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# Chinese multi-center study of lung scintigraphy and CT pulmonary angiography for the diagnosis of pulmonary embolism

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**Abstract** To evaluate diagnostic value of the PISA-PED and PIOPED II criteria for lung scintigraphy and compare it with CT pulmonary angiography (CTPA) for the detection of pulmonary embolism (PE). Five hundred and forty-four consecutive patients with suspected PE were enrolled. All patients underwent lung ventilation/perfusion (V/P) scan, chest radiography, and CTPA. Two readers used the PIOPED II criteria, and 2 used the PISA-PED criteria for the interpretation of lung scintigraphy. CTPA scans were interpreted by two experienced radiologists. Lung scintigraphy and CTPA were categorized as PE present, absent or non-diagnostic. PE was present in 321 of 544 patients. Using PIOPED II criteria, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were 85.1, 82.5, 88.1, and 78.4% respectively for V/P scan. Using PISA-PED criteria, sensitivity, specificity, PPV, and NPV were 86.0, 81.2, 86.8, and 80.1% respectively, and none was non-diagnostic. Sensitivity, specificity, PPV, and NPV were 81.7, 93.4, 94.9, and 77.3%, respectively for CTPA. PISA-PED interpretation has similar diagnostic accuracy to PIOPED II interpretation, does not have non-diagnostic scan, with lower cost and radiation, thus should be considered as a choice for patients with suspected PE.

**Keywords** Lung scintigraphy · CTPA · Chest radiography · Pulmonary embolism · Diagnosis

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## Introduction

The overall mortality in patients with pulmonary embolism (PE) who are untreated can be as high as 30% [1] while the correct diagnosis and appropriate therapy can significantly lower mortality to 2.5–10%

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[2–4]. Therefore, the accurate and prompt diagnosis of PE is very important. Pulmonary angiography is traditionally considered the gold standard of diagnosis of PE. However, it is infrequently performed because it is an invasive and expensive method with high rate of recurrence and complication and requires experienced radiologists/physicians to both perform the test and interpret the results.

Over recent years, contrast-enhanced multi-slice spiral CT pulmonary angiography (CTPA) has shown promising results [5, 6] in diagnosing PE. As a result, there has been increasing enthusiasm for the use of CTPA, and the numbers of CTPA performed in the past few years have increased significantly. However, CTPA is not applicable in patients who have contraindications to iodinated contrast material, and the radiation dose of CTPA has been identified as a problem of public health [7]. Ventilation/perfusion (V/P) scan and the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) criteria have been widely used as the first line assessment for PE. As well known, non-diagnostic reading is a main flaw of the PIOPED criteria [8]. Taking a different approach, the Prospective Investigative Study of Pulmonary Embolism Diagnosis (PISA-PED) criteria use a simplified classification method for lung perfusion scan (not using lung ventilation scan at all), which with few non-diagnostic readings and promising accuracy [9]. The sensitivity and specificity of such an approach was recently reported to be high, without non-diagnostic reading [10]. However, data regarding the performance of PISA-PED criteria are still scarce and inconsistent [9–11]. Therefore, the aim of this study was to evaluate diagnostic accuracy of the PIOPED II criteria and the PISA-PED criteria for lung scintigraphy interpretation and compare it with CTPA.

## Materials and methods

### Study population

A prospective study was conducted by four medical centers (Cardiovascular Institute and Fu Wai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College; Beijing Hospital; Beijing Tong Ren Hospital, Capital Medical University; Beijing An Zhen Hospital, Capital Medical University) from June 2007 to January 2011. This study was approved by our local ethics committee, and the informed consents were obtained from the patients who were enrolled. Five hundred and forty-four consecutive patients (235 men, 309 women, mean age of 53.3 $\pm$ 16.9 years-old, range 20–91 years-old) with suspected PE were enrolled. All patients had a normal serum creatinine level and were willing to undergo lung V/P scan, chest radiography, and CTPA. Exclusion criteria included pregnant women and patients who were currently experiencing circulatory shock or had hypotension or renal failure, were hemodynamically unstable, were on ventilatory support, received anticoagulation, or had a history of allergy to contrast media.

