

The value of the computed tomographic obstruction index in the identification of massive pulmonary thromboembolism

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PURPOSE

In this study, the pulmonary arterial computed tomography obstruction index ratio, which indicates the degree and extent of thrombotic arterial occlusion, was calculated in cases with pulmonary thromboembolism. Our objectives were to investigate the value of this index for the identification of cases with massive pulmonary thromboembolism and to search for correlations between this index and clinical parameters.

MATERIALS AND METHODS

Data from 68 patients were evaluated retrospectively. For the clinical evaluation, the Wells scoring system was used. Pulmonary computed tomographic angiography examinations were acquired using an eight-channel multidetector computed tomography. The presence of arterial filling defects was recorded, and the clot burden was quantified based on the degree and extent of thrombotic arterial occlusion.

RESULTS

According to the Wells scoring system, the patients were assigned to low ($n=14$), moderate ($n=34$), and high clinical ($n=20$) possibility groups, and the difference among the mean pulmonary arterial computed tomography obstruction index ratios of the three groups was significant ($P = 0.001$). A positive correlation was observed between the pulmonary arterial computed tomography obstruction index ratio and the Wells score ($r=0.470$, $P < 0.001$). The pulmonary arterial computed tomography obstruction index ratio cut-off point was determined to be 40% for the discrimination of massive and non-massive cases (sensitivity, 72.7%; specificity, 91.4%).

CONCLUSION

We found that in cases where the pulmonary arterial computed tomography obstruction index ratio was above 40%, a diagnosis of massive pulmonary thromboembolism was demonstrated. Furthermore, a positive correlation between the obstruction index and the Wells score suggested the use of a clinical evaluation as a means of developing a recommendation regarding the thrombotic load.

Key words: • pulmonary embolism • thromboembolism
• X-ray computed tomography • pulmonary artery

Pulmonary thromboembolism (PTE) is a common clinical condition that is difficult to diagnose due to its nonspecific features. The mortality rate approaches to 30% if left untreated (1). The clinical presentation can be asymptomatic, but PTE can also result in cardiogenic shock due to massive emboli (2). The rapid establishment of a diagnosis of massive PTE is important for the initiation of life-saving thrombolytic therapy. Although pulmonary angiography is the gold standard for the diagnosis of PTE, its disadvantages, including its invasiveness, costliness, unavailability in every medical center, and its associated risks, make the use of noninvasive diagnostic methods important (3). The use of spiral and multi-detector computed tomographic angiography (CTA) is a priority in therapeutic plans for PTE due to multiple advantages, such as more rapid accessibility, noninvasiveness, higher rates of consensus among interpreters, better compliance by especially hemodynamically impaired patients, and quicker diagnostic yield when compared with pulmonary angiography and V/P scanning (4, 5). With the aid of pulmonary arterial CTA (PCTA), the PCTA obstruction index ratio (CTPAOIR), which indicates the degree and extent of thrombotic arterial occlusion, can be calculated (6).

In this study, the CTPAOIR was calculated in cases of PTE diagnosed by PCTA, and we sought to address the following questions:

- 1) What is the value of this index in the identification of cases with massive PTE with an indication of thrombolytic therapy?
- 2) Is there any association between the CTPAOIR, the Wells clinical score, symptoms, and parameters of arterial blood gasses (ABG)?

Materials and methods

Data from 89 PTE patients whose diagnoses were made by PCTA between January 2006 and May 2010 were retrospectively analyzed. Sixty-eight patients with complete clinical and radiologic records were evaluated. The research was performed according to the World Medical Association Declaration of Helsinki. Complaints on admission, physical examination findings, risk factors, ABG values, and echocardiographic findings were registered, and PCTA microfilms were copied from a radiologic database. The Wells score was used for the determination of clinical possibilities (Table 1) (7). The Wells score was calculated retrospectively by an investigator who was blind to the PCTA imaging results.

