Quantitative Evaluation of the Attenuation Value of Pulmonary Thrombus on Unenhanced Computed Tomography

MAKI ICHINOSE\textsuperscript{1, 2, 3}, TOMOHISA NOMURA\textsuperscript{2}, YASUSEI OKADA\textsuperscript{3}, HIROSHI INAGAWA\textsuperscript{3}, MANABU SUGITA\textsuperscript{2}

\textsuperscript{1}Department of Anesthesiology, Showa General Hospital, Tokyo, Japan
\textsuperscript{2}Department of Emergency and Disaster Medicine, Juntendo University Graduate School of Medicine, Tokyo, Japan
\textsuperscript{3}Department of Emergency, Showa General Hospital, Tokyo, Japan

Objective: To identify pulmonary thromboembolism (PTE) using the thrombus attenuation value on unenhanced computed tomography (CT).

Design: Single-center retrospective study (January 2015–March 2020).

Methods: Patients who underwent both unenhanced and enhanced CT for suspected PTE were enrolled. Patients with a hyperdense lumen on unenhanced CT and thrombi in the peripheral pulmonary artery (PA) were excluded. Patients were classified into two groups: thrombi (thrombi detected in PA by enhanced CT) and non–thrombi (attenuations of the main PA evaluated as thrombi). Mean CT attenuation values of the thrombi, main PA, and pulmonary trunk (blood pool) were measured. The attenuation values of the thrombus (T) and the thrombus to blood-pool (T/P), thrombus to hemoglobin (T/Hb), and thrombus to hematocrit (T/Ht) ratios were evaluated. The cut-off attenuation value of the thrombus was calculated by a receiver operating characteristic curve and its accuracy in detecting PTE was determined.

Results: Of the 260 patients enrolled, 40 were included, of whom 24 had confirmed PTE. The mean T was 27.25 Hounsfield units (HU) and 36.66HU (p<0.001), and the T/P ratio was 0.74 and 0.99 (p=0.004) in the PTE and non–PTE groups, respectively. The thrombus cut-off value for PTE diagnosis was 30.85 HU. The sensitivity and specificity were 79.9% and 87.5%.

Conclusions: Measuring and evaluating the attenuation value for the central PA and T/P ratio on unenhanced CT improves the diagnostic ability of central PTE in patients suspected to have PTE but cannot tolerate contrast medium.

Key words: attenuation value of thrombus, pulmonary thromboembolism, unenhanced computed tomography (CT)

Introduction

Pulmonary thromboembolism (PTE) is a life-threatening disease with a mortality rate of 11.9\%\textsuperscript{1}. Approximately 350,000 cases of PTE and 85,000 PTE–related deaths occur each year in Japan\textsuperscript{2}. The gold standard for definitive diagnosis of PTE is enhanced computed tomography (CT). However, the use of contrast media may be a concern for...
Ichinose M, et al: Attenuation value of pulmonary thrombus on unenhanced computed tomography

certain patients, such as those with allergies to contrast media, patients medicated with biguanides, or those suffering from renal dysfunction. For these patients, detection of pulmonary thrombi on unenhanced CT could be useful for diagnosis and initiation of therapy for PTE.

High-density regions on unenhanced CT scans, or the hyperdense lumen sign, are known indicators of recent PTE. Current reports have shown that the CT attenuation value of the hyperdense lumen sign is 50–80 Hounsfield units (HU). However, the attenuation of the clots gradually decreases with time and becomes equal to or less than that of the blood pool. Therefore, pulmonary thrombi are rarely detected on unenhanced CT with the exception of the hyperdense lumen sign. We need to find other methods to detect PTE on unenhanced CT and there are no studies that measure the CT attenuation value of thrombi.

The purpose of this study was to examine the usefulness of the thrombus attenuation value on unenhanced CT for the diagnosis of PTE. We also assessed the cut-off CT values for PTE diagnosis using unenhanced CT in patients with PTE. This is the first study that quantitively evaluated the CT attenuation value of thrombi.

Materials and methods

This study reviewed outpatients who presented with dyspnea, chest pain, syncope, and dizziness, showed low saturated oxygen in arterial blood and right heart load, and underwent enhanced CT at Showa General Hospital from January 2015 to March 2020.