The clinical suspicion of PE was made by the referring physicians that were based on patients' signs and symptoms, laboratory findings, patients' medical history and predisposing factors. Objective clinical probability was assessed by the Wells test [12]. All patients underwent CTPA, V/P scan and chest radiography. The interval between CTPA and V/P scan ranged from 1 to 3 days. Pulmonary contrast angiography was performed in patients in whom pulmonary embolism was not conclusively diagnosed or ruled out by the noninvasive tests. Patients who received thrombolytic therapy before the examinations were excluded. All patients' original imaging data was available.

### Lung ventilation and perfusion scan

Lung perfusion scan was performed using a single or double-head gamma camera equipped with low-energy, high-resolution, parallel-hole collimators (Infinia Hawkeye 4, GE, USA; e.cam Signature, Siemens, Germany). Images were acquired in a 128 $\times$ 128 matrix and eight views (anterior, posterior, left anterior oblique, left lateral, left posterior oblique, right anterior oblique, right lateral and right posterior oblique) were acquired as previously described [13]. Perfusion imaging began with an intravenous injection of 185–370 MBq (5–10 mCi) of $^{99m}$Tc-macro-aggregated albumin with the patient in supine position. 500 kilo-counts per projection was collected. Ventilation imaging was performed after inhalation of 10 mCi of $^{99m}$Tc-Technegas over 5–8 respiratory cycles in a similar manner. All patients remained in supine position throughout the examination.

### CT pulmonary angiography

CTPA was done using 64-detector CT scanner (LightSpeed VCT, GE, USA,Brilliance 64, PHILIPS, Holland and Aquilion 64, Toshiba, Japan). An intravenous injection of 75–85 mL of contrast medium was made at 5 mL/s using a double power injector. Scans were started with an injection-to-scan delay of approximately 14 s. Scan parameters were 120 kV and 300 mA, using a thin collimation of 64 × 0.625 mm. Patients underwent CTPA in the supine position with a breath-hold, and scans were performed from the level of the aortic arch to 2 cm above the diaphragm. Interpretation was based on effective axial slice thickness of 1.25 mm. These images were assessed on a separated workstation.

### Contrast pulmonary angiography

Pulmonary angiography was performed on an Allura Xper FD10/10 angiographic unit (Philips, Holland). The machine obtained 25 images per second with a 1,024 × 1,024 matrix. The patient's right or left common femoral vein was cannulated and a 6F-sheath (Cordis, USA) was introduced. For angiograms of the main pulmonary arteries, 30–40 mL of nonionic contrast material, iohexol (Omnipaque 350, GE Health-Ireland, USA) was injected at a rate of 15–20 mL/s by power injector through a 6-F pig tail catheter (Cordis, USA). Sub-selective studies used 10–15 mL of contrast material by either hand or power injector at approximately 5–8 mL/s through a 5-F curved tip catheter (Cordis, USA). Anterior and supplemental oblique projections were obtained. All pulmonary angiography images were obtained by using the same imaging parameters and assessed by two experienced physicians.

### Imaging interpretation

Four observers who were unaware of the results of CTPA interpreted the lung scintigraphy. A consensus between the two referees was reached by discussing each case. The lung V/P scans were interpreted by two experienced observers, using the PIOPED II criteria [8]. The results of V/P scans were categorized as PE present, PE absent, and non-diagnostic. Lung perfusion scans combined with chest radiographs were interpreted by another two observers, using the PISA-PED criteria [9]. The results of the perfusion scans combined with chest radiographs were categorized as PE present, PE absent.

