referred to the Department of Nuclear Medicine at Rigshospitalet or Frederiksberg Hospital, Denmark, for V/Q SPECT as a first-line imaging procedure. The number of eligible patients was 196. Patients with positive D-dimer results (>5.5 nmol/L) or a clinical assessment with a Wells score greater than 2 were included and underwent V/Q SPECT, low-dose CT, and pulmonary MDCT angiography in a single session. Patient follow-up was 6 mo. Results: A total of 81 simultaneously studies were available for analysis, of which 38% were from patients with PE. V/Q SPECT had a sensitivity of 97% and a specificity of 88%. When low-dose CT was added, the sensitivity was still 97% and the specificity increased to 100%. Perfusion SPECT with low-dose CT had a sensitivity of 93% and a specificity of 51%. MDCT angiography alone had a sensitivity of 69% and a specificity of 100%. Conclusion: We conclude that V/Q SPECT in combination with low-dose CT without contrast enhancement has an excellent diagnostic performance and should therefore probably be considered first-line imaging in the workup of PE in most cases.

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Key Words: clinical cardiology; SPECT/CT; CT angiography; V/Q SPECT; pulmonary embolism
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V/Q SPECT and Low-Dose CT vs. MDCT in PE • Gütte et al. 1987

Acute pulmonary embolism (PE) is a severe and potentially fatal disease, with a mortality rate of approximately 30% if untreated. The incidence is 2 per 1,000 persons per year in Western countries (1–4).

PE is usually diagnosed through a combination of clinical assessment, blood sampling with D-dimer testing, and imaging with either pulmonary ventilation-perfusion (V/Q) scintigraphy or pulmonary multidetector CT (MDCT) angiography.

Pulmonary CT angiography has been shown to have a higher diagnostic accuracy and specificity than conventional planar V/Q scintigraphy (5,6). Thus, in many institutions, MDCT is first-line imaging in the daily clinical routine for patients suspected of PE (7–9). In addition, MDCT is fast, can yield an alternative diagnosis, and has a high degree of interobserver agreement (6,7,10,11).

Accordingly, in recent years the role of V/Q scintigraphy in the diagnosis of PE has diminished. Among the weaknesses of V/Q scintigraphy, if performed as traditional planar scintigraphy using Prospective Pulmonary Embolism Diagnosis (PIOPED) interpretation criteria (12), are high proportions of equivocal studies (9,12) as well as moderate interobserver agreement (6). Yet, the introduction of 3-dimensional V/Q SPECT technology instead of 2-dimensional planar V/Q scintigraphy has in pilot data suggested high diagnostic accuracy for SPECT (13–15).
Perfusion-SPECT

Ventilation-SPECT

Pulmonary low dose CT without a contrast agent (LDCT)
Final diagnosis

- Consensus reading by side-by-side reading of all lesions detected on the pulmonary MDCT angiography, V/Q SPECT and low-dose CT
- ECG
- Transthoracic echocardiography
- Doppler US examinations of the lower extremity veins
- Clinical data and 6 month follow-up from hospital files and telephone interviews.
Results

100 patients were included
81 simultaneous studies were available for analysis.
38% patients had pulmonary embolism as final diagnosis

<table>
<thead>
<tr>
<th></th>
<th>V/Q-SPECT</th>
<th>MDCT</th>
<th>Q-SPECT + LDCT</th>
<th>V/Q-SPECT + LDCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity (%)</td>
<td>97</td>
<td>68</td>
<td>93</td>
<td>97</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>88</td>
<td>100</td>
<td>51</td>
<td>100</td>
</tr>
<tr>
<td>PPV (%)</td>
<td>82</td>
<td>100</td>
<td>57</td>
<td>100</td>
</tr>
<tr>
<td>NPV (%)</td>
<td>98</td>
<td>83</td>
<td>91</td>
<td>98</td>
</tr>
<tr>
<td>Accuracy (%)</td>
<td>86</td>
<td>88</td>
<td>68</td>
<td>99</td>
</tr>
</tbody>
</table>
V/Q-SPECT

False positive: 6 patients
- Interlobar fissure and paraseptal fluid
- COPD
- Atelectasis
- Pneumonia

False negative: 1 patient
- Large thrombosis in a segment artery as seen on the MDCT
Fissure mimicking pulmonary embolism

Perfusion-SPECT

CT

Perfusion-SPECT + CT
Pleural effusion mimicking PE on perfusion SPECT
False negative: 10 patients

