Multidetector-Row Computed Tomography Management of Acute Pulmonary Embolism

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Background The purpose of this study was to evaluate the usefulness and safety of multidetector-row computed tomography (MDCT) pulmonary angiography and indirect venography management of acute pulmonary embolism (PE), including indication for inferior vena cava (IVC) filter.

Methods and Results Seventy-one consecutive patients who were clinically suspected of PE and underwent 16-slice MDCT pulmonary angiography and indirect venography were enrolled. Management included indication of IVC filter for patients with extensive deep venous thrombosis (DVT) in submassive or massive PE. A right ventricular to left ventricular short-axis diameter by MDCT >1.0 was judged as submassive PE. All patients were followed for 1 year. MDCT identified 50 patients with venous thromboembolism and 47 patients had acute PE: 4 were judged as massive, 14 as submassive, and 29 as non-massive by MDCT; 3 patients had DVT alone and 7 patients had caval or iliac DVT. Only 1 patient with massive PE and DVT near the right atrium died of recurrence. No other patients died of PE.

Conclusion Management based on MDCT pulmonary angiography combined with indirect venography is considered to be safe and reliable in patients with suspected acute PE. (Circ J 2007; 71: 1948–1954)

Key Words: Computed tomography; Pulmonary embolism; Vena cava filters

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g-e-adjusted mortality rates of pulmonary embolism (PE) increased significantly between 1951 and 2000, and the rate of successful treatment of acute PE has been increasing in Japan. Three clinical surveys have been performed by Tohoku University and the calculated number of new patients with pulmonary thromboembolism in Japan has been increasing, the most recent total being 4,108 (3.22 per 100,000). Mutidetector-row computed tomography (MDCT) is now widely available, making it possible to directly visualize thrombus and enabling alternative diagnoses. The clinical validity of using MDCT and D-dimer to rule out PE has been reported, and recently, the results of the largest study (PIOPED II study) using either MDCT pulmonary angiography (MDCTA) or MDCTA combined with indirect venography (MDCTA-CTV) were reported showing that MDCTA-CTV had a higher sensitivity than MDCTA alone, with similar specificity. However, MDCTA-CTV was inconclusive in 10.6% of patients because of poor image quality of either CTA or CTV. Several reports have suggested that right ventricular (RV) dysfunction assessed by MDCT helped predict mortality during follow-up and it is possible to evaluate RV dysfunction indicating submassive PE without echocardiography.

Kucher et al reported a reduction in mortality from the use of inferior vena cava (IVC) filters in massive PE, and Sakuma et al reported that several patients died of recurrence with submassive PE and even with non-massive PE. Since 2003, we have routinely placed IVC filters in patients with massive or submassive PE with extensive deep venous thrombosis (DVT) on MDCTA-CTV. Echocardiography is used to assess RV dysfunction at that time. In the present study, the RV to left ventricular (LV) short-axis diameter was also calculated by MDCT, and the patients were reclassified: RVD/LVD >1.0 was judged as RV dysfunction (submassive PE) according to van der Meer et al.

The purpose of this study was to evaluate the usefulness and safety of MDCTA-CTV-oriented management of acute PE, including IVC filter indication.

Methods

Patients

Between January 2003 and December 2005, 71 consecutive inpatients and outpatients (26 males, 45 females; mean age 58±17 years, range 17–86) suspected of having acute PE and who had not undergone diagnostic testing for PE were enrolled. Exclusion criteria were contraindication to the use of iodine contrast material (eg, history of allergy to contrast medium, renal insufficiency, pregnancy). All patients underwent MDCTA and indirect venography within 1 week from onset.
Computed Tomography (CT) Protocol

CT was performed with a 16-slice MDCT scanner (LightSpeed Ultra, GE Medical Systems, Milwaukee, WI, USA). Digital scout CT images of the chest, abdomen, and lower extremities to the upper calf level were obtained. For MDCTA, a total of 100 ml of non-ionic contrast material was injected at a rate of 3 ml/s with a power injector via an intravenous catheter in the antecubital vein. MDCTA scanning was started during the phase peak of main pulmonary arterial enhancement, and the scanning delay was 20–25 s. The patient was scanned from the lung apex to the level of the diaphragm while breathholding (9–20 s). Gantry rotation time was 0.5 s and the imaging parameters were 0.625-mm collimation with a pitch of 13.75 used in fast mode. Images were reconstructed from the raw data set at 2.5-mm intervals and 1.25-mm thickness.