The CTPA scans were assessed by two experienced radiologists who were unaware of the results of lung scintigraphy. The main, lobar, segmental, and subsegmental arteries were examined. Complete visualization of a main, lobar, or segmental arteries required that the branch should be followed to its bifurcation. Readers scored their degree of diagnostic certainty by using a three-point scale (PE present, PE absent and non-diagnostic).

A composite reference standard was used to diagnose or rule out pulmonary embolism as previously described [5]. The final diagnosis was made at a consensus meeting taking into account clinical data, all available laboratory recorders, imaging information such as echocardiography, CTPA, V/Q, right heart cardiac catheterization, and pulmonary angiography, the opinions of the physicians responsible for treatment, and clinical follow-up of at last 6 months.

### Statistical analysis

All statistical analyses were done using SPSS 11.5 (SPSS Inc, American). Results were expressed as mean values ± standard deviations (SD) when appropriate. Kappa test was used to analyze the degree of agreement between the image modalities. The differences between the image modalities were tested for significance using Chi-square test. Statistical significance was defined as $P < 0.05$.

## Results

Clinical characteristics of the studied population were summarized in Table 1. Wells test showed that 218 (218/544, 40.1%) patients had low probability of PE (Wells score < 2), and 236 (236/544, 43.4%) patients had intermediate probability of PE (Wells score = 2–6), and 90 (90/544, 16.5%) patients had high probability of PE (Wells score > 6). D-dimer test was performed in all patients, of which 431 (431/544, 79.2%) patients had elevated D-dimer levels. Radionuclide deep venography or Doppler ultrasonography of leg veins was performed in all patients, of which 141 (141/544, 25.9%) patients had positive findings. Pulmonary angiography was performed in 57 (57/544,

**Table 1** Clinical characteristics of study population (n = 544)

| | All patients (n = 544) | Patients with PE (n = 321) | Patients without PE (n = 223) |
|---|---|---|---|
| Gender (men/women) | 235/309 | 149/172 | 86/137 |
| Age (years) | 53.3 ± 16.9 | 56.2 ± 15.2 | 49.1 ± 18.4 |
| Heart Rate (beats/min) | 83.7 ± 15.7 | 86.0 ± 15.1 | 80.3 ± 16.0 |
| RF (cycles/min) | 18.8 ± 4.1 | 18.7 ± 2.4 | 18.9 ± 5.7 |
| Systolic BP (mm Hg) | 121.2 ± 19.6 | 122.4 ± 19.7 | 119.6 ± 19.3 |
| Diastolic BP (mm Hg) | 77.3 ± 11.1 | 77.9 ± 11.2 | 76.3 ± 10.9 |
| Wells score | 3.2 ± 2.8 | 3.9 ± 2.8 | 2.2 ± 2.6 |

*RF* respiratory frequency, *BP* blood pressure

10.5%) patients in whom PE was diagnosed in 31 (31/57, 54.4%) patients and excluded in 26 (26/57, 45.6%) patients.

The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and proportion of non-diagnostic results for the PIOPED II interpretation, the PISA-PED interpretation, and CTPA are depicted in Table 2. There was no statistically significant difference in sensitivity, specificity, NPV and PPV ($P > 0.05$) between the PIOPED II and the PISA-PED interpretation. The CTPA showed significantly higher specificity and PPV ($P < 0.05$), but similar sensitivity and NPV in comparison to both PIOPED II and PISA-PED interpretation ($P > 0.05$).

Proportion of non-diagnostic results on the PIOPED II interpretation and CTPA is significant, but there was no non-diagnostic result on the PISA-PED interpretation ($P < 0.05$). After excluding the non-diagnostic results, the agreement was good between the PIOPED II and the PISA-PED interpretation (Kappa value = 0.97), and moderate between the PIOPED II interpretation and CTPA (Kappa value = 0.59), and between the PISA-PED interpretation and CTPA (Kappa value = 0.58).