All studies were performed using the GE® light-speed VCT 64 detector (GE Healthcare, Hino, Japan) or the Canon Aquilion® One 320 (Canon, Ota city, Tokyo, Japan) detector. The parameters were varied among the unenhanced and enhanced CT examinations, with slice thickness ranging from 3 mm to 5 mm at axial, coronal, and sagittal views. Patients were administered intravenous injections of 2 ml/kg non-ionic contrast medium (Iopromide: Iopromide Injection FRI® 300 mgI/ml, FujiPharma, Toyama, Japan) at a rate of 3 ml/s. Scans were obtained 30 seconds after injection.

CT images were evaluated on a picture archiving and communications system workstation. Based on the enhanced CT images, patients were divided into the PTE group (thrombi were detected) (Figure 1A) or the non-PTE group (thrombi were not detected). Patients who underwent both enhanced and unenhanced CT were included. The central type of PTE was defined as a filling defect in the pulmonary trunk or in the main, lobar, and segmental pulmonary arteries (PAs). We excluded peripheral PTE filling defects in the subsegmental and more peripheral arteries. Patients who showed a hyperdense lumen sign on unenhanced CT were also excluded. The hyperdense lumen sign is a clot with hyperdensity in the PA on unenhanced CT (Figure 1B). In the central PTE group, patients who met the inclusion criteria were labeled as the thrombi group. Patients who met the inclusion

Figure 1 A: Thrombi (arrow) in pulmonary artery on enhanced computed tomography. B: Hyperdense lumen sign (arrow): the same position of thrombi in Figure 1A.
criteria in the non-PTE group were labeled as the non-thrombi group. CT attenuation values were then measured on unenhanced CT images. In the thrombi group, attenuation values were measured in relation to the thrombus after referring to its position in the enhanced CT image. The attenuation values of the pulmonary trunk were also measured after confirming that there was no thrombus on the enhanced CT image. In the non-thrombi group, the attenuation value of the PAs was evaluated and compared to the attenuation value of the thrombi in the thrombi group. The attenuation value of the pulmonary trunk was also evaluated. These measurements were performed by placing the region of interest (ROI) in the scans, after which the computer automatically calculated the average attenuation values (in HU) for the selected foci (Figure 2A, 2B and 3). Each ROI was about 4–6 mm in diameter with an area of 12–28 mm², which was the maximum diameter possible without exceeding the diameter of the segmental PA. Although no specific window setting was used consistently in this study, results were best seen with narrow window settings (window width=330 HU, window level=30 HU). To reduce bias without affecting the partial volume effect, 3-5 ROIs were placed for each image.

Medical records were reviewed to assess the baseline characteristics of patients, including the presenting signs and symptoms, clinical diagnosis, indications for the procedure, and laboratory workups. The mean (± standard deviation [SD]) attenuation values (in HU) of the thrombus and main PA were compared. The thrombus attenuation value on unenhanced CT is related to the

![Figure 2](image1.png) Placing the region of interest (ROI) (●) on unenhanced computed tomography (CT) in the thrombi group. ROIs were placed on the thrombus (A) after referring to its position in the enhanced CT image (B).

![Figure 3](image2.png) Placing the region of interest (ROI) (●) on unenhanced computed tomography (CT) in the non-thrombi group. ROIs were placed on the pulmonary trunk and the left and right main pulmonary arteries.
patient’s hematocrit (Ht) and hemoglobin (Hb) levels\(^4\,^5\). Therefore, we also assessed the ratio of the attenuation value of thrombus (T) to Hb (T/Hb ratio), Ht (T/Ht ratio), and PA (T/P ratio). Receiver operating characteristic (ROC) analysis was performed to set the threshold of the diagnostic performance of unenhanced CT in detecting PTE. Sensitivity, specificity, positive and negative predictive values (PPV and NPV, respectively), and positive and negative likelihood ratios (PLR and NLR, respectively) as well as their 95% confidence intervals (CIs) for the diagnosis of PTE were calculated for each unenhanced CT finding. Continuous variables were tested by t-test or Mann–Whitney U test, discontinuous variables were tested by Fisher’s exact test, and p-values <0.05 were considered significant. All statistical analyses were performed using EZR\(^6\) (Saitama Medical Center, Jichi Medical University, Saitama, Japan).

This study protocol was approved by the ethics committee of Showa General Hospital (approval number REC-240m). All patients provided written informed consent.

