



Investigation of the relationship between the PaO₂/FiO₂ ratio and Wells score in patients diagnosed with acute pulmonary embolism

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Abstract

Aim: In order to make a definitive diagnosis of acute pulmonary embolism (APE), patients to undergo computed tomography angiography (CTA) are selected according to certain criteria. This study aimed to examine the partial oxygen pressure PaO₂/inspired oxygen concentration ratio (P/F) as a new parameter to be used for this purpose in addition to the Wells score, which is one of the methods of determining clinical probability.

Materials and Methods: This study was prospectively conducted between July 1, 2022, and October 1, 2022, and included 80 patients that presented to the emergency department with acute dyspnea and were diagnosed with APE using CTA. The Wells scores of the patients were recorded at the time of their presentation to the emergency department. IBM SPSS v. 20.0 was used for the statistical analysis of the data.

Results: Of the cases included in the study, seven had a low probability, 57 had an intermediate probability, and 16 had a high probability of APE. The PaO₂ values of the patients were 56.7±8.0, 56.1±11.2, and 51.8±9.9 mmHg for the low, intermediate, and high probability groups, respectively. According to the Wells scores, the P/F ratios of the patients with low, intermediate, and high probability were determined as 205.5±72.2, 198.5±62.5, and 183.5±43.6, respectively.

Conclusion: There was a negative correlation between the P/F ratio and Wells score, but this was not statistically significant. Therefore, it may not be appropriate to evaluate the P/F ratio in making a decision to perform CTA in clinical practice.



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Introduction

Acute pulmonary embolism (APE) is a common and sometimes fatal form of venous thromboembolism [1]. In the emergency department, the diagnosis of APE is primarily based on clinical suspicion. The growing number of computed tomography angiography (CTA) procedures performed in light of increased clinical suspicion has resulted in a higher rate of APE detection [2].

APE risk factors should be determined in patients during clinical evaluation. Following the identification of APE risk factors, many scoring systems have been designed, with the most well-known being the Wells score [3]. According to this scoring system, CTA is recommended for high-probability patients, while in intermediate and low-probability patients, it is recommended to measure D-dimer values to support the diagnosis [4]. However, D-dimer levels can be affected by many factors, such as malignancy, chronic inflammatory conditions, and age [5].

Therefore, the Wells score and D-dimer test results used in APE risk assessment are not always useful when diagnosing APE.

Hypoxia and accompanying hypocarbia are seen in patients with pulmonary embolism. Therefore, in patients presenting to the emergency department with the complaint of dyspnea, APE is primarily considered in the presence of hypoxia and hypocarbia in the analysis of blood gas samples taken at the time of presentation [6]. During the evaluation of hypoxia, the ratio of partial oxygen pressure (PaO₂) to inspired oxygen concentration (FiO₂) (P/F) is frequently used. Severe hypoxia has been reported in patients with a P/F ratio of <200. It is also known that mortality increases in patients with APE that have a low P/F ratio [7].

In patients presenting to the emergency department with acute dyspnea, the definitive diagnosis of APE is made using CTA. Echocardiography is one of the radiological examinations that can be used other than CTA. However, its dependency on the practitioner limits its use in emergency

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departments [8]. However, due to various reasons, such as radiation exposure and contrast agent administration during the procedure and complications that may be caused by contrast material, patients to undergo CTA should be selected according to certain criteria. The Wells score and the D-dimer test are commonly used to determine the clinical probability of APE in these patients. However, the results of the D-dimer test can be misleading, and there is a need for additional parameters to support the Wells score. Therefore, in our study, we aimed to examine the relationship between the Wells score and P/F ratio in patients diagnosed with APE based on CTA.

Materials and Methods

Study design and patient selection

This study was prospectively conducted in the emergency department of a tertiary hospital between July 1, 2022, and October 1, 2022. Ethical approval for the study was obtained from the local clinical research ethics committee (Ataturk University Clinical Research Ethics Committee, number: 31/06, date: 30/06/2022). The study was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from the patients to participate in the study or their first-degree relatives through a face-to-face interview. G-Power 3.1 software was used to calculate the sample size for the study. During this process, the medium effect size was taken as 0.5, type 1 error as 0.05 and power as 0.80. Considering 10% missing data, the sample size for the study was calculated as 38 patients for each group calculated (76 patients with an allocation ratio of 1:1).

