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Present diagnostic strategies for acute pulmonary thromboembolism; results of a questionnaire in a retrospective trial conducted by the Respiratory Nuclear Medicine Working Group of the Japanese Society of Nuclear Medicine

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The aim of this study is to re-evaluate and clarify the diagnostic role of ventilation/perfusion lung scintigraphy in Japan, now that single-detector-row helical CT and multidetector-row CT are available in clinical practice. The Respiratory Nuclear Medicine Working Group of the Japanese Society of Nuclear Medicine distributed a questionnaire to institutions in Japan equipped with scintillation cameras as of September 2001. Of 1,222 institutions, 239 returned effective answers (19.6%). The most frequent combination for initial diagnosis of acute pulmonary thromboembolism was chest radiography, perfusion lung scintigraphy, and contrast-enhanced CT (111 institutions, 46.4%). The questionnaire revealed that the validity and usage of perfusion lung scintigraphy and those of contrast-enhanced CT were equivalent in the present clinical situation. On the other hand, the diagnostic value of ventilation lung scintigraphy in suspected pulmonary thromboembolism has not been established in Japan. Even though contrast-enhanced CT is widely used in Japan, perfusion lung scintigraphy is still required to determine disease severity and monitor its progress.

Key words: questionnaire, pulmonary thromboembolism, perfusion lung scintigraphy, ventilation lung scintigraphy, contrast-enhanced helical CT

INTRODUCTION

PULMONARY THROMBOEMBOLISM is a potentially fatal disease for which treatment is highly effective if an accurate early diagnosis is made. Ventilation/perfusion lung scintigraphy has been used extensively as the primary imaging method for evaluating patients suspected of having pulmonary thromboembolism.

The most comprehensive prospective study to date addressing the role of ventilation/perfusion lung scintigraphy is the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) study,[1] a multicenter trial evaluating the efficacy of various conventional methods for diagnosing acute pulmonary thromboembolism. Because the results of ventilation/perfusion lung scintigraphy were nondiagnostic in approximately 70% of the patients included in the PIOPED study,[1] we may need to conduct further studies to exclude or confirm the diagnosis of pulmonary thromboembolism.

Pulmonary angiography has been the gold standard imaging method for the diagnosis of pulmonary

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thromboembolism, but this method is invasive and an alternative modality is desirable.

Helical computed tomography (CT) is a minimally invasive technique that has shown great promise in the diagnosis of central thromboembolism. Current contrast-enhanced helical CT can detect small emboli in subsegmental branches of the pulmonary artery.[2] This ability could reduce the need for additional pulmonary angiography,[2] and helical CT would then be more useful than ventilation/perfusion lung scintigraphy as a first-line test in patients suspected of having pulmonary thromboem bolism.[2]

In recent years, the development of multidetector-row CT, fast gantry rotation speed, and special reconstruction algorithms allow more rapid and accurate CT assessment of vessel visualization in middle and peripheral lung zones. Compared with helical CT (single-detector-row CT), multidetector-row CT significantly improves detection of peripheral pulmonary emboli.[3] With these techniques, we can easily obtain a three-dimensional (3D) image of a pulmonary artery.

Therefore, the recent widespread use of helical CT and multidetector-row CT provides precise information about the existence of emboli in pulmonary arteries. This technology seems to change the diagnostic role of ventilation/perfusion lung scintigraphy.

The aim of this study is to re-evaluate and clarify the diagnostic role of the ventilation/perfusion lung scintigraphy in Japan, now that a helical CT and multidetector-row CT are widely available in clinical practice.

MATERIALS AND METHODS

The Respiratory Nuclear Medicine Working Group of the Japanese Society of Nuclear Medicine conducted a questionnaire study. The questionnaire covered the following areas: 1) annual examination numbers of CT, pulmonary angiography, perfusion lung scintigraphy, ventilation lung scintigraphy and magnetic resonance imaging (MRI); 2) classification of conventional CT, helical CT and multidetector-row CT; 3) a standard combination of the imaging studies for the initial diagnosis of acute pulmonary thromboembolism; 4) a standard combination of the imaging studies for monitoring the therapeutic effect on pulmonary thromboembolism; 5) the present diagnostic strategy: first line study, decision making, diagnostic criteria, a study for monitoring, and an emergency system; and 6) responders' opinions about an ideal diagnostic strategy (Appendix).