Sixty-eight patients were scanned on an eight-channel multislice computed tomography (CT) scanner (Lightspeed Ultra 3X, GE Medical Systems, Milwaukee, Wisconsin, USA). A contrast-enhanced multislice CT of the pulmonary arteries was performed from the lung apices to the lowest level of the hemidiaphragm in a supine position during suspended inspiration or shallow breathing, depending on the patients' level of dyspnea. The images were obtained on multidetector CT using

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Table 1. The Wells scoring system (7)

Variable	Score
Clinical signs of DVT	3
Alternative diagnosis less likely than PTE	3
Heart rate >100 beats/min	1.5
Recent surgery or immobilization	1.5
Previous DVT or PTE	1.5
Hemoptysis	1
Cancer	1
Clinical possibility	<2: Low 2–6: Moderate >6: High

DVT, deep vein thrombosis; PTE, pulmonary thromboembolism.

120 kVp, 350 effective mAs, a collimation of 8×1.25 mm, a slice thickness of 1.25 mm, a reconstruction interval of 2.5 mm, and a table speed of 13.50 per 0.60 s rotation time (pitch 1.35). The field of view was appropriately adjusted to the size of the patient, and an acquisition matrix of 512×512 was used. A total volume of 120 mL of iodine-based nonionic contrast material (300 mgI/mL) was injected through an antecubital vein using a power injector at a rate of 4 mL/s. The SmartPrep technique was used for contrast timing. CT data were transferred electronically to a Workstation (AW 4.2, GE Medical Systems). All axial images were viewed on the workstation using standard mediastinal (level, 40 HU; width, 350 HU) and lung window settings (level, -700 HU; width, 1000 HU). However, the observers were free to perform and review multiplanar reconstructions and to change the window and level settings to optimize the visualization of the vessels. Thrombi, as assessed by PCTA, were localized in the common pulmonary, lobar, and segmental arteries. For each patient, the CTPAOIR was estimated based on the consensus of two radiologists. The calculation was performed as follows. The pulmonary arteries in the lungs were divided into 10 segmental branches as upper lobe (n=3), middle lobe and lingula (n=2), and lower lobe (n=5). Based on the locations, when thrombi were observed in proximal (common, lobar) pulmonary arteries, each segment distal to the thrombus

was calculated as one point, and the total number of segmental arteries yielded the total score. The observation of an isolated thrombus within the segmental artery without any thrombi within the proximal artery was rated as one point. According to the degree of pulmonary arterial occlusion, contrast material observed in the vicinity of an arterial filling defect was interpreted as a partial thrombotic occlusion, while the absence of contrast uptake by distal pulmonary vascular structures was defined as a complete occlusive thrombus. Consequently, partial or complete occlusive thrombi were considered as partial and complete obstructions, respectively. The relevant coefficients were 0, 1, and 2 for vascular patency, partial, and complete obstruction, respectively. The CTPAOI was estimated by multiplying the number of segmental arteries (at least 1, at most 20) with the degree of obstruction (at least 0, at most 2 points):

$$CTPAOI = n \times d$$

n, number of segmental arteries;
d, degree of obstruction.

The maximum possible total score that corresponds to a 100% obstruction index is 40. After determination of the CTPAOI, the value of the CTPAOIR was calculated according to the following formula (6):

$$CTPAOIR = \text{Epsilon}(n \times d) / 40 \times 100$$

The echocardiography records were evaluated. Echocardiographic

examinations were acquired on the same day as the PCTA. Any echocardiography findings of PTE, such as right ventricular hypokinesis or akinesis, right ventricular dilatation, interventricular septal paradoxical movement and pulmonary hypertension (i.e., pulmonary artery systolic pressure >38–40 mmHg) were coded as abnormal findings. None of the patients had a patent foramen ovale.

Cases with PTE were divided into two groups as massive and non-massive. The presence of cardiogenic shock and/or arterial hypotension (systolic arterial pressure <90 mmHg) and thrombus, as evidenced by PCTA in one or both common pulmonary arteries or more than 50% of pulmonary vascular bed occlusion by a thrombus, was defined as massive embolism. All the cases that did not meet these criteria were termed non-massive embolisms (8). Thrombolytic (recombinant tissue plasminogen activator infusion at a rate of 100 mg/2 h) therapy was applied in all the cases with massive PTE.

