Introduction

Emboli, such as a thrombi formed in the venous system, air, fat, amniotic fluid, tumor cell masses, and foreign bodies, reach the lung via the bloodstream and obstruct the pulmonary arterial system, the functional blood vessel of the lung, inducing an acute or chronic pulmonary circulatory disorder in the lung. This pathological condition is called pulmonary thromboembolism. Pulmonary infarction represents the hemorrhagic necrosis of peripheral lung tissue resulting from pulmonary arterial obstruction, but its incidence is not high. Emboli are considered to be derived from thrombi released from areas of deep vein thrombosis in the legs and pelvic region in 50–80% of cases, and pulmonary thromboembolism was present in 50–60% of cases with deep vein thrombosis. Therefore, pulmonary thromboembolism may be a complication of deep vein thrombosis; the two together are termed venous thrombosis.

The incidence of pulmonary thromboembolism is high in Western countries, and, reportedly, more than 200,000 cases are diagnosed and 50,000 die yearly in the U.S.A. In contrast, the annual number of diagnoses in Japan was calculated to be 3,492, markedly lower than in Western countries. However, pulmonary thromboembolism was present in 30–64% of consecutive autopsies in Western countries; the corresponding figure in Japan was 11–24%. The difference is smaller than was the case with clinical diagnoses, suggesting that pulmonary thromboembolism is probably not a rare disease in Japan, but that the rate of clinical diagnosis is low due to a deficiency in perceiving the disease.

To increase the rate of diagnosis of this disease, clinical evaluation is important. In clinical evaluation, the investigation of risk factors, such as recent surgery, the presence of a malignant tumor, long-term bed rest, obesity, symptoms at onset, including dyspnea and chest pain, and arterial blood gas analysis and plasma D-dimer measurement before the initiation of inhaled oxygen are mentioned. However, there is no clinical symptom specific to this disease, and the pathology varies depending on the number of emboli. It is difficult to diagnose this disease based on these clinical features alone, and definitive diagnosis by imaging is essential. Diagnostic imag-
The diagnosis of pulmonary thromboembolism includes chest radiography, echocardiography, nuclear medicine, computed tomography (CT), magnetic resonance imaging (MRI), and pulmonary arteriography. Of these test methods, CT has recently been considered the most useful and is being increasingly employed.

**The Diagnosis of Pulmonary Thromboembolism by CT, Including the Diagnosis of Leg Vein Thrombosis**

CT was not frequently used for the diagnosis of pulmonary thromboembolism in the past era of conventional CT. The region in which this form of CT could make a diagnosis was limited to the central region from the main pulmonary artery to the intermediate pulmonary arterial trunk because of the poor continuity of images due to a thick slice width and a long acquisition time which reduced the enhancement of the pulmonary artery and thrombus separation.

The advent of helical CT facilitated the generation of information with superior continuity in the cranio-caudal direction within a short period of time. The diagnostic performance for pulmonary thromboembolism was also improved because continuous CT acquisition enabled acquisition of high-contrast, thin cross-sectional images of the pulmonary artery within a short time. Both the sensitivity and specificity for detecting pulmonary thromboembolisms in the central area extending to the segmental pulmonary artery were improved to about 90%.

Multidetector-row CT (MDCT) was developed subsequent to helical CT. In MDCT, multiple detector rows are arranged in the cranio-caudal direction, and multiple CT images can be obtained per single rotation of the X-ray tube. Although just 10 years have passed since the advent of MDCT equipped with 4 detector rows, the development of CT has been rapid, and 64-row MDCT is currently the main trend. The clinical advantages of MDCT compared to helical CT are predominantly the improvement of temporal and spatial resolution, enabling the scanning of a wider area within a shorter time without reducing spatial resolution in the cranio-caudal direction. The current 64-row MDCT scanner is capable of acquiring 1-mm or thinner slices of the entire lung within about 5–10 seconds. The sensitivity and specificity of MDCT for pulmonary thromboembolism are 96% and 88% respectively, a diagnostic performance that may be clinically satisfactory. In addition, favorable continuity in the axial direction of MDCT image data can be utilized for the evaluation of a thrombus in the pulmonary artery in coronal and sagittal views by multiplanar reformation (MPR) and the stereoscopic evaluation of lesions by 3-dimensional CT angiography as well as CT endoscopy (Fig. 1).