The questionnaire papers were distributed to 1,222 institutions in Japan equipped with scintillation cameras as of September 2001. Data were collected up to November 30, 2001. Data were recorded and analyzed with the use of the Microsoft Excel® Spreadsheet software program.

Table 1 Annual examination numbers of chest CT, pulmonary angiography, perfusion lung scintigraphy, and ventilation lung scintigraphy

	Total numbers			Numbers performed for initial diagnosis		Numbers performed for monitoring	
	Average	Maximum	Minimum	No.	%*	No.	%*
chest CT	1976	9000	15	2506	0.5	1338	0.3
pulmonary angiography	7.9	120	0	860	45.6	287	15.2
perfusion lung scintigraphy	58.5	1255	0	6071	43.4	2438	17.4
ventilation lung scintigraphy	18.1	753	0	1224	28.3	429	9.9

*: (numbers performed for initial diagnosis/total numbers) × 100

Table 2 A standard combination of study for the initial diagnosis of acute and chronic pulmonary thromboembolisms

Acute pulmonary thromboembolism	No.	%
chest radiography + perfusion lung scintigraphy + contrast-enhanced CT	111	46.4
chest radiography + ventilation/perfusion lung scintigraphy + contrast-enhanced CT	29	12.1
chest radiography + perfusion lung scintigraphy	20	8.4
chest radiography + perfusion lung scintigraphy + contrast-enhanced CT + pulmonary angiography	19	7.9
chest radiography + perfusion lung scintigraphy + pulmonary angiography	15	6.3
Chronic pulmonary thromboembolism	**No.**	**%**
chest radiography + perfusion lung scintigraphy	84	35.1
chest radiography + perfusion lung scintigraphy + contrast-enhanced CT	60	25.1
chest radiography + ventilation/perfusion lung scintigraphy + contrast-enhanced CT	19	7.9
chest radiography + contrast-enhanced CT	16	6.7
chest radiography + ventilation/perfusion lung scintigraphy	12	5

RESULTS

Of the 1,222 institutes, 239 (19.6%) effectively answered question 1. These institutes performed 472,264 chest CT examinations and 13,982 perfusion lung scintigraphy. Perfusion lung scintigraphy was the most frequently performed examination for initial diagnosis and monitoring, and CT was the second (Table 1). The numbers of pulmonary angiography and ventilation lung scintigraphy for initial diagnosis and monitoring were far less than those of perfusion lung scintigraphy and CT. Regarding perfusion lung scintigraphy, 2,199 of SPECT (15.7%) and 1,625 instances of lower limb venography (11.6%) were added to conventional planar imaging. Ventilation lung scintigraphy was conducted at 108 of the 239 institutions (45.0%). Of these 108 institutions, 69 (63.9%) conducted ventilation lung scintigraphy for initial diagnosis, and 44 (40.7%) conducted it for monitoring the therapeutic effect. The radioactive tracers used for ventilation lung scintigraphy were ^{133}Xe-gas in 32 institutions, ^{81m}Kr in 69, ^{99m}Tc-gas in 17, ^{99m}Tc-DTPA in 1, and ^{99m}Tc-HSA-D in 1. Magnetic resonance imaging for diagnosing pulmonary thromboembolism was conducted in 93 cases at 23 institutions (9.6%).

Question 2 revealed that conventional CT was installed in 18 institutions, helical CT in 191, and multidetector-row CT in 57 (24%).