MDCTV was performed 3 min after initial contrast material injection. Axial venous images were obtained from the level of the upper calves to the level of the diaphragm during breathholding (~20 s). The imaging parameters were 1.25-mm collimation with a pitch of 27.5 used in fast mode. Images were reconstructed from the raw data set at 5-mm intervals and 2.5-mm thickness.

MDCTA-CTV images of all patients were reloaded from the optic disks to a workstation for retrospective review by 2 trained pneumologists who were specialists in CT.

Thrombi and emboli were defined as low-attenuating partial or complete intraluminal filling defects surrounded by a high-attenuating ring of enhanced blood seen on at least 2 consecutive transverse images. Streaking artifacts were distinguished from clots in several ways according to Cham et al.10

Classification of PE

PE was classified as massive, submassive, and non-massive.9,11 Massive PE was defined as shock when the patient had hypotension (systolic blood pressure (SBP) <90 mmHg or a decrease in SBP of at least 40 mmHg for a period of less than 15 min) not caused by newly emerged arrhythmia, hypovolemia or sepsis, and was accompanied by clinical signs of organ hypoperfusion and hypoxia (eg, impaired consciousness, urine output <30 ml/h, cold and clammy extremities). Submassive PE was defined as RV dysfunction by echocardiographic criteria and/or MDCT criteria (Fig 1). Non-massive PE was defined as normal hemodynamics without RV dysfunction.
Echocardiography

Echocardiography was performed by a cardiologist within 24h before or after diagnosis of PE by MDCTA-CTV. Criteria for RV dysfunction included a dilated, hypokinetic RV, an increased RV to LV ratio caused by interventricular septal bulging into the LV, and estimated systolic pulmonary arterial pressure (SPAP) higher than 35 mmHg. SPAP was calculated by the modified Bernoulli equation, and right atrial pressure was estimated as 5, 10, 15 or 20 mmHg, on the basis of the size and respiratory change of the IVC using previously described techniques. In 4 cases echocardiographic assessment was not performed because of trivial PE.

CT sign of RV Dysfunction

CT scans were retrospectively evaluated by measuring the minor axes of the right and left ventricles of the heart in the transverse plane at their widest points between the inner surface of the free wall and the surface of the interventricular septum. The maximum dimension may be found at different levels, and the RV/LV ratio was then calculated. CT scans were considered to show no RV dysfunction if the ratio was 1.0 or less, but were positive if the ratio was greater than 1.0, as recommended in the literature. RV dysfunction on CT was compared with that on echocardiography and according to SPAP, and the CT classification for submassive PE was used in this study.

CT Obstruction Index

To quantify the pulmonary arterial obstruction by thrombi, the CT obstruction index was calculated according to Qanadli et al. The index is defined as the number of segmental artery branches that are blocked and corrected by a factor of 1 for partial blockage or a factor of...
2 for a completely obstructive PE. With this scoring system, the highest possible score is 40 (thrombus completely obstructing the pulmonary trunk), which corresponds to a 100% obstruction index.

**Diagnosis of Extensive DVT and Limited DVT by MDCT**

The proximal site of DVT (caval, iliac, femoral, popliteal, calf) was investigated in each patient and although proximal DVT is generally defined as proximal to popliteal and distal DVT as calf, according to the upper level of DVT¹⁵ we used our original criteria. Extensive DVT was defined as the proximal site of DVT being proximal to femoral thrombi with at least 2 slices (1 cm) (Fig 2a). Limited DVT was defined as the proximal site of DVT being popliteal or calf thrombi with at least 2 slices (Fig 2b). No DVT was defined as non-detection of DVT, including unconfirmed DVT <1 cm. The association of the presence or level of DVT with the severity of PE (CT obstruction index and RV/LV) was investigated.