Statistical analysis

The Chi-square test was used to compare the categorical variables. The categorical variables were shown as counts and percentages. All the continuous variables demonstrated normal distribution according to the Kolmogorov-Smirnov normality test. Therefore, a one-way ANOVA test was used to compare the continuous variables among the three groups. When the one-way ANOVA results were significant, the Sheffe test was used for pairwise comparisons. Two independent sample t tests were used to compare the continuous variables between the two groups. Pearson's correlation analysis was used to determine the correlation between the variables. Continuous variables were presented as the mean and standard deviation. ROC (Receiver Operating Characteristic) curve analysis was used to determine the cut-off value of CTPAOIR in the discrimination between massive and non-massive pulmonary thromboembolism. *P* values < 0.05 were considered statistically significant. The analyses were performed using a commercially available software (Statistical Package for Social Sciences version 18.0, SPSS Inc., Chicago, Illinois, USA).

Results

The clinical records of 27 (40%) women and 41 (60%) men with a mean age of 60 ± 13 years were evaluated. The majority ($n=60$, 88%) of the cases had risk factors for PTE. A history of previous surgery and immobilization were present in 49 (82%) patients. Malignancy was observed in nine (15%) patients, deep vein thrombosis (DVT) was present in 16 (27%) patients, and cardiopulmonary disease was present in 16 (27%) patients.

The most frequently observed complaint on admission was dyspnea ($n=54$, 79%). Other complaints in the order of frequency were angina pectoris ($n=44$, 65%), palpitations ($n=30$, 44%), hemoptysis ($n=23$, 34%), swollen and painful legs ($n=15$, 22%), and syncope ($n=4$, 6%). The presence of cardiogenic shock and/or arterial hypotension (systolic arterial pressure <90 mmHg) and thrombus, as evidenced by PCTA in one or both common pulmonary arteries or more than 50% of pulmonary vascular bed occlusion by a thrombus, was defined as a massive embolism, while all the cases that did not meet these criteria were termed non-massive embolisms. According to this definition, 33 (49%) patients with massive PTE and 35 (51%) patients with non-massive PTE were identified. The mean CTPAOIR values were estimated as 52.9 ± 21 in cases with massive PTE and 21.8 ± 15 in cases with non-massive PTE. The mean CTPAOIR was 36.9 ± 23.9 in both groups combined, and the difference between the means was significant ($P < 0.001$). To assess the ability of CTPAOIR to predict patients with massive PTE, a ROC curve was constructed, and the area under the curve was calculated ($AUC=0.887$, $P < 0.001$) (Fig. 1). When the cut-off point for the CTPAOIR was chosen as 40%, the sensitivity was 72.7%, and the specificity was 91.4%.

Based on the Wells scoring system, low, moderate, and high clinical possibilities were detected in 14 (21%), 34 (50%), and 20 (29%) cases, respectively. The mean Wells scores were found to be 5.31 ± 2.31 , 3.77 ± 2.53 , and 4.52 ± 2.53 in patients with massive embolisms, non-massive embolisms, and in both groups combined, respectively, and the difference between the mean values was significant ($P = 0.011$).