### Results

A total of 260 patients were enrolled in the study; 200 were diagnosed with PTE and 60 were not, confirmed based on enhanced CT examination. Of the 200 patients with PTE, 151 did not undergo unenhanced CT examination and were excluded. Among the 49 patients with PTE who underwent both enhanced and unenhanced CT, 33 were of the central type, of whom 9 showed a hyperdense lumen sign and were also excluded. From the 60 patients in the non-PTE group, 17 underwent both enhanced and unenhanced CT, of whom 1 showed a hyperdense lumen sign and was excluded. After applying the exclusion criteria, a total of 40 patients were included in the analyses. Twenty-four of these patients had an acute central PTE (thrombi group), and sixteen had no thrombi in the PA (non-thrombi group) (Figure 4). There was no significant difference in age, renal function, or Hb values at the time of imaging between the two groups. D-dimer, fibrin, and fibrinogen degeneration...
tive product (FDP) were significantly higher in the thrombi group than in the non-thrombi group (Table 1).

The mean attenuation values of pulmonary blood pools in the thrombi and non-thrombi groups were 40.01±12.19 HU and 38.07±9.37 HU, respectively (p=0.594). The mean attenuation values of thrombi in the thrombi group and main PA in the non-thrombi group were 27.25±7.94 HU and 36.66±6.10 HU, respectively (p<0.001). The T/Hb ratio, T/Ht ratio, and T/P ratio in the PTE group were significantly lower than those in the non-thrombi group (Table 2). There was no significant difference in the attenuation values between the two CT devices.

The performance of unenhanced CT for PTE diagnosis is shown in Table 3. According to the ROC curve (Figure 5), a thrombus cut-off value of 30.85 HU and a T/P ratio cut-off value of 0.835 were associated with moderately accurate diagnosis of PTE (area under the curve=83.3 and 77.5, respectively). The thrombus sensitivity, specificity, PPV, NPV, and PLR were 79.2%, 87.5%, 90.5%, 73.7%, and 6.33, respectively (Table 3). The T/P

![Figure 5](image-url) Receiver operating characteristic (ROC) curve of thrombus and the thrombus/pulmonary blood pool ratio. Solid line indicates the ROC of computed tomography (CT) attenuation values of thrombus. The cut-off values are 30.85 Hounsfield units (HU) for thrombus, 0.875 HU for specificity, and 0.792 for sensitivity. Dotted line indicates the ROC of the thrombus/pulmonary blood pool ratio. The cut-off values are 0.835 for the thrombus/pulmonary blood pool ratio, 0.875 for specificity, and 0.667 for sensitivity.
hyperdense lumen has a high diagnostic perfor-
our study, only 9 of 49 patients
6
Ichinose M, et al: Attenuation value of pulmonary thrombus on unenhanced computed tomography

...showed good accuracy. Our results indicate poten-
tial benefits of using measurements of thrombus
value of 30.85 HU calculated from the ROC curve
than that in the blood pool. The thrombus cut-off
value was lower in the thrombi group than in the
value for PTE diagnosis. The thrombus attenuation
can be explained by the processes undergone by the clot itself while lodged within the PA system. As a thrombus retracts, its water
content decreases, which concentrates the hemo-
globin and raises the CT attenuation value of
thrombi to 50–80 HU. The attenuation of clots
decreases gradually to the same as or lower than
that of the blood13,7,8,11-15). Acute thrombi—clinically
judged to be <8 days old—have an average attenu-
ation value of 66 HU, whereas those older than 8
days have a lower value14). In PTE, thrombi are
primarily caused by deep venous thrombosis
(DVT). As DVT has varied symptoms (and can be
asymptomatic in some cases), it is difficult to accu-
rate stly determine when a DVT had formed. This
study included emergency outpatients, but it is
possible that several days had passed since the clot
had formed. This is probably why the CT images
showed a hypoattenuation clot.

The attenuation value of thrombosis is related to
the age of clots and Hb and Ht levels4,5). To elimi-
nate any bias because of the Hb and Ht factors, we
also evaluated the T/Hb, T/Ht, and T/P ratios. Our
hypothesis is that T/Hb, T/Ht and T/P ratios are
more useful than the attenuation value of T alone.
There were significant differences for T/Hb, T/Ht
and T/P ratios, but sensitivity, PPV, and PLR of
the T/Hb and T/Ht ratios were lower than those of
the thrombus. The attenuation of a blood-pool
CT value becomes 1.7–2.0 HU lower when the Hb
drops 1 g/dL10). This was a very small change, and
so there were no noticeable changes in the T/Hb
and T/Ht ratios. Sun et al.10 stratified Hb levels
into 4 classes and attempted to determine the effect
of the Hb value on the accuracy of PTE identifica-
tion. However, patients with anemia were not more
likely to be diagnosed as truly positive for PTE.