**Management**

Our patient management is summarized in Fig 3. All patients with confirmed venous thromboembolism (VTE) were administered intravenous unfractionated heparin for at least 5 days; the aim being prolongation of the activated partial thromboplastin time by a factor of 1.5–2.5. Warfarin was given with the aim of an international normalized ratio of 2–3 for at least 3 months. Thrombolytic therapy was performed in cases of massive or submassive PE, after considering absolute or relative contraindications of thrombolytic therapy. IVC filters were placed in cases of massive or submassive PE with extensive (proximal to femoral) DVT by MDCT, although echocardiography was used in assessing RV dysfunction in addition to MDCT findings at that time. IVC filters were also placed in cases of recurrent PE despite adequate anticoagulation therapy. All patients considered not to have VTE received no additional anticoagulation therapy, although a few patients were treated by preventive therapy with heparin before the diagnosis was confirmed.

**Follow-up**

All patients were followed for at least 1 year by their physicians. Clinical recurrence of VTE, survival period, and cause of death were investigated.

**Statistical Analysis**

Statistical analysis was performed with commercially available software (Statview 5.0 for Macintosh, Tokyo, Japan). Comparisons of 2 groups were analyzed by unpaired t-test and chi-square test, where appropriate. Pearson's correlation coefficient was also used to compare RV/LV and estimated SPAP. Comparisons of 3 groups were tested with 1-way analysis of variance, with Sheffe’s test for multiple comparisons. A p-value of less than 0.05 was considered significant.

**Results**

The enhancement of the pulmonary arteries on MDCT was excellent for a confident diagnosis of PE in all patients, whereas that of the deep veins was fair in 69 patients for a

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>n (%)</th>
</tr>
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<tbody>
<tr>
<td>Pneumonia or atelectasis</td>
<td>6 (28.6)</td>
</tr>
<tr>
<td>Angina or left ventricular failure</td>
<td>4 (19.0)</td>
</tr>
<tr>
<td>Acute exacerbation of COPD</td>
<td>3 (14.3)</td>
</tr>
<tr>
<td>Drug-induced pneumonia</td>
<td>3 (14.3)</td>
</tr>
<tr>
<td>Bronchial asthma attack</td>
<td>2 (9.5)</td>
</tr>
<tr>
<td>Eosinophilic pneumonia</td>
<td>1 (4.8)</td>
</tr>
<tr>
<td>Pleuritis carcinomatosa</td>
<td>1 (4.8)</td>
</tr>
<tr>
<td>Psychogenic dyspnea</td>
<td>1 (4.8)</td>
</tr>
</tbody>
</table>

COPD, chronic obstructive pulmonary disease.

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Fig. 5. Course and prognosis of acute pulmonary embolism according to MDCTA-CTV. Extensive DVT, proximal to femoral DVT; limited DVT, popliteal or calf DVT; PE recurrence, recurrence of PE within one year of follow-up; PE-related death or PE-unrelated death, death within 1 year of follow-up (see Fig 3 for other abbreviations).
confident diagnosis of DVT. The diagnosis of DVT was initially inconclusive in 2 patients, but no further examination for DVT was performed because of non-massive PE and trivial popliteal DVT.

Of the 71 patients, 50 (70.4%) were diagnosed with DVT or PE, and 47 had PE. Isolated DVT was observed in 3 patients and VTE was excluded in 21 patients.

Among 38 of the 47 patients with PE, 13 were judged as submassive and 25 as non-massive by echocardiography, and the other 9 patients were not classified by echocardiography (4 patients were judged as massive type, 1 as a poor study, and 4 patients did not have echocardiography). The classification remained unchanged in 31 (82%) of the 38 patients in terms of the MDCAT-CTV criteria based on RVod/LVod, and 7 cases were reclassified. Finally, 4 patients were judged as massive, 14 as submassive, and 29 as non-massive by RVod/LVod on MDCAT-CTV. RVod/LVod was 1.01±0.316 (0.569–2.538), and in 20 patients in whom SPAP could be measured the ratio correlated well with SPAP (r=0.68 p=0.0006) by echocardiography (an RVod/LVod of 1 corresponded to SPAP of approximately 30 mmHg).

The CT obstruction index was 31.9±18.9% (range 2.5–67.5%), and was well correlated with RVod/LVod (r=0.60, p<0.0001). It also correlated with SPAP by echocardiography (r=0.451, p=0.0453).