In the subgroup analysis of 218 patients with low probability of PE (Wells score < 2), the prevalence of PE was 88 of 218 (40.4%). The diagnostic results for the PIOPED II interpretation, the PISA-PED interpretation, and CTPA are showed in Table 3. The PIOPED II and PISA-PED interpretation showed no statistically significant difference in sensitivity, specificity, NPV, and PPV ($P > 0.05$). Both PIOPED II and PISA-PED interpretation had significantly lower specificity and PPV than CTPA ($P < 0.05$), and had similar sensitivity and NPV to CTPA ($P > 0.05$). After excluding the non-diagnostic results, the agreement was good between the PIOPED II and the PISA-PED interpretation (Kappa value = 0.99), and was moderate between the PIOPED II interpretation and CTPA (Kappa value = 0.58), and was also moderate between the PISA-PED interpretation and CTPA (Kappa value = 0.56).

In the subgroup analysis of 236 patients with medium probability of PE (Wells score = 2–6), the prevalence of PE was 165 of 236 (69.9%). The diagnostic results for the PIOPED II interpretation, the PISA-PED interpretation, and CTPA are showed in Table 4. There was no statistically significant difference in sensitivity, NPV, and PPV between them ($P > 0.05$). Regard to specificity, the PIOPED II interpretation was similar to both the PISA-PED interpretation and CTPA ($P > 0.05$), and CTPA was significantly higher than the PISA-PED interpretation ($P < 0.05$). After excluding the non-diagnostic results, the agreement was good between the PIOPED II and the

**Table 2** Diagnostic results of the PIOPED interpretation, the PISA-PED interpretation, and CTPA in all patients (n = 544)

| Index | PIOPED interpretation | PISA-PED interpretation | CTPA |
|---|---|---|---|
| Sensitivity | 85.1% (245/288) | 86.0% (276/321) | 81.7% (259/317) |
| Specificity | 82.5% (156/189) | 81.2% (181/223) | 93.4% (197/211) |
| PPV | 88.1% (245/278) | 86.8% (276/318) | 94.9% (259/273) |
| NPV | 78.4% (156/199) | 80.1% (181/226) | 77.3% (197/255) |
| Non-diagnostic | 12.3% (67/544) | 0.0% (0/544) | 2.94% (16/544) |

Numbers are percentages, with raw data in parentheses. Sensitivity, specificity, PPV, and NPV are calculated after excluding non-diagnostic cases

**Table 3** Diagnostic results of the PIOPED interpretation, the PISA-PED interpretation, and CTPA in the patients with low probability of PE (n = 218)

| Index | PIOPED interpretation | PISA-PED interpretation | CTPA |
|---|---|---|---|
| Sensitivity | 81.5% (66/81) | 81.8% (72/88) | 78.4% (69/88) |
| Specificity | 83.8% (93/111) | 83.1% (108/130) | 95.2% (119/125) |
| PPV | 78.6% (66/84) | 76.6% (72/94) | 92.0% (69/75) |
| NPV | 86.1% (93/108) | 87.1% (108/124) | 86.2% (119/138) |
| Non-diagnostic | 11.9% (26/218) | 0.0% (0/218) | 2.3% (5/218) |

Numbers are percentages, with raw data in parentheses. Sensitivity, specificity, PPV, and NPV are calculated after excluding non-diagnostic cases

**Table 4** Diagnostic results of the PIOPED interpretation, the PISA-PED interpretation, and CTPA in the patients with intermediate probability of PE (n = 236)

| | PIOPED interpretation | PISA-PED interpretation | CTPA |
|---|---|---|---|
| Sensitivity | 84.3% (123/146) | 84.9% (140/165) | 80.9% (131/162) |
| Specificity | 82.5% (47/57) | 78.9% (56/71) | 92.4% (61/66) |
| PPV | 92.5% (123/133) | 90.3% (140/155) | 96.3% (131/136) |
| NPV | 67.1% (47/70) | 69.1% (56/81) | 66.3% (61/92) |
| Non-diagnostic | 14.0% (33/236) | 0.0% (0/236) | 3.4% (8/236) |