In question 3, the most frequent combination for initial diagnosis of acute pulmonary thromboembolism was chest radiography, perfusion lung scintigraphy, and con-

Table 3 Results of present status and response

	Present status	Response			
	No.	agree No.	undetermined No.	disagree No.	no opinion No.
1 We perform perfusion lung scintigraphy as the first method for evaluating patients with suspected acute pulmonary thromboembolism.	82	64	93	36	46
2 We perform contrast-enhanced CT as the first method for evaluating patients with suspected acute pulmonary thromboembolism.	73	55	84	57	43
3 We perform perfusion lung scintigraphy or contrast-enhanced CT as the first method for evaluating patients with suspected acute pulmonary thromboembolism. If the results of the first method do not suggest pulmonary thromboembolism, another method is performed to confirm the diagnosis.	68	103	56	38	42
4 In the situation in which perfusion lung scintigraphy is performed as the first method for evaluating pulmonary thromboembolism and a chest radiography suggests normal findings, we do not perform the ventilation lung scintigraphy.	38	63	56	65	55
5 In the situation in which perfusion lung scintigraphy is performed as the first method for evaluating pulmonary thromboembolism and a chest radiography suggests normal findings, we perform ventilation lung scintigraphy.	34	50	65	70	54
6 In the situation in which ventilation/perfusion lung scintigraphy is performed as the first method for evaluating pulmonary thromboembolism and the results suggest pulmonary thromboembolism, we do not perform further examinations.	14	21	55	103	60
7 We essentially use the PIOPED criteria to evaluate for pulmonary thromboembolism.	33	46	109	38	46
8 We mainly perform perfusion lung scintigraphy for monitoring pulmonary thromboembolism.	132	143	44	12	40
9 We mainly perform contrast-enhanced CT for monitoring pulmonary thromboembolism.	37	26	82	77	54
10 We perform perfusion lung scintigraphy as the first method for evaluating patients with suspected acute pulmonary thromboembolism. If the results suggest pulmonary thromboembolism, we conduct pulmonary angiography for the treatment of pulmonary thromboembolism.	38	65	73	54	47

trast-enhanced CT (Table 2). In question 4 regarding monitoring for chronic pulmonary thromboembolism, a combination of chest radiography and perfusion lung scintigraphy was most frequently used. The second most frequent combination was chest radiography, perfusion lung scintigraphy, and contrast-enhanced CT (Table 2).

The replies to questions 5 and 6 are summarized in Table 3. For evaluating acute pulmonary thromboembolism (rows 1–3 in Table 3), the numbers of institutions using perfusion lung scintigraphy as a first method, those using contrast-enhanced CT, and those using either method which could be performed earlier as a first method were almost the same. Of the physicians who replied, 43% thought that whichever method that could be performed earlier would be used as a first method for evaluating acute pulmonary thromboembolism and the other method would be used to confirm the diagnosis if the results of the first method did not suggest pulmonary thromboembolism.

The necessity of interventional radiology for pulmonary thromboembolism was controversial, and only 38 of 239 institutions (16%) performed it.

The chest radiography as an alternative test to ventilation lung scintigraphy was also controversial, as shown in rows 4 and 5 (Table 3).

In only 14 institutions (6%), positive results of the ventilation/perfusion lung scintigraphy were used as a final diagnosis of pulmonary thromboembolism. Of the physicians who replied, 43% said that we should perform further examinations if ventilation/perfusion lung scintigraphy was conducted as a first method and the results suggested pulmonary thromboembolism (row 6 in Table 3).

The PIOPED criteria were used by only 33 institutions (14%). Of the physicians who replied, 109 had not determined the usefulness of the PIOPED criteria (row 7 in Table 3).

In 132 institutions (55%), perfusion lung scintigraphy was employed as the most suitable method for monitoring pulmonary thromboembolism. Conversely, contrast-enhanced CT was used as the most suitable method for monitoring pulmonary thromboembolism in only 37 institutions (15%). Although 143 physicians thought that perfusion lung scintigrapny should be used as a monitoring method, 77 physicians (32%) disagreed, preferring the use of contrast-enhanced CT for monitoring pulmonary thromboembolism.

There were 85 institutions (36%) with a 24-hour emergency system for pulmonary angiography, and only 39 institutions (16%) with a 24-hour emergency system for perfusion lung scintigraphy. Of the physicians who replied, 102 (43%) desired a 24-hour emergency system for perfusion lung scintigraphy.