DVT was found in 34 of 47 (72.3%) patients with PE, although 2 patients with trivial popliteal DVT were judged as inconclusive at diagnosis. The upper level of DVT was caval in 2 patients, iliac in 5, femoral in 20, popliteal in 6, and calf in 1.

The relationship between residual DVT and severity of PE is shown in Fig 4. The CT obstruction index was higher in patients with extensive (proximal to femoral) DVT compared with those with limited (popliteal to calf) DVT or no DVT. However, RVod/LVod was similar regardless of the site of DVT.

The final diagnosis of no VTE is shown in Table 1. Pneumonia or atelectasis was found in 6 (28.6%) of the 21 cases, and 16 (76%) were respiratory diseases. D-dimer was positive in all patients with PE or DVT.

Treatment and Clinical Course

The actual treatments and prognoses of the 71 patients are summarized in Fig 5. In 13 patients with submassive PE with extensive DVT who were supposed to have filters placed, 8 underwent filter placement: 1 patient was excluded from filter placement because of absence of RV dysfunction by echocardiography and 3 patients did not have filters placed because of a few thrombi <4 slices (2 cm) in the femoral vein. We could not place filters in the remaining patient because of IVC thrombi near the right atrium, and the patient died of recurrence of PE. We used permanent filters (Greenfield filter; Medi-tech/Boston Scientific, Watertown, MA, USA) in 2 patients and temporary-permanent filters (Gunther tulip retrievable vena cava filter: Cook, Bjaeverskov, Denmark) in 8 patients, but we did not retrieve them in any patients because of residual DVT or trapped emboli in the IVC filters. We placed a filter in a patient with non-massive PE because she had progressive DVT despite anticoagulation. Two patients with non-massive PE received thrombolytic therapy, 1 of whom had progressive DVT and the other had already been monitored by Swan-Ganz catheter, and low-dose thrombolysis with urokinase was performed.

During the 1-year follow-up of the 50 patients with VTE, only 1 patient, already described above, died of PE recurrence, and 5 patients died of cancer. No other patients had recurrence of PE in that time, although DVT recurred in 1 patient who had filter placement and in 2 patients without filters, all of whom needed to have warfarin stopped for 1 to several weeks because of surgery or invasive examination. In the 21 patients without PE, 2 died of cancer and 1 of pneumonia, but none had PE or DVT during follow-up.

Discussion

We found that MDCAT-CTV was useful for confirming PE and DVT, and that the patients diagnosed as not having PE or DVT did not have VTE during 1-year follow-up. Furthermore, it was safe to place filters only in the patients with submassive or massive PE with extensive DVT based on the findings of MDCAT-CTV.

Several issues need to be considered in the interpretation of the results. We planned to place filters in cases of submassive or massive PE with proximal to femoral DVT. Decousus et al reported an initial beneficial effect for IVC filters for the prevention of PE, but excessive recurrence of DVT. Recently, temporary filters have been used to reduce the recurrence of PE in the acute phase, especially in Japan, but adverse effects may result (ie, infection, obstruction of filters, hematoma at insertion site). Further precise indications for filters for the prevention of PE with high risks are required. Kucher et al reported that IVC filters were associated with a reduction in 90-day mortality in massive PE and several reports suggest that submassive PE because of RV dysfunction on echocardiography or CT identifies high-risk patients. Sakuma et al also reported that in a Japanese registry IVC filters reduced mortality and no patients died of recurrence of PE in cases of non-massive PE in contrast to submassive or massive PE. Therefore, we used our criteria for the indication for filter use.

We regarded RVod/LVod >1 on MDCCTV as indicating submassive PE and RVod/LVod ≤1 as non-massive PE, but these classifications were changed in 7 patients (8%) from the original assessment of RV dysfunction on echocardiography. Classification of RV dysfunction by echocardiography is generally used, but recently its assessment using RVod/LVod on CT and the ability to predict prognosis has been reported. We used the criteria of RVod/LVod according to van der Meer et al because RVod/LVod ≤1 excluded PE mortality. They also reported that RVod/LVod >1.5, 1< RVod/LVod ≤1.5 predicted 15% and 8% mortality, respectively. Our criteria of RVod/LVod >1 as the submassive type may overestimate RV dysfunction.