Numbers are percentages, with raw data in parentheses. Sensitivity, specificity, PPV, and NPV are calculated after excluding non-diagnostic cases

**Table 5** Diagnostic results of the PIOPED interpretation, the PISA-PED interpretation, and CTPA in the patients with high probability of PE (n = 90)

| Index | PIOPED interpretation | PISA-PED interpretation | CTPA |
|---|---|---|---|
| Sensitivity | 91.8% (56/61) | 94.1% (64/68) | 88.1% (59/67) |
| Specificity | 76.2% (16/21) | 77.3% (17/22) | 85.0% (17/20) |
| PPV | 91.8% (56/61) | 92.8% (64/69) | 95.2% (59/62) |
| NPV | 76.2% (16/21) | 81.0% (17/21) | 68.0% (17/25) |
| Non-diagnostic | 8.9% (8/90) | 0.0% (0/90) | 3.3% (3/90) |

Numbers are percentages, with raw data in parentheses. Sensitivity, specificity, PPV, and NPV are calculated after excluding non-diagnostic cases

PISA-PED interpretation (Kappa value = 0.95), and was moderate between the PIOPED II interpretation and CTPA (Kappa value = 0.56), and was also moderate between the PISA-PED interpretation and CTPA (Kappa value = 0.52).

In the subgroup analysis of 90 patients with high probability of PE (Wells score > 6), the prevalence of PE was 68 of 90 (75.6%). The diagnostic results for the PIOPED II interpretation, the PISA-PED interpretation, and CTPA are showed in Table 5. There was no statistically significant difference in sensitivity, specificity, NPV, and PPV between them ($P > 0.05$). After excluding the non-diagnostic results, the agreement was good between the PIOPED II and the PISA-PED interpretation (Kappa value = 0.93), and was moderate between the PIOPED II interpretation and CTPA (Kappa value = 0.50), and was also moderate between the PISA-PED interpretation and CTPA (Kappa value = 0.55).

## Discussion

This is to our best knowledge the first Chinese Multicenter study of lung scintigraphy and CTPA for the diagnosis of PE in a large number of patients. There

are several significant findings from the present study. First, lung scintigraphy and CTPA has similar sensitivity for the diagnosis of PE although CPTA has slightly higher specificity than lung scintigraphy; Second, the PIOPED II and the PISA-PED interpretation have comparable accuracy for the diagnosis of PE; Finally, the PISA-PED interpretation without the need of ventilation scan is fast and simpler than the PIOPED II interpretation, thus is of significant advantage in the setting of acute PE.

It should be pointed out that this study used a composite reference test to diagnose PE that was based on all imaging modalities, all available laboratory records, clinical data, and the opinions of the physicians responsible for treatment and follow-up of at last 6 month. Pulmonary angiography was not performed in all patients. Majority patients acquired final diagnosis by non-invasive tests. This was necessary, since it was deemed to be unethical to require pulmonary angiography in all recruited patients. The PIOPED II study [5, 8] and many other studies [14, 15] also used a composite reference test to diagnose PE. According to previous reports [5, 8, 16–19], the composite reference test could accurately diagnose and exclude PE. Furthermore, pulmonary angiography had been performed in 57 patients in whom PE could not be definitively excluded or diagnosed by non-invasive methods in this study. Therefore, the accuracy of final diagnosis was not adversely affected by using the composite reference test to diagnose PE. In recent years, V/Q single-photon emission computed tomography has emerged as a mature technique for the diagnosis of PE and has been shown to be clearly superior to planar V/Q [20].

The PISA-PED criteria differ substantially from the PIOPED II criteria: first, lung ventilation scan is omitted, which can increase technical simplicity while reduce cost, risk, and radiation dose. Previous reports [21, 22] have suggested that ventilation scan can be omitted without affecting diagnostic accuracy. Second, lung perfusion images are classified according to the shape of perfusion defects regardless of their number or size, and the presence of matching chest radiography abnormalities is not considered in the evaluation of perfusion defects. Using these criteria, the reader is constrained to choose between only two categories of abnormal scan or choose non-diagnostic category, which can reduce the number of non-diagnostic readings. With PISA-PED criteria, none was non-diagnostic in our study as well as in the PIOPED II study [10].