The use of CT for the diagnosis of pulmonary thromboembolism facilitates not only the direct visualization of a thrombus in the pulmonary artery, but also evaluation of the presence or absence of pulmonary infarction and atelectasis, altered attenuation in the lung fields, presence or absence of pleural effusion, and severity of cardiomegaly and pericardial effusion. In addition, pneumonia, diseases of the great vessels, chronic obstructive pulmonary disease and pleural lesions, which may result in symptoms similar to those of pulmonary arterial thrombosis, can be excluded.

Furthermore, the introduction of MDCT led to the advent of CT venography to identify deep vein thrombus in the pelvic region and down to the lower limbs subsequent to the examination of pulmonary thromboembolism by CT pulmonary arteriography, as a serial examination. This examination is not complex. The pelvic region and lower limbs is continuously imaged starting at 4–4.5 minutes after the initiation of contrast medium administration for chest CT examination, and the thin slices acquired in this way are displayed as scrolling images to search for a venous filling-defect that represents the thrombus. Imaging may be started from the abdominal region as necessary, and a thrombus in the inferior vena cava can be evaluated at the same time (Fig. 2). MDCT for deep vein thrombosis subsequent to the diagnosis of pulmonary thromboembolism has been reported to have a diagnostic performance characterized by a 97% sensitivity and 100% specificity.

**Changes in the Frequency of Employing Imaging Diagnosis for Pulmonary Thromboembolism**

On comparison of the frequency of use of various diagnostic imaging tests between the first (January 1994–October 1997) and second (November 1997–October 1999) registration periods based on reports by the Japanese Society of Pulmonary Embolism Research, the frequency of use of pulmonary blood flow scintigraphy in the first and second registration periods were 74.1 and 76.7% (p = 0.50), respectively; pulmonary ventilation scintigraphy, 28.2 and 23.0% (p = 0.64); pulmonary arteriography, 45.3 and 56.8%; CT, 13.9 and 57.6% (p
Fig. 1 Various imaging diagnoses of pulmonary arterial thromboembolism by pulmonary arterial CT angiography.
A: Thin (0.6 mm) cross-sectional image. Overriding thrombi are clearly visualized in both pulmonary arterial trunks (arrows).
B: Multiplanar reconstruction of the right pulmonary artery. A continuous thrombus is present in the right pulmonary artery extending into the ascending and descending branches (arrow).
C: Three-dimensional CT image reconstructed by volume-rendering technique. A thrombus in the left pulmonary artery is three-dimensionally visualized (arrow).
D: Evaluation of a thrombus in the pulmonary artery by a CT endoscopic technique. Continuous overriding thrombi in both pulmonary arteries are presented stereoscopically.

<0.0001); MRI, 2.3 and 6.2% (p = 0.019); and transesophageal echocardiography, 0.6 and 3.9% (p = 0.015), respectively, showing that CT has rapidly been employed for the diagnosis of pulmonary thromboembolism. The spread of helical CT and MDCT enabled the minimally invasive detection of thrombi in segments or subsegments of the pulmonary artery within a short time, which may have facilitated the use of CT. On comparison between the 2nd and 3rd (until August 2003) registration periods, the frequency of use of CT for the imaging diagnosis of pulmonary thromboembolism did not change statistically (57.6→62.2%, p = 0.23), but those of pulmonary arteriography (56.8→36.7%, p <0.0001), pulmonary blood flow scintigraphy (76.7→62.2%, p <0.0001), and MRA (6.2→1.6%, p = 0.0014) decreased.

A Diagnostic Tree for Acute Pulmonary Thromboembolism in PIOPED II

Investigators from the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) II trial recommends CT pulmonary arteriography or its use in combina-
tion with CT venography as the initial investigation when the D-dimer is positive, regardless of a low, intermediate, or high possibility of pulmonary thromboembolism based on clinical evaluation.28) Unfortunately, however, the diagnostic performance of CT is not 100%. Comprehensive decision-making should be based on performance of an additional, appropriate test, such as ultrasonography, MRI, nuclear medical examination, or angiography.