One non–PTE patient showed a hyperdense

| Parameter | Sensitivity (%) | Specificity (%) | AUC | PPV (%) | NPV (%) | PLR | NLR |
|-----------|----------------|----------------|-----|---------|---------|-----|-----|
| T≤30.85   | 79.2 (57.8,92.9) | 87.5 (61.7,98.4) | 83.3 (69.4,97.3) | 90.5 (69.6,98.8) | 73.7 (48.8,90.9) | 6.3 (1.7,23.5) | 0.2 (0.1,0.5) |
| T/Hb≤2.53 | 62.5 (40.6,81.2) | 87.5 (61.7,98.4) | 72.9 (56.5,89.3) | 88.2 (63.6,98.5) | 60.9 (38.5,80.3) | 5.0 (1.3-19.0) | 0.4 (0.2,0.7) |
| T/Ht≤0.83 | 62.5 (40.6,81.2) | 87.5 (61.7,98.4) | 72.9 (56.5,89.3) | 88.2 (63.6,98.5) | 60.9 (38.5,80.3) | 5.0 (1.3-19.0) | 0.4 (0.2,0.7) |
| T/P≤0.835 | 66.7 (44.7,84.0) | 87.5 (61.7,98.4) | 77.5 (62.7,92.2) | 88.9 (65.3,98.6) | 63.6 (40.7,82.8) | 5.3 (1.4-20.1) | 0.4 (0.2,0.7) |

Values (95% confidence interval); P: computed tomography value for pulmonary artery blood pool (Hounsfield unit); T: computed tomography value for thrombus (Hounsfield unit); Hb: hemoglobin (g/dL); H: hematocrit (%); AUC: area under the curve; PPV: positive predictive value; NPV: negative predictive value; PLR: positive likelihood ratio; NLR: negative likelihood ratio

Discussion

A thrombus in the pulmonary trunk or main PA
is a life-threatening disease, and a prompt diag-
nosis is critical for a favorable outcome. Recent
reports have shown that several signs of PTE have
been observed via unenhanced CT, including a
hyperdense lumen sign, PA dilatation, and wedge-
shaped consolidation3-9. Among these signs, the
hyperdense lumen has a high diagnostic perfor-
ance, but it only occurs in 50-70% of cases8,9. In
our study, only 9 of 49 patients (18%) showed a
hyperdense lumen sign.

To date, no study has evaluated the CT attenua-
tion value for patients with PTE using quantitative
indicators on unenhanced CT images. This study
aimed to evaluate the thrombus attenuation cut-off
value for PTE diagnosis. The thrombus attenuation
value was lower in the thrombi group than in the
non–thrombi group. Additionally, the attenuation
value of thrombus in the thrombi group was lower
than that in the blood pool. The thrombus cut-off
value of 30.85 HU calculated from the ROC curve
showed good accuracy. Our results indicate poten-
tial benefits of using measurements of thrombus
attenuation values on unenhanced CT to detect
PTE. This study is the first to evaluate the useful-
ness and reliability of thrombus attenuation value
on unenhanced CT in patients with PTE.

The blood pool attenuation value is mainly deter-
mained by the protein content of red blood cells and
it increases linearly with Ht10). The blood pool
attenuation value is 20–60 HU7,8), whereas the
density of the thrombus is determined by the
concentration of red blood cells and fibrin. From a
pathologic point of view, the different densities of
ratio sensitivity and specificity were 66.7% and
87.5%, respectively.
lumen sign in our study. The descending aorta showed several calcifications in her unenhanced CT. This may occur with atherosclerotic disease of the PA. We misunderstood a calcification for a hyperdense lumen sign.

In conclusion, the T/Hb ratio and T/Ht ratio were not useful for the diagnosis of PTE, but the thrombus attenuation value and the T/P ratio were useful. Patients in whom PTE is clinically suspected, attenuation values should be measured at multiple points in the main and lobar PAs and a few points in the pulmonary trunk. PTE is suspected when the attenuation value is below 30.85 HU or when the T/P ratio is below 0.835, and thus an enhanced CT can confirm the presence of PTE.

There are several limitations to this study. This study was retrospective in nature. The thrombus attenuation values in unenhanced CT were measured after the thrombi were detected by enhanced CT and cut-off values were not considered in a healthy population. In future studies, we will assess whether PTE can be found via unenhanced CT with a fixed window width of 45 and window level of 70, which was obtained from this present study. The minimum and maximum pulmonary blood attenuation values were 20.15 HU and 71.55 HU. The minimum and maximum thrombus attenuation values were 11.75 HU and 44.75 HU. In addition, this was a single-center study with a small sample size, and a larger sample size could improve the accuracy of our results.