In our study, there was a relatively high prevalence of PE, 59.01%, which could have been due to the high-risk patient population in our medical centers. This rate of PE is higher than that in both the PIOPED I and the PIOPED II patients, who showed prevalence rates of 33% and 19% respectively [10, 23]. Our results demonstrated that the PIOPED II and the PISA-PED interpretation had slightly lower specificity than CTPA, and the sensitivities of them were higher but did not differ significantly from CTPA. Different from our results, the specificity of lung perfusion scan combined with chest radiography was comparable to CTPA in the PISA-PED study [9]. In comparison to the PIOPED II study [10], the PIOPED II and the PISA-PED interpretation showed similar sensitivities (85.1% vs. 84.9% and 86.0% vs. 80.4%, respectively) and somewhat lower specificities (82.5% vs. 92.7% and 81.2% vs. 96.6%) in our study. It may be related to the differences in the patient samples. Our study included patients with severely ill and high prevalence of PE while the majority of the PIOPED II patients were outpatients, with a 19% prevalence of PE. It may be also related to the difference in definition of PE between different observers. The frequency of different readings from lung perfusion scans likely will vary depending on skill and experience of observers.

CTPA showed promising diagnostic accuracy in this study and previous studies [5, 6], and outcome studies [24, 25] have shown that the diagnosis of PE can safely be excluded by negative results on CTPA. However, CTPA may lead to complications in patients who have reduced renal function and iodine allergy. In the PIOPED II study, 18.5% of patients had elevated creatinine and 3.7% of patients were allergic to contrast material [5]. In addition, the radiation dose of CTPA has been identified as a problem of public health, especially in younger women. The breast dose with CTPA in an average 60-kg woman is 20 mGy/breast [26]. Because of the risk of cancer after such exposures to radiation, an imaging test with lower dose may be preferred, such as lung perfusion scan. Finally, CTPA also had non-diagnostic results, that was 2.9% of patients in our study and 6.2% of patients in the PIOPED II study [5], further imaging test should be required for those patients.

In conclusion, the PISA-PED interpretation has diagnostic accuracy similar to the PIOPED II

interpretation. Although the specificity of CTPA is slightly higher than the PISA-PED or the PIOPED II interpretation, the PISA-PED interpretation at lower cost and with lower radiation dose, thus should be considered as a choice for patients with suspected PE.

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**Conflict of interest** None.