- Septic emboli (echo and V/Q-SPECT)
- Sub segment defects on V/Q-SPECT

4 out of 10, was later found on the MDCT by head-to-head comparison with the V/Q-SPECT
Conclusion

V/Q-SPECT with low-dose CT

- Excellent diagnostic performance
- Considered first-line imaging in the work-up of PE.
Future directions – PE diagnosis

- Is SPECT truly superior to planar imaging?
- Does V/Q-SPECT improve mortality and morbidity?
- Independent “Criterion Standard”? 
- Which diagnostic criteria for V/Q-SPECT?
- Is the anatomic information from low-dose CT superior to that from chest radiography?
- How does V/Q-SPECT in combination with low-dose CT compare with CT angiography in a multi-institutional setting?
Original article

Comparison of V/Q SPECT and planar V/Q lung scintigraphy in diagnosing acute pulmonary embolism
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Purpose Planar ventilation/perfusion (V/Q) scintigraphy is currently the standard method for the diagnosis of pulmonary embolism (PE) in most nuclear medicine centers. However, recent studies have shown a superior sensitivity and specificity when applying V/Q single photon emission computed tomography (SPECT) in diagnosing PE. This study evaluated the diagnostic performance of three-dimensional V/Q SPECT in comparison with planar V/Q scintigraphy.

Materials and methods Consecutive patients suspected of acute PE from June 2006 to February 2008 were referred to the Department of Nuclear Medicine at Frederiksberg Hospital, Denmark to a V/Q SPECT, as the first-line imaging procedure. Patients with positive D-dimer ($>0.5 \text{mg/l}$) or after clinical assessment with a Wells score of more than 2 were included and had a V/Q SPECT, low-dose CT, planar V/Q scintigraphy, and pulmonary multidetector computer tomography angiography performed the same day. Ventilation studies were performed using $^{81}$Kr. Patient follow-up was at least 6 months.

Results A total of 36 patient studies were available for analysis, of which 11 (31\%) had PE. V/Q SPECT had a sensitivity of 100\% and a specificity of 87\%. Planar V/Q scintigraphy had a sensitivity of 64\% and a specificity of 72\%.

Conclusion We conclude that V/Q SPECT has a superior diagnostic performance compared with planar V/Q scintigraphy and should be preferred when diagnosing PE. Nucl Med Commun 31:82–86 © 2010 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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Keywords: lung scintigraphy, pulmonary embolism, V/Q SPECT

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<table>
<thead>
<tr>
<th>V/Q planar</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>64 (40–83)</td>
</tr>
<tr>
<td>Specificity</td>
<td>72 (61–80)</td>
</tr>
<tr>
<td>PPV</td>
<td>50 (31–65)</td>
</tr>
<tr>
<td>NPV</td>
<td>82 (70–91)</td>
</tr>
<tr>
<td>Accuracy</td>
<td>70 (55–81)</td>
</tr>
<tr>
<td>Nondiagnostic rate</td>
<td>0 (0–7)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>V/Q SPECT</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>100 (79–100)</td>
</tr>
<tr>
<td>Specificity</td>
<td>87 (78–87)</td>
</tr>
<tr>
<td>PPV</td>
<td>77 (60–77)</td>
</tr>
<tr>
<td>NPV</td>
<td>100 (89–100)</td>
</tr>
<tr>
<td>Accuracy</td>
<td>90 (78–91)</td>
</tr>
<tr>
<td>Nondiagnostic rate</td>
<td>8 (2–22)</td>
</tr>
<tr>
<td>Examination</td>
<td>Effective (whole body) dose (mSv)</td>
</tr>
<tr>
<td>-------------------------------------</td>
<td>------------------------------------</td>
</tr>
<tr>
<td>Chest PA plus lateral</td>
<td>0.07</td>
</tr>
<tr>
<td>Perfusion lung scan</td>
<td>0.8</td>
</tr>
<tr>
<td>Ventilation-perfusion lung scan</td>
<td>1.2-2.0</td>
</tr>
<tr>
<td>CT pulmonary angiography</td>
<td>1.6-8.3</td>
</tr>
<tr>
<td>CT venography</td>
<td>5.7</td>
</tr>
<tr>
<td>Pulmonary DSA</td>
<td>3.2-30.1</td>
</tr>
<tr>
<td>Natural yearly background radiation</td>
<td>2.5</td>
</tr>
<tr>
<td>Allowable yearly maximal exposure in radiation workers</td>
<td>50</td>
</tr>
</tbody>
</table>

Abbreviations: PA, pulmonary artery; CTV, computed tomographic venous phase imaging; DSA, digital subtraction angiography.
V/Q mismatch

PE was diagnosed if one or more perfusion defects (>0.5 segment) with normal ventilation were present.