Our results show that the probability of PTE was extremely high in patients who had a central PA attenuation value below 30.85 HU and a T/P ratio below 0.835. This study suggests that assessing the attenuation value for the central PA and T/P ratio on unenhanced CT improves the diagnostic ability of central PTE in patients with suspected to have PTE but who cannot tolerate contrast medium, and whose unenhanced CT does not show hyperdense lumen sign, PA dilatation and wedge-shaped consolidation.

Acknowledgments
We are grateful to the radiation technologist for help with data collection.

Funding
The authors received no financial support for the research.

Authors’ contributions
MI conceived and designed the study, collected and analyzed the data, drafted the manuscript, and revised it critically for important intellectual content. TN interpreted the data and drafted and revised the manuscript. YU interpreted the CT data. MS, HI, and YO revised the manuscript critically and provided important intellectual content. All authors have read and approved the final version of manuscript.

Conflicting interest statement
The authors declare no conflicting interests.

References
1) Sakuma M, Okada O, Nakamura M, et al: Japanese society of pulmonary embolism research. Recent developments in diagnostic imaging techniques and management for acute pulmonary embolism: multicenter registry by the Japanese Society of pulmonary embolism research. Intern Med, 2003; 42: 470–476.
2) Nakamura M, Yamada M, Ito M: Current management of venous thromboembolism in Japan: current epidemiology and advances in anticoagulant therapy. J Cardio, 2015; 66: 451–459.
3) Tatco VR, Piedad IH: The validity of hyperdense lumen sign in non-contrast chest CT scans in the detection of pulmonary thromboembolism. Int J Cardiovasc Imaging, 2011; 27: 433–440.
4) Sun S, Semionov A, Xie X, Kosiu J, Mesurolle B: Detection of central pulmonary embolism on non-contrast computed tomography: a case control study. Int J Cardiovasc Imaging, 2014; 30: 639–646.
5) Gotway MB, Webb WR: Acute pulmonary embolism: visualization of high attenuation clot in the pulmonary artery on noncontrast helical chest CT. Emerg Radiol, 2000; 7: 117–119.
6) Okechukwu N, Currna-Melendez MC, Weyer A, Micksus TJ: The hyperdense lumen sign: the tale of the elusive pulmonary embolism. BMJ Case Rep, 2014; 2014: bcr2014205986.
7) Kanne JP, Gotway MB, Thoongsuwan N, Stern EJ: Six cases of acute central pulmonary embolism revealed on unenhanced multidetector CT of the chest. AJR Am J Roentgenol, 2003; 180: 1661–1666.
8) Mohamed ND, Othman MH, Hassan LS, Yousef HA: The accuracy of non-contrast chest computed tomographic scan in the detection of pulmonary thromboembolism. J Curr Med Res Pract, 2019; 4: 61–66.
9) Chien CH, Shih FU, Chen CY, Chen CH, Wu WL, Mak CW: Unenhanced multidetector computed tomography findings in acute central pulmonary embolism. BMC Med Imaging, 2019; 19: 65.
10) Wegener, OH: Whole–body computerized tomography, second edition. Cambridge: Blackwell Scientific Publication, 1993: 87–88.
11) Morita S, Ueno E, Masukawa A, Suzuki K, Machida H,
Fujimura M: Hyperattenuating signs at unenhanced CT indicating acute vascular disease. Radiographics, 2010; 30: 111–125.
12) New PF, Aronow S: Attenuation measurements of whole blood and blood fractions in computed tomography. Radiology, 1976; 121: 635–640.
13) Swensen SJ, McLeod RA, Stephens DH: CT of extra-crani al hemorrhage and hematomas. AJR Am J of Roentgenol, 1984; 142: 907–912.
14) Yankelevitz DF, Gamsu G, Shah A, et al: Optimization of combined CT pulmonary angiography with lower extremity CT venography. AJR Am J Roentgenol, 2000; 174: 67–69.
15) Cobelli R, Zompatori M, De Luca G, Chiari G, Brasciani P, Marcato C: Clinical usefulness of computed tomography study without contrast injection in the evaluation of acute pulmonary embolism. J Comput Assist Tomogr, 2000; 29: 6–12.