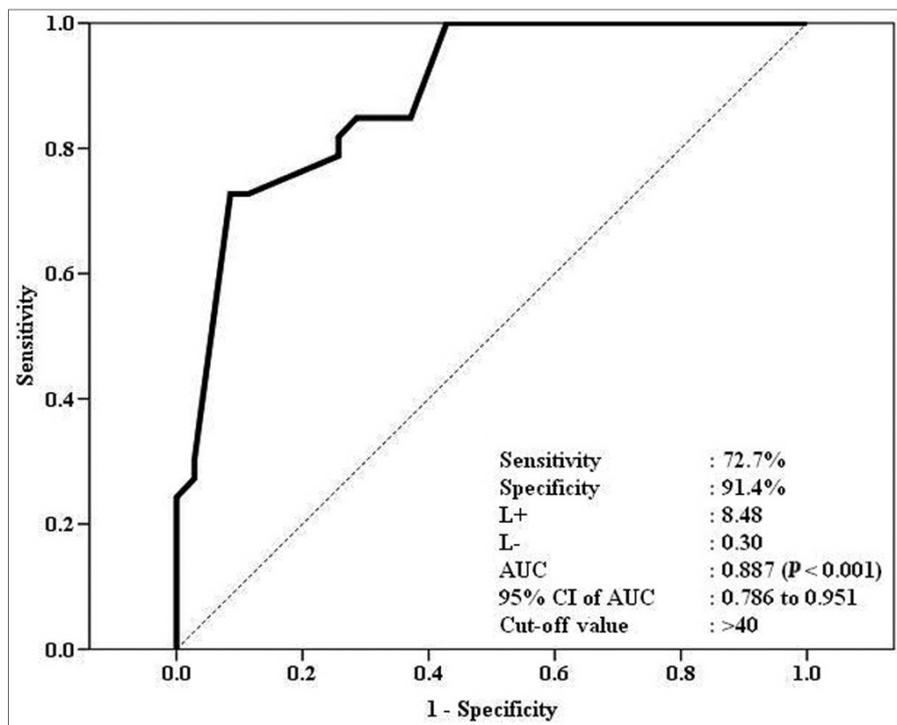


Figure 1. The cut-off value of the pulmonary arterial computed tomographic angiography obstruction index ratio (CTPAOIR) in the discrimination between massive and non-massive pulmonary thromboembolism. AUC, area under the curve; CI, confidence interval.

Table 2. The CTPAOIR values according to the Wells clinical possibilities

Clinical possibility	n	CTPAOIR (mean \pm standard deviation)	P
Low	14	23.39 \pm 20.53	0.001 ^a
Moderate	34	33.23 \pm 20.32	
High	20	52.50 \pm 24.26	

CTPAOIR, pulmonary arterial computed tomographic angiography obstruction index ratio.

^aThe group with high clinical possibility score had significantly increased CTPAOIR values relative to the groups with low and moderate clinical possibility scores ($P < 0.05$). No significant difference was found between the groups with low and moderate clinical possibility scores ($P > 0.05$).

Table 3. The CTPAOIR values in patients with or without dyspnea and syncope

	CTPAOIR (mean \pm standard deviation)	P
Dyspnea	Yes (n=54)	40.64 \pm 24.03
	No (n=14)	22.32 \pm 17.16
Syncope	Yes (n=4)	68.75 \pm 23.93
	No (n=59)	34.44 \pm 22.62

CTPAOIR, pulmonary arterial computed tomographic angiography obstruction index ratio.

Based on the Wells classification of the clinical possibilities, the difference between the mean CTPAOIR values of the three groups was statistically significant ($P = 0.001$). In pairwise comparisons differences between mean CTPAOIR values of cases with low and

high and also with moderate and high clinical possibilities were observed ($P = 0.001$ vs. 0.009) (Table 2). The mean CTPAOIR values in cases with dyspnea and syncope were higher than in those without these features ($P = 0.009$ vs. 0.005) (Table 3).