DISCUSSION

The limitation of this questionnaire study was a bias as to the sampling of institutions with nuclear medicine examination facilities. Small hospitals were apparently excluded from this study. We had an initial plan to compare the questionnaire data among groups of hospitals on the basis of size, but we did not conduct it because of this bias. A relatively high proportion of institutions had multi-detector-row CT facilities, more than we had initially expected, which would result in the same bias.

We confirmed that perfusion lung scintigraphy along with a CT scan as a noninvasive study was most frequently performed for initial diagnosis and monitoring of acute pulmonary thromboembolism. The literature suggests that ventilation lung scintigraphy should be combined with perfusion lung scintigraphy to obtain the best clinical information on acute pulmonary thromboembolism.

The medical insurance system covers ventilation lung scintigraphy with ^{81m}Kr, ^{133}Xe, and ^{99m}Tc-gases. In cases in which ^{81m}Kr and ^{133}Xe were employed for ventilation lung scintigraphy, these radioactive gases were not available for 24 hours because of an insufficient delivery system. The ^{99m}Tc-gas could be prepared in each institution throughout 24 hours a day, but a special device was required to generate the radioactive gas. The ^{99m}Tc-DTPA and ^{99m}Tc-HSA-D were clinically available in the USA and Europe for aerosol scintigraphy as a substitution for ventilation lung scintigraphy.[4,5] In Japan, however, the medical insurance system does not cover aerosol scintigraphy. These various inconveniences interfere with the widespread use of ventilation lung scintigraphy.

As an initial diagnostic tool for detecting pulmonary thromboembolism, contrast-enhanced CT tends to be an alternative method to ventilation/perfusion lung scintigraphy because of the high detectability for emboli and additional information about the lung field,[6] but most institutions performed both contrast-enhanced CT and perfusion lung scintigraphy (Table 2). Because perfusion lung scintigraphy is necessary to determine disease severity and to monitor disease progression (Table 3), it could be included in a combination of initial diagnostic tools, regardless of its ability to detect emboli. Pulmonary angiography was not commonly used as a diagnostic method because of its invasiveness, and it was replaced by contrast-enhanced CT (Table 2). For monitoring pulmonary thromboembolism, popular combinations of diagnostic tools were chest radiography and pulmonary perfusion scintigraphy or the two with contrast-enhanced CT. The combination of chest radiography and contrast-enhanced CT was seldom found in this study (Table 2).

Most respondents could not determine the most appropriate method for making an initial diagnosis in patients with suspected pulmonary thromboembolism (Table 3). As a result, the validity and usage of perfusion lung scintigraphy and those of contrast-enhanced CT were equivalent in the present clinical situation.

The use of ventilation lung scintigraphy in cases in

which perfusion lung scintigraphy was performed as an initial method and had normal results were seen on a chest radiography was controversial (Table 3). Even if the ventilation/perfusion lung scintigraphy revealed positive results in patients with suspected pulmonary thromboembolism, further examinations such as contrast-enhanced CT and pulmonary angiography were required in this study. In Japan, because ventilation lung scintigraphy is not popular, the validity of ventilation lung scintigraphy is not recognized. In a report of the 4th nation-wide survey in 1997, 50,400 perfusion lung scintigraphy were conducted annually; on the other hand, 9,740 ventilation lung scintigraphy were conducted.[7]

Although Grewal et al. reported that ventilation/perfusion lung scintigraphy was more sensitive than helical CT for detecting clinically suspected pulmonary thromboembolism,[8] no multi-institutional comparative study was reported. Since we did not ask about the diagnostic accuracy of ventilation/perfusion lung scintigraphy and contrast-enhanced CT in this questionnaire, a further multi-institutional prospective study is recommended to establish the future role of the two methods.

The PIOPED criteria were not widely used because of their complexity[1] and the replacement of contrast-enhanced CT, which was not included in these criteria.