## References

1. Soudry G, Dibos PE (2000) Gated myocardial perfusion scan leading to diagnosis of unsuspected massive pulmonary embolism. Ann Intern Med 132:845
2. Dalen JE, Alpert JS (1975) Natural history of pulmonary embolism. Prog Cardiovasc Dis 17:259–270
3. Carson JL, Kelley MA, Duff A et al (1992) The clinical course of pulmonary embolism. N Engl J Med 326:1240–1245
4. Barritt DW, Jordan SC (1960) Anticoagulant drugs in the treatment of pulmonary embolism. A controlled trial. Lancet 1:1309–1312
5. Stein PD, Fowler SE, Goodman LR et al (2006) Multidetector computed tomography for acute pulmonary embolism. N Engl J Med 354:2317–2327
6. Musset D, Parent F, Meyer G et al (2002) Diagnostic strategy for patients with suspected pulmonary embolism: a prospective multicentre outcome study. Lancet 360:1914–1920
7. Brenner DJ, Hall EJ (2007) Computed tomography: an increasing source of radiation exposure. N Engl J Med 357:2277–2284
8. Sostman HD, Stein PD, Gottschalk A et al (2008) Acute pulmonary embolism: sensitivity and specificity of ventilation-perfusion scintigraphy in PIOPED II study. Radiology 246:941–946
9. Miniati M, Pistolesi M, Marini C et al (1996) Value of perfusion lung scan in the diagnosis of pulmonary embolism: results of the prospective investigative study of acute pulmonary embolism diagnosis (PISA-PED). Am J Respir Crit Care Med 154:1387–1393
10. Sostman HD, Miniati M, Gottschalk A et al (2008) Sensitivity and specificity of perfusion scintigraphy combined with chest radiography for acute pulmonary embolism in PIOPED II. J Nucl Med 49:1741–1748
11. McLean RG, Carolan M, Bui C et al (2004) Comparison of new clinical and scintigraphic algorithms for the diagnosis of pulmonary embolism. Br J Radiol 77:372–376
12. Wells PS, Anderson DR, Rodger M et al (2000) Derivation of a simple clinical model to categorize patients probability of pulmonary embolism: increasing the models utility with the SimpliRED D-dimer. Thromb Haemost 83:416–420
13. Wang F, Fang W, Lv B et al (2009) Comparison of lung scintigraphy with multi-slice spiral CT in the diagnosis of pulmonary embolism. Clin Nucl Med 34:424–427
14. Reinartz P, Wildberger JE, Schaefer W et al (2004) Tomographic imaging in the diagnosis of pulmonary embolism: a comparison between V/Q lung scintigraphy in SPECT technique and multislice spiral CT. J Nucl Med 45:1501–1508
15. Katsouda E, Mystakidou K, Rapti A et al (2005) Evaluation of spiral computed tomography versus ventilation/perfusion scanning in patients clinically suspected of pulmonary embolism. In Vivo 19:873–878
16. Turkstra F, Kuijer PM, van Beek EJ et al (1997) Diagnostic utility of ultrasonography of leg veins in patients suspected of having pulmonary embolism. Ann Intern Med 126:775–781
17. Henry JW, Relyea B, Stein PD (1995) Continuing risk of thromboemboli among patients with normal pulmonary angiograms. Chest 107:1375–1378
18. Kipper MS, Moser KM, Kortman KE et al (1982) Longterm follow-up of patients with suspected pulmonary embolism and a normal lung scan. Perfusion scans in embolic suspects. Chest 82:411–415
19. Wells PS, Ginsberg JS, Anderson DR et al (1998) Use of a clinical model for safe management of patients with suspected pulmonary embolism. Ann Intern Med 129:997–1005
20. Bajc M, Neilly JB, Miniati M et al (2009) EANM guidelines for ventilation/perfusion scintigraphy: part 2. algorithms and clinical considerations for diagnosis of pulmonary emboli with V/P (SPECT) and MDCT. Eur J Nucl Med Mol Imag 36:1528–1538
21. Goldberg SN, Palmer EL, Scott JA et al (1994) Pulmonary embolism: prediction of the usefulness of initial ventilation–perfusion scanning with chest radiographic findings. Radiology. 193:801–805
22. Stein PD, Terrin ML, Gottschalk A et al (1992) Value of ventilation/perfusion scans compared to perfusion scans alone in acute pulmonary embolism. Am J Cardiol 69:1239–1241
23. The PIOPED Investigators (1990) Value of the ventilation/perfusion scan in acute pulmonary embolism. Results of the prospective investigation of pulmonary embolism diagnosis (PIOPED). JAMA 263:2753–2759
24. Perrier A, Roy P-M, Sanchez O et al (2005) Multidetector-row computed tomography in suspected pulmonary embolism. N Engl J Med 352:1760–1768
25. The Christopher Study Investigators (2006) Effectiveness of managing suspected pulmonary embolism using an algorithm combining clinical probability, D-dimer testing, and computed tomography. JAMA 295:172–179
26. Parker MS, Hui FK, Camacho MA (2005) Female breast radiation exposure during CT pulmonary angiography. AJR 185:1228–1233