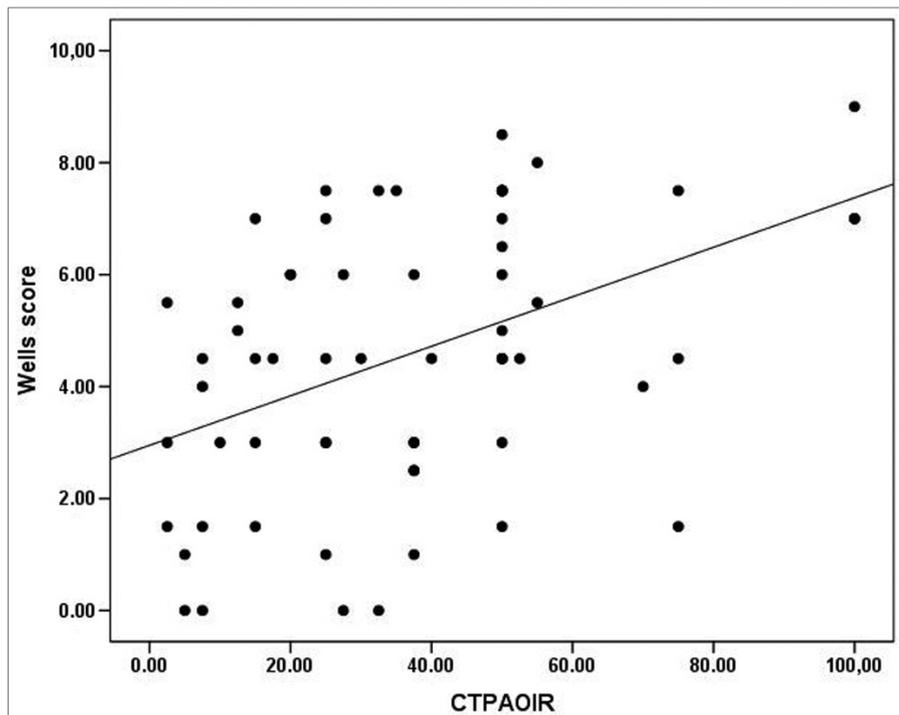


Figure 2. The correlation between the pulmonary arterial computed tomographic angiography obstruction index ratio (CTPAOIR) and the Wells score.

Echocardiography records were obtained for a total of 48 patients. All the patients (n=33) in the massive PTE group had right ventricular dilatation and at least one echocardiographic abnormality. Analyses of ABG were performed in 61 cases, and hypoxemia (n=54, 89%), hypocapnia (n=45, 74%), and an increased alveoloarterial oxygen gradient (AaDO₂) were found. A positive significant correlation was observed between the CTPAOIR, the Wells score (Fig. 2), and AaDO₂ as an ABG parameter. No correlations were observed between partial oxygen pressure (PO₂), partial carbon dioxide pressure (PCO₂), relevant symptoms, risk factors, pulmonary artery pressure (PAP), and the CTPAOIR (Table 4).

PCTA images of patients with massive pulmonary embolism and high CTPAOIR are shown in Figs. 3a and 3b.

The rate of in-hospital mortality was 4.4% (n=3). These cases had massive embolism.

Discussion

In this study, the association between the clinical findings and the CTPAOIR with respect to the extent of the thrombotic process in PTE was evaluated. This evaluation showed that the obstruction index in cases with massive PTE managed with thrombolytic therapy was greater than 40%, and this was significantly correlated with the Wells score. A clinical evaluation is important in the establishment of a diagnosis of PTE, which is responsible for 10% of cases of in-hospital mortality. In the diagnostic algorithm, clinical evaluation ranks before imaging methods and guides further investigations. For definitive

diagnosis, clinical evaluation should be considered together with an objective method (9, 10). Currently, the Wells, Geneva, Modified Geneva and Miniati scoring systems formulated based on risk factors and clinical findings have been used in the diagnosis of PTE (7, 11–13). When the findings were scored and the threshold of the Wells scoring system with numerical limits was defined, higher sensitivity and lower negativity rates were reported. In the study by Wells et al. (7) entitled “Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED)”, scored and standardized clinical data and a diagnosis of PTE were found to be established in groups with high (66.7%), moderate (20.5%), and low (3.6%) clinical possibilities. In our study, the Wells scoring system was used in the evaluation of clinical possibility, and the mean Wells score for both groups combined was calculated to be 4.57±2.43. Low, moderate, and high clinical possibilities were detected in 19%, 52%, and 29% of the cases, respectively.