The clinical usefulness of interventional radiology for pulmonary thromboembolism had been proposed,[9] but some clinicians doubt its effectiveness.[10] In this study, the need for interventional radiology for pulmonary thromboembolism in patients with positive results of perfusion lung scintigraphy was controversial.[11]

In summary, we re-evaluated the diagnostic role of ventilation/perfusion lung scintigraphy in Japan, now that a helical CT (single-detector-row CT) and multidetector-row CT are available in clinical practice. The questionnaire revealed that the validity and usage of perfusion lung scintigraphy and those of contrast-enhanced CT were equivalent in the present clinical situation. On the other hand, the diagnostic value of ventilation lung scintigraphy in suspected cases of pulmonary thromboembolism was not established in Japan. Even if contrast-enhanced CT was widely used in Japan, perfusion lung scintigraphy would still be required to determine disease severity and monitor disease progression.

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APPENDIX: THE QUESTIONNAIRE

Question 1

Please indicate the total number of annual examinations for the purpose of diagnosing of pulmonary thromboembolism.

Chest CT
- Total number [ ]
  - No. for initial diagnosis [ ]
  - No. for monitoring [ ]

Pulmonary angiography
- Total number [ ]
  - No. for initial diagnosis [ ]
  - No. for monitoring [ ]

Perfusion lung scintigraphy
- Total number [ ]
  - No. for initial diagnosis [ ]
  - No. for monitoring [ ]

Ventilation lung scintigraphy
- Total number [ ]
  - No. for initial diagnosis [ ]
  - No. for monitoring [ ]

MRI
- Total number [ ]
  - No. for initial diagnosis [ ]
  - No. for monitoring [ ]

Regarding perfusion lung scintigraphy, do you conduct SPECT or RI lower limb venography in addition to conventional planar imaging?

SPECT No. [ ]
RI lowers limb venography No. [ ]

What kind of radioactive gas do you use for ventilation lung scintigraphy? Please check.

( ) ^{133}Xe ( ) ^{81m}Kr ( ) ^{99m}Tc-gas ( ) ^{99m}Tc-DTPA aerosol
( ) another radioactive gas _____

Question 2

What kind of CT is installed in your institution?

[ ] conventional CT
[ ] helical (single-detector-row) CT
[ ] multidetector-row CT

Question 3

Which combination is the standard method for the initial diagnosis of acute pulmonary thromboembolism in your institute?

[ ] Chest radiography + ventilation/perfusion lung scintigraphy + contrast-enhanced CT + pulmonary angiography
[ ] Chest radiography + perfusion lung scintigraphy + contrast-enhanced CT
[ ] Chest radiography + ventilation/perfusion lung scintigraphy + pulmonary angiography
[ ] Chest radiography + perfusion lung scintigraphy + pulmonary angiography
[ ] Chest radiography + ventilation/perfusion lung scintigraphy + contrast-enhanced CT
[ ] Chest radiography + perfusion lung scintigraphy + contrast-enhanced CT
[ ] Chest radiography + contrast-enhanced CT + pul-

monary angiography
[ ] Chest radiography + perfusion lung scintigraphy
[ ] Chest radiography + ventilation/perfusion lung scintigraphy
[ ] Chest radiography + contrast-enhanced CT
[ ] Contrast-enhanced CT + pulmonary angiography
[ ] Ventilation/perfusion lung scintigraphy + contrast-enhanced CT
[ ] Perfusion lung scintigraphy + contrast-enhanced CT
[ ] Contrast-enhanced CT
[ ] Another combination

Question 4
Which combination is the standard method for monitoring chronic pulmonary thromboembolism in your institute?
[ ] Chest radiography + ventilation/perfusion lung scintigraphy + contrast-enhanced CT + pulmonary angiography
[ ] Chest radiography + perfusion lung scintigraphy + contrast-enhanced CT
[ ] Chest radiography + ventilation/perfusion lung scintigraphy + pulmonary angiography
[ ] Chest radiography + perfusion lung scintigraphy + pulmonary angiography
[ ] Chest radiography + ventilation/perfusion lung scintigraphy + contrast-enhanced CT
[ ] Chest radiography + perfusion lung scintigraphy + contrast-enhanced CT
[ ] Chest radiography + contrast-enhanced CT + pulmonary angiography
[ ] Chest radiography + perfusion lung scintigraphy
[ ] Chest radiography + ventilation/perfusion lung scintigraphy
[ ] Chest radiography + contrast-enhanced CT
[ ] Contrast-enhanced CT + pulmonary angiography
[ ] Ventilation/perfusion lung scintigraphy + contrast-enhanced CT
[ ] Perfusion lung scintigraphy + contrast-enhanced CT
[ ] Contrast-enhanced CT
[ ] Another combination