Only 1 patient (2.1%) in our series died of recurrence of PE, although 5 patients died of malignancy, similar to previous reports. Our study may have included mild disease, compared with the previous study (5.8%) resulting in lower mortality from PE. The mean RVod/LVod ratio was 1.02±0.36, and only 4 patients (in our series 8.5%) had RVod/LVod >1.5. These data were not as severe as the 1.17±0.36 and 15% reported by van der Meer who excluded hemodynamically unstable patients? On the other hand, the CT obstruction index in our series was 31.9±18.9%, similar to their 31.8±22.9%. In patients in our series with 1< RVod/LVod≤1.5, mortality was 0% compared with 8% in the van der Meer report, a discrepancy that is possibly related to our filter placement in such patients with extensive DVT. In the patient with IVC thrombi near the right atrium
who died, we used thrombolytic therapy on the basis of reports of successful treatment of right atrial thrombi.20,21 The indication of thrombolytic therapy for thrombi near the right atrium needs to be further investigated.

In the PIOPED II study, MDCTA-CTV was inconclusive in 10.6% of patients because image quality was poor. In our series, only 3% of the patients were diagnosed inconclusive because of marginal image quality, with lower thickness possibly enabling us to detect limited DVT. The frequency of DVT in PE was 70.4% in our series, which is lower than that in Girard et al’s report,15 but was similar to that of Hull et al22 and of Simonneau et al.23 The difficulties in detecting calf DVT might be related to the lower frequency of DVT; however, without the use of IVC filters we did not find any recurrence of PE in the patients with no-DVT or limited DVT, including 2 patients with initially inconclusive DVT because of trivial popliteal DVT. In addition, MDCTV found caval or iliac DVT, which can be difficult to find using leg ultrasound, in 7 (20.6%) patients. These data may justify the management of patients by MDCTA-CTV.

The obstruction index was higher in patients with extensive (proximal to femoral) DVT compared with those with limited (popliteal to calf) DVT or no DVT, but the RV/LVo was similar regardless of the extent of DVT or its site. Emboli formed prior to the diagnosis of acute PE and RV remodeling might be related to these discrepancies.

Similarly, Girard et al reported that the mean pulmonary vascular obstruction index by pulmonary angiography was significantly lower in patients with normal venography than in patients with detectable DVT by venography15 and van der Meer reported that a high CT obstruction index predicted poor prognosis of PE.5 It may be important to detect residual DVT by MDCTA-CTV in patients with a high CT obstruction index, as well as RV/LVo >1, although in our series the CT obstruction index correlated with RV/LVo.

Patients without PE did not have recurrence of PE or DVT. The high negative predictive value in CTA-CTV, as previously reported,3,4 was confirmed. In this series 76% of patients without PE were finally diagnosed as having respiratory disease, which suggests the advantages of CT for the differential diagnosis of PE.

We did not evaluate the clinical probability24,25 before examination by MDCTA. Nevertheless, our pretest probability was 47 (66.2%) of 71, much higher than that (30.7%) of a previous study in which MDCTA was performed in patients with high clinical probability or intermediate to low clinical probability with positive D-dimer test.26 We could have performed CT in only patients with high clinical probability and then more patients with low to intermediate clinical probability might have been missed enrollment into MDCT.

Study limitations

Our study was retrospective and the patient population was small. The assessment of submassive or non-massive PE was changed from the original assessment by echocardiography, and filters were not placed in several patients who were originally scheduled to have them. Further indications for filters in cases of submassive DVT with residual DVT should be examined, but our data warrant avoiding the placement of filters in cases of non-massive PE or DVT alone.

In conclusion, MDCTA-CTV was useful for confirming PE and DVT, and for excluding PE, and our study, for the first time, showed management of PE, including indications for the safe insertion of filters, as assessed by MDCTA-CTV.

Acknowledgments

This study was supported in part by a grant to the Respiratory Failure Research Group from the Japanese Ministry of Health, Labor, and Welfare of Japan, Grants-in-Aid for Scientific Research from the Ministry of Education, Science and Culture of Japan (19590833).

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Circulation Journal Vol.71, December 2007