The clinical findings in patients with PTE depend upon the extent of embolism (massive/non-massive), the number of emboli (single/multiple), their reproducibility, their location, their rate of resolution, and the cardiopulmonary capacity of the patient (14). In more than 90% of the cases with PTE, dyspnea, tachypnea or angina was found. Syncope is rarely seen. However, its presence indicates a severe decrease in hemodynamic capacity. Pleuritic chest pain develops as a result of pleural irritation due to pulmonary infarct arising from distally located emboli, while retrosternal chest pain suggests right ventricular ischemia (15). Massive PTE is a rapidly developing, life-threatening disease that results in death if it is left undiagnosed (16). Thrombolytic therapy is the first and most effective treatment alternative for the majority of

Table 4. Correlations (as Pearson correlation coefficient, r) between the CTPAOIR values and the parameters of arterial blood gases and the Wells score

	pO ₂	pCO ₂	AaDO ₂	Wells score	PAP
CTPAOIR	-0.131	-0.177	0.264 ^a	0.470 ^a	0.267

^aP < 0.05

CTPAOIR, pulmonary arterial computed tomographic angiography obstruction index ratio; pO₂, partial pressure of oxygen; pCO₂, partial pressure of carbon dioxide; AaDO₂, alveoloarterial oxygen gradient; PAP, pulmonary artery pressure.

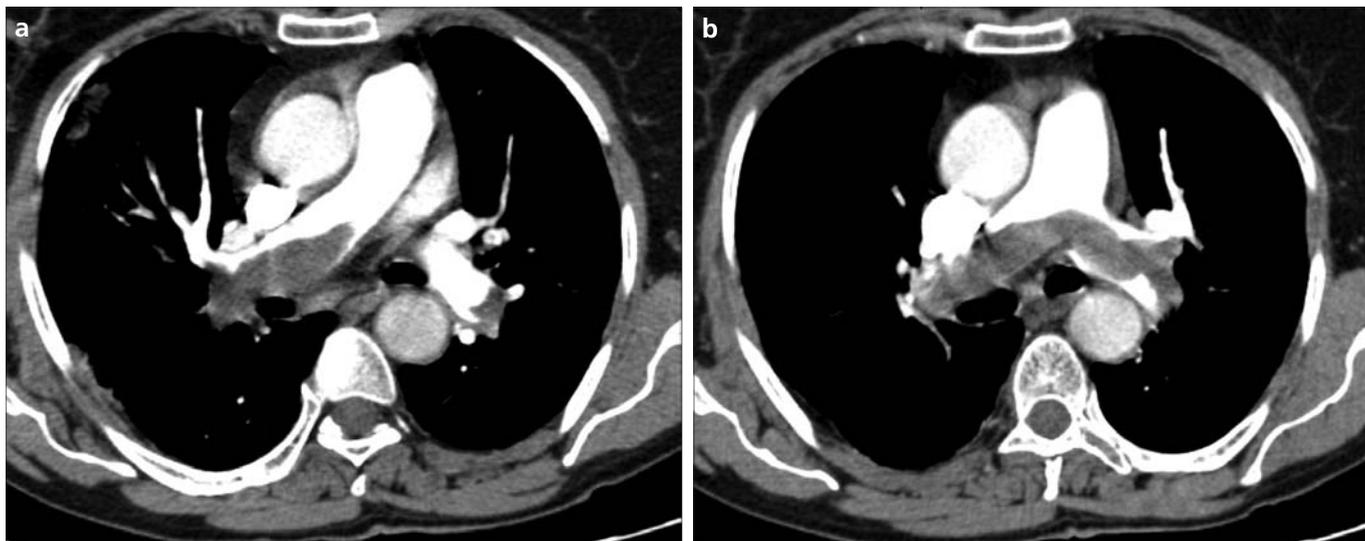


Figure 3. a, b. Axial CTA images of a 70-year-old woman with bilateral multiple pulmonary emboli. The mediastinal window setting shows a saddle thrombus in the main pulmonary arteries, which received a pulmonary artery obstruction index of 75%. The Wells score was 7.5.

the patients diagnosed with massive PTE. It is life saving in hemodynamically unstable patients (17). We detected massive and non-massive PTE in 49% and 51% of our cases, respectively. Thrombolytic therapy was used for cases with massive PTE. The most frequently observed complaints were shortness of breath and chest pain. Syncope was present in four cases with massive PTE.