Question 5
Please respond by checking the statement that reflects the present condition in your institute.
[ ] We perform perfusion lung scintigraphy as the first method for evaluating patients with suspected acute pulmonary thromboembolism.
[ ] We perform contrast-enhanced CT as the first method for evaluating patients with suspected acute pulmonary thromboembolism.
[ ] We perform perfusion lung scintigraphy or contrast-enhanced CT as the first method for evaluating patients with suspected acute pulmonary thromboembolism. If the results of the first method do not suggest pulmonary thromboembolism, another method is performed to confirm the diagnosis.
[ ] In the situation in which perfusion lung scintigraphy is performed as the first method for evaluating pulmonary thromboembolism and a chest radiography suggests normal findings, we do not perform ventilation lung scintigraphy.
[ ] In the situation in which perfusion lung scintigraphy is performed as the first method for evaluating pulmonary thromboembolism and a chest radiography suggests normal findings, we perform ventilation lung scintigraphy.
[ ] In the situation in which ventilation/perfusion lung scintigraphy is performed as the first method for evaluating pulmonary thromboembolism and the results suggest pulmonary thromboembolism, we do not perform further examinations.
[ ] We essentially use the PIOPED criteria to evaluate for pulmonary thromboembolism.
[ ] We mainly perform perfusion lung scintigraphy for monitoring pulmonary thromboembolism.
[ ] We mainly perform contrast-enhanced CT for monitoring pulmonary thromboembolism.
[ ] We perform perfusion lung scintigraphy as the first method for evaluating patients with suspected acute pulmonary thromboembolism. If the results suggest pulmonary thromboembolism, we conduct pulmonary angiography for the treatment of pulmonary thromboembolism.
[ ] Perfusion lung scintigraphy is available as a 24-hour emergency service.

Question 6
Please respond by checking the statement that reflects your ideal diagnostic strategy. Please check as follows: agree = 1, undetermined = 2, disagree = 3.
[ ] We perform perfusion lung scintigraphy as the first method for evaluating patients with suspected acute pulmonary thromboembolism.
[ ] We perform contrast-enhanced CT as the first method for evaluating patients with suspected acute pulmonary thromboembolism.
[ ] We perform perfusion lung scintigraphy or contrast-enhanced CT as the first method for evaluating patients with suspected acute pulmonary thromboembolism. If the results of the first method do not suggest pulmonary thromboembolism, another method is performed to confirm the diagnosis.
[ ] In a situation in which perfusion lung scintigraphy is performed as the first method for evaluating pulmonary thromboembolism and a chest radiography suggests normal findings, we do not perform ventilation lung scintigraphy.
[ ] In a situation in which perfusion lung scintigraphy is performed as the first method for evaluating pulmonary thromboembolism and a chest radiography suggests normal findings, we perform ventilation lung

scintigraphy.

[ ] In a situation in which ventilation/perfusion lung scintigraphy is performed as the first method for evaluating pulmonary thromboembolism and the results suggest pulmonary thromboembolism, we do not perform further examinations.

[ ] We essentially use the PIOPED criteria to evaluate for pulmonary thromboembolism.

[ ] We mainly perform perfusion lung scintigraphy for monitoring pulmonary thromboembolism.

[ ] We mainly perform contrast-enhanced CT for monitoring pulmonary thromboembolism.

[ ] We perform perfusion lung scintigraphy as the first method to evaluate patients with suspected acute pulmonary thromboembolism. If the results suggest pulmonary thromboembolism, we conduct pulmonary angiography for the treatment of pulmonary thromboembolism.

[ ] Perfusion lung scintigraphy is available as a 24-hour emergency service.

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