- **Acute PE**
- chronic PE
- Vasculitis
- Radiation fibrosis
- Hypoplastic pulmonal artery
- Hilus tumor
- Interstitial pneumonia
Exclusion

96 patients

- 49 patients: Impaired kidney function (\(p\)-creatinine >0.120 mmol/l)
- 14 patients: Women under the age of 40 years
- 11 patients: Not able to cooperate
- 8 patients: Technical issues
- 6 patients: A decision not to participate in the study
- 3 patients: Other reasons
- 3 patients: Absence of peripheral venous access
- 2 patients: Allergy to iodine contrast agents
Perspectives

• With use of combined scanners, V/Q-SPECT in combination with low-dose CT without contrast enhancement can “revitalize” lung scintigraphy and should probably be considered first-line imaging test in diagnosing PE
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Department of Clinical Physiology and Nuclear Medicine, Frederiksberg Hospital, Denmark

Department of Cardiology, Rigshospitalet, Copenhagen University Hospital, Denmark

Cluster for Molecular Imaging, Faculty of Health Sciences, University of Copenhagen.
V/Q-SPECT with a wrong diagnosis

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Sex</th>
<th>Symptoms on admission</th>
<th>Comorbidity</th>
<th>Wells score</th>
<th>D-dimer</th>
<th>SPECT</th>
<th>SPECT + LDCT</th>
<th>MDCT</th>
<th>Consensus</th>
<th>Echo</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>80</td>
<td>Male</td>
<td>Dyspnoea, fatigue, coughing</td>
<td></td>
<td>0</td>
<td>0.6</td>
<td>PE</td>
<td>No PE</td>
<td>No PE</td>
<td>No PE</td>
<td>Normal</td>
<td>1 small unmatched defect on the V/Q-SPECT corresponded to a fissure on the LDCT</td>
</tr>
<tr>
<td>86</td>
<td>Male</td>
<td>Dyspnoea, vertigo, vomiting, abdominal pain</td>
<td>CHF, atrial fibrillation, hypertension</td>
<td>0</td>
<td>11</td>
<td>PE</td>
<td>No PE</td>
<td>No PE</td>
<td>No PE</td>
<td>LVEF 25%, dilated LV, mild MI, AI and TI</td>
<td>Negative US of the lower extremities veins. Moderate mismatched defects on the V/Q-SPECT corresponded to fissures on the LDCT</td>
</tr>
<tr>
<td>81</td>
<td>Male</td>
<td>Dyspnoea, new cardiac arrhythmia</td>
<td>Ulcerative colitis, indwelling venous infusion catheter, COPD</td>
<td>1.5</td>
<td>0.7</td>
<td>PE</td>
<td>No PE</td>
<td>No PE</td>
<td>No PE</td>
<td>NA</td>
<td>2 moderate unmatched defects on V/Q-SPECT were shown to be regional emphysema on LDCT. See figure 1 and 2.</td>
</tr>
<tr>
<td>81</td>
<td>Male</td>
<td>Dyspnoea</td>
<td>CHF, apoplexia cerebri, hypertension, mesothelioma</td>
<td>1</td>
<td>4</td>
<td>PE</td>
<td>No PE</td>
<td>No PE</td>
<td>No PE</td>
<td>Mild AI</td>
<td>1 small unmatched defect on the V/Q-SPECT corresponded to a fissure on the LDCT</td>
</tr>
<tr>
<td>78</td>
<td>Male</td>
<td>Dyspnoea, new cardiac arrhythmia</td>
<td>COPD</td>
<td>1.5</td>
<td>0.8</td>
<td>PE</td>
<td>No PE</td>
<td>No PE</td>
<td>No PE</td>
<td>NA</td>
<td>1 small unmatched defect on the V/Q-SPECT corresponded to atelectasis on the LDCT</td>
</tr>
<tr>
<td>86</td>
<td>Female</td>
<td>Dyspnoea, coughing, haemoptysis</td>
<td>COPD, CHF, DVT in the past</td>
<td>3.5</td>
<td>0.7</td>
<td>PE</td>
<td>No PE</td>
<td>No PE</td>
<td>No PE</td>
<td>NA</td>
<td>1 small unmatched defect on the V/Q-SPECT corresponded to airspace filling area on the LDCT</td>
</tr>
<tr>
<td>66</td>
<td>Male</td>