In recent years, developments in computed tomographic technology have guided the the diagnostic process for PTE. Particularly, the usage of spiral multi-detector tomography has allowed for the establishment of diagnosis without a requirement for invasive interventions. Studies performed previously have demonstrated the sensitivity and specificity of PCTA in the diagnosis of PTE to be greater than 90% (18–20). In the PIOPED II study, the positive predictive values in the presence of high and moderate clinical possibilities were reported to be 96% and 90%, respectively (21). In cases where the PCTA was in concordance with the clinical possibility, higher predictive values were obtained (22). In the guidelines of the British Thoracic Society, PCTA is ranked first, before ventilation/perfusion scanning, in the diagnostic algorithm for PTE (23). Erdur et al. (24) reported that spiral or multi-detector-row CTA is widely applied, surpassing other imaging modalities for the diagnosis of PTE in Turkey. Additionally, PCTA is

superior to scintigraphy in terms of detecting parenchymal abnormalities. In a study investigating the relationship of parenchymal and pleural abnormalities with acute pulmonary embolism, it was found that only wedge-shaped opacities showed significant correlation with the presence and severity of PE (25).

Qanadli et al. (6) formulated a CT obstruction index that indicates the extent of the thrombotic process and their arterial occlusion, as demonstrated by PCTA. In a study by van der Meer et al. (26), an association was found between PTE-related mortality during a three-month follow-up period and the tomographic obstruction index. Another study revealed a higher obstruction index in patients who died PTE (27). Therefore, the CTPAOIR can be evaluated as a prognostic factor. In our study, the significance of higher CTPAOIR values could not be analyzed due to the extremely low rates of in-hospital mortality (n=3). However, the significant CTPAOIR values obtained in cases with massive PTE with higher mortality risk substantiates this perspective.

Unlike other studies, in our study, the CTPAOIR cut-off value discriminating between cases with massive and non-massive PTE was calculated. This value was estimated to be higher than 40%. Based on this finding, it might be postulated that a diagnosis of massive PTE can be made in conditions with indices above 40%, and

thrombolytic therapy should be administered. Furthermore, because the risk of mortality in massive PTE is increased, this index might represent an indirect indicator of the risk of mortality. Our findings are in accordance with those of van der Meer et al. (26) who found an 11.2-fold increased risk of mortality related to PTE in cases with indices above 40%. In the current study, the mean CTPAOIR values in groups with low, moderate, and high possibilities were compared, and significant differences were found among them. Additionally, in analyses of correlation, a significant positive correlation was observed between the CTPAOIR values and the Wells scores. The detection of a correlation between the Wells score and the CTPAOIR, which is an objective method of measurement, suggested that the Wells clinical scoring system, with its higher sensitivity for the PTE diagnosis, might provide information regarding a patient's thrombotic burden. This finding has vital importance for the rapid identification of cases with PTE, especially in emergency centers. The detection of a correlation between the CTPAOIR and the alveolar-arterial oxygen gradient suggested that gas exchange is impaired in relation to the thrombus burden.

Our study has several limitations. This is a retrospective study, and a remarkable number of patients were not included in the study due to

incomplete data. This restricts the sample size. In this study, the percentage of massive embolism cases was extremely high. This suggests that anticoagulant prophylaxis has not been administered often enough, as the majority of cases in the study population have a history of surgery and immobilization.

As a conclusion, we identified a correlation between the CTPAOIR, which reveals the extent of thrombotic spread in PTE, and the clinical findings, demonstrating that the index of obstruction in cases with massive PTE receiving thrombolytic therapy was above 40%. Furthermore, a positive correlation between the CTPAOIR and the Wells score suggested that clinical evaluation might provide an insight into the thrombotic load. Further prospective studies should analyze the role of the CTPAOIR in the therapeutic decision process related to cases with submassive PTE for which the treatment method and prognosis are currently debatable.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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