**Advantages and Limitations of MDCT in Comparison with Other Methods of Diagnostic Imaging**

Compared to pulmonary blood flow scintigraphy, CT is advantageous in that it can be performed readily and completed within a short time, the reading of images is relatively straightforward, the sensitivity and specificity exceed 90% when the range is limited to the pulmonary arterial segments, showing superior diagnostic performance,22, 28) and the differentiation of many diseases is possible. On comparison with pulmonary arteriography, CT is less invasive and applicable for performance of repeated tests, as may be required in the evaluation of therapeutic effects (Fig. 3). In addition, CT is superior in detecting mural thrombus in the pulmonary artery and intravenous floating thrombus, detection of which is difficult on angiography (Fig. 4). A limitation of CT is that the evaluation of regions distal to the subsegmental pulmonary artery may be difficult in some cases. The use of iodine contrast medium...
Fig. 3 CT venography before and after catheter intervention for left femoral vein thrombus.

**A:** A continuous thrombus was present in the left femoral vein (arrow). Pain was severe, and thrombolytic therapy was performed.

**B:** After thrombolysis, the left femoral vein has re-opened although some residual thrombus is present. Clinical symptoms remitted.

Fig. 4 Comparison of pulmonary arteriography (**A**) and pulmonary arterial CT angiography (**B**): A discordant case.

A mural thrombus (arrow) is present in A1+2 and A3 of the left ascending branch detected by pulmonary arterial CT angiography (**B**) but was not clearly visualized on pulmonary arteriography (**A**).

is also necessary, and its administration carries a risk in patients with allergy and renal dysfunction. Radiation dose of MDCT for pulmonary thromboembolism is relatively high, thus low X-ray kilo-volt peak technique and reduced milliampere second should be used especially in young patients. Needless to say, it is not applicable for the evaluation of hemodynamics such as measurement of the pulmonary arterial blood pressure.

**Conclusion**

Pulmonary thromboembolism is not a rare disease in
Japan. When the disease cannot be ruled out based on clinical evaluation, confirmation through diagnostic imaging is necessary. MDCT should be employed because evaluation of the pulmonary artery by MDCT is minimally invasive and applicable within a short period of time with a high-level of diagnostic performance. Since pulmonary thromboembolism may be a complication of deep vein thrombosis in the legs, the simultaneous investigation of deep vein thrombus at this site by MDCT may provide useful information in deciding on a comprehensive therapeutic strategy for this disease.