<td>Dyspnoea, DVT</td>
<td>Myelomatosis</td>
<td>4</td>
<td>0.7</td>
<td>No PE</td>
<td>No PE</td>
<td>PE</td>
<td>PE</td>
<td>NA</td>
<td>MUDCT demonstrated a partial occlusion of a seventh segment order pulmonary arterial. Positive US of the lower extremities veins.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Sex</th>
<th>Symptoms on admission</th>
<th>Comorbidity</th>
<th>Wells score</th>
<th>D-dimer</th>
<th>SPECT + LDCT</th>
<th>MDCT</th>
<th>Consensus</th>
<th>Echo</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>80</td>
<td>Female</td>
<td>Dyspnoea</td>
<td>COPD, CHF, surgery for ulcerative colitis within a month, DVT in the past, atrial fibrillation</td>
<td>3</td>
<td>2.9</td>
<td>PE</td>
<td>PE</td>
<td>No PE</td>
<td>PE</td>
<td>NA PE was on the head-to-head comparison found on the MDCT angiography</td>
</tr>
<tr>
<td>90</td>
<td>Female</td>
<td>Dyspnoea</td>
<td>Hypertension</td>
<td>3</td>
<td>0.8</td>
<td>PE</td>
<td>PE</td>
<td>No PE</td>
<td>PE</td>
<td>NA PE was on the head-to-head comparison found on the MDCT angiography</td>
</tr>
<tr>
<td>48</td>
<td>Female</td>
<td>Dyspnoea, vertigo, DVT</td>
<td>Indwelling venous infusion catheter, ulcerative colitis</td>
<td>3</td>
<td>3.2</td>
<td>PE</td>
<td>PE</td>
<td>No PE</td>
<td>PE</td>
<td>Mild TI PE was on the head-to-head comparison found on the MDCT angiography</td>
</tr>
<tr>
<td>81</td>
<td>Male</td>
<td>Dyspnoea</td>
<td>COPD</td>
<td>0</td>
<td>0.5</td>
<td>PE</td>
<td>PE</td>
<td>No PE</td>
<td>PE</td>
<td>Normal PE was on the head-to-head comparison found on the MDCT angiography</td>
</tr>
<tr>
<td>68</td>
<td>Male</td>
<td>Chest pain, new cardiac arrhythmia</td>
<td>Surgery for c. prostate within a month</td>
<td>2.5</td>
<td>21</td>
<td>PE</td>
<td>PE</td>
<td>No PE</td>
<td>PE</td>
<td>Mitral valvular exocresence, mild MI PE was on the head-to-head comparison found on the MDCT angiography. See figure 3.</td>
</tr>
<tr>
<td>52</td>
<td>Female</td>
<td>Dyspnoea, fatigue, vertigo</td>
<td>C. mamma</td>
<td>1</td>
<td>2</td>
<td>PE</td>
<td>PE</td>
<td>No PE</td>
<td>PE</td>
<td>NA 2 moderate wedge-shaped mismatched defects on the V/Q-SPECT, no abnormal findings in the corresponding area on CT.</td>
</tr>
<tr>
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<td>Female</td>
<td>Dyspnoea</td>
<td>C. mamma</td>
<td>1</td>
<td>2.2</td>
<td>Inconclusive</td>
<td>PE</td>
<td>No PE</td>
<td>PE</td>
<td>Mild pulmonary hypertension, mild TI 1 moderate mismatched defect on the V/Q-SPECT, no abnormal findings in the corresponding area on CT.</td>
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<td>86</td>
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<td>Chest pain</td>
<td>Hypertension, DVT in the past</td>
<td>3</td>
<td>12</td>
<td>PE</td>
<td>PE</td>
<td>No PE</td>
<td>PE</td>
<td>NA One large wedge-shaped mismatched segmental perfusion defect on the V/Q-SPECT, no abnormal findings in the corresponding area on CT.</td>
</tr>
<tr>
<td>63</td>
<td>Female</td>
<td>Dyspnoea, New cardiac arrhythmia</td>
<td>Esophageal cancer, thrombus in indwelling venous infusion catheter</td>
<td>2.5</td>
<td>3</td>
<td>PE</td>
<td>PE</td>
<td>No PE</td>
<td>PE</td>
<td>Mild TI One large mismatched wedge-shaped defect on the V/Q-SPECT, no abnormal findings in the corresponding area on CT.</td>
</tr>
</tbody>
</table>