REFERENCES

1) Hull RD, Hirsh J, Carter CJ, Jay RM, Dodd PE, Ockelford PA, et al. Pulmonary angiography, ventilation lung scanning, and venography for clinically suspected pulmonary embolism with abnormal perfusion lung scan. Ann Intern Med. 1983; 98: 891–9.
2) Sandler D, Martin J. Autopsy proven pulmonary embolism in hospital patients: are we detecting enough deep vein thrombosis? J R Soc Med. 1989; 82: 203–5.
3) Huismann MV, Böller HR, ten Cate JW, van Royen EA, Vreeken J, Kersten MJ, et al. Unexpected high prevalence of silent pulmonary embolism in patients with deep venous thrombosis. Chest. 1989; 95: 498–502.
4) Moser KM, Fedullo PF, LitteJohn JK, Crawford R. Frequent asymptomatic pulmonary embolism in patients with deep venous thrombosis. JAMA. 1994; 271: 223–5.
5) Dalen J, Alpert J. Natural history of pulmonary embolism. Prog Cardiovasc Dis. 1975; 17: 259–70.
6) Coon WW, Willis PW 3rd, Keller JB. Venous thromboembolism and other venous disease in the Tecumseh community health study. Circulation. 1973; 48: 839–46.
7) Prevention of venous thrombosis and pulmonary embolism. NIH Consensus Development. JAMA. 1986; 256: 744–9.
8) Kumasaka N, Sakuma M, Shirato K. Incidence of pulmonary thromboembolism in Japan. Jpn Circ J. 1999; 63: 439–41.
9) Freiman D, Suyemoto J, Wessler S. Frequency of pulmonary thromboembolism in man. N Engl J Med. 1965; 272: 1278–80.
10) Diebold J, Lohrs U. Venous thrombosis and pulmonary embolism. A study of 5039 autopsies. Pathol Res Pract. 1991; 187: 260–6.
11) Lindblad B, Eriksson A, Bergqvist D. Autopsy-verified pulmonary embolism in a surgical department: analysis of the period from 1951 to 1988. Br J Surg. 1991; 78: 849–52.
12) Mizukami Y, Murai Y, Fukushima Y, Saiki S. Pulmonary embolism in 200 consecutive autopsies of elderly persons. Ko-to-jun. 1976; 24: 979–84. (in Japanese)
13) Nakano T, Ito S, Takezawa H. Epidemiology of pulmonary embolism. Jpn Med J. 1980; 2949: 43–7.
14) Ito M. Pathology of pulmonary arterial embolism. Koto-jun. 1991; 39: 567–72. (in Japanese)
15) Nakamura Y, Yoshitani T, Imakita M, et al. Histopathological study of vein thrombosis and pulmonary thromboembolism leading to pulmonary infarction. Jpn J Phlebol. 1996; 7: 17–22.
16) Murashima S, Nakagawa T, Sakuma H, et al. Imaging diagnosis of acute pulmonary thromboembolism. J Med Imaging. 2003; 19: 1182–91.
17) Hoshi T, Kanai T, Shimizu Y, et al. Pulmonary vascular disease. Gazoshindan. 2001; 21: 1085–95. (in Japanese)
18) Ohtaki M, Endo J, Koizumi A, et al. Imaging diagnosis of pulmonary thromboembolism: Era of CT diagnosis of pulmonary thromboembolism. Rinho. 2003; 48: 20–32. (in Japanese)
19) Remy-Jardin M, Remy J, Deschildre F, Artaud D, Beregi JP, Hossein-Foucher C, et al. Diagnosis of acute pulmonary embolism with spiral CT: comparison with pulmonary angiography and scintigraphy. Radiology. 1996; 200: 699–706.
20) Drucker EA, Rivitz SM, Shepard JA, Boiselle PM, Trotman-Dickenson B, Welch TJ, et al. Acute pulmonary embolism: assessment of helical CT for diagnosis. Radiology. 1998; 209: 235–41.
21) Hayashi H, Takagi R, Ichikawa T, Kumazaki T. New technology of helical scanning CT: For understanding of multidetector-row CT. Nichidokuiho. 1999; 44: 330–41. (in Japanese)
22) Coche E, Verschuren F, Keyeux A, Goffette P, Goncette L, Hainaut P, et al. Diagnosis of acute pulmonary embolism in outpatients: comparison of thin-collimation multi-detector row spiral CT and planar ventilation-perfusion scintigraphy. Radiology. 2003; 229: 757–65.
23) Patel S, Kazerooni EA, Cascade PN. Pulmonary embolism: optimization of small pulmonary artery visualization at multi-detector row CT. Radiology. 2003; 227: 455–60.
24) Loud PA, Katz DS, Klippenstein DL, Shah RD, Grossman ZD. Combined CT venography and pulmonary angiography in suspected thromboembolic disease. AJR. 2000; 174: 61–5.
25) Loud PA, Katz DS, Bruce DA, Klippenstein DL, Grossman ZD. Deep venous thrombosis with suspected pulmonary embolism; detection with combined CT venography and pulmonary angiography. Radiology. 2001; 219: 498–502.
26) Sakuma S, Okada S, Nakamura M, Nakinishi N, Miyahara Y, Yamada N, et al. Present conditions and problems of diagnosis and treatment for pulmonary embolism. Jpn J Angiol. 2003; 43: 207–9.
27) Sakuma S, Nakamura M, Nakinishi N, et al. Results of the 3rd registration for individual pulmonary thromboembolism survey form: Report from the Japanese Society of Pulmonary Embolism Research Joint Working Group. Ther Res. 2004; 25: 1134–5.