The study included patients that presented to the emergency department with acute dyspnea and were diagnosed with APE using CTA. Patients with previously known chronic obstructive pulmonary disease, asthma or idiopathic pulmonary fibrosis, or cardiovascular disease that could cause hypoxia, those with chronic hypoxia due to other reasons, those with CTA contraindications, such as pregnancy and contrast allergy, those aged <18 years, those with metabolic conditions, such as renal failure and liver failure, and those that underwent cardiopulmonary resuscitation were excluded from the study. Further excluded were cases in which CTA images were not of adequate quality to visualize the pulmonary arteries due to the use of insufficient contrast material, limited visualization of the vascular bed, or presence of patient- or device-related artifacts. Our primary outcome was to determine the role of partial oxygen pressure PaO_2 /inspired oxygen concentration ratio (P/F) ratio in diagnosing pulmonary embolism.

CTA was performed in 225 patients who presented to the emergency department with the complaint of acute dyspnea and had a preliminary diagnosis of APE. APE was radiologically diagnosed in 136 of these patients. However, 23 patients had radiological findings (such as atelectasis, cardiomegaly, and right ventricular dilatation) indicating conditions that could cause hypoxia (chronic lung or cardiovascular disease); therefore, these patients were excluded from the study. In addition, nine patients that were initially planned to be included in the study were excluded due to the insufficient amount of contrast used

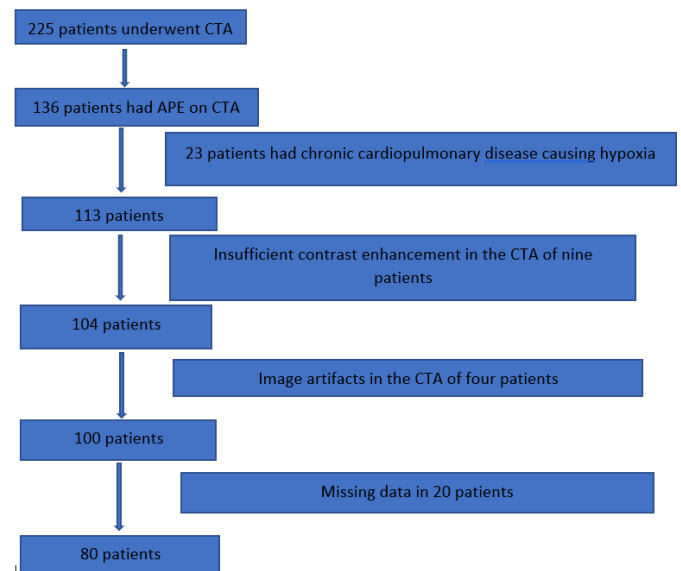


Figure 1. Flow chart of patient selection.

during CTA. In a further four patients, the diagnosis of APE could not be proven using CTA due to image artifacts caused by device-related factors during the procedure; therefore, these patients were also excluded from the study. Lastly, during the clinical examination of the patients, 20 were excluded from the sample due to missing data. After applying the exclusion criteria, 80 patients were prospectively included in the sample (Figure 1).

Data collection

The patients' fingertip oxygen saturation, blood pressure, and heart rate measurements were performed and Wells scores were recorded by an emergency department physician who evaluated the patients at the time of their presentation. While calculating the Wells score, the presence of deep vein thrombosis and tachycardia and the history of immobilization, venous thromboembolism, hemoptysis, malignancy, and deep vein thrombosis were taken into account. As a result, the total score obtained was defined as low probability if 0-1, intermediate probability if 2-6, and high probability if ≥ 7 (Table 1). The oxygen support status of the patients and the amount of oxygen they

Table 1. Wells scoring.

Characteristics	Score
Alternative diagnosis less likely than pulmonary embolism	3 points
Clinical signs of deep vein thrombosis	3 points
Previous pulmonary embolism or deep vein thrombosis	1.5 points
Heart rate > 100 beats/minute	1.5 points
Recent surgery or immobilization	1.5 points
Hemoptysis	1 point
Cancer	1 point
Low probability: 0-1 point, intermediate probability: 2-6 points, high probability: ≥ 7 points	

received per minute were recorded, and the FiO_2 levels were calculated using these values. While calculating the FiO_2 levels, the formula $21 + (4 \times \text{oxygen support level in 4 minutes})$ was used and the result was expressed as a percentage. For the patients who did not require oxygen support, FiO_2 was accepted as 0.21 [9]. Arterial blood gas samples were taken from the patients with heparinized blood gas injectors at the time of presentation to the emergency department. The PaO_2 values were recorded from the taken arterial blood gas analysis, and the P/F ratios were calculated.

Statistical analysis

IBM SPSS v. 20.0 (SPSS Inc., Chicago, IL, United States) was used for the statistical analysis of the obtained data. Continuous variables were expressed as mean (standard deviation) or median [interquartile range (IQR)] values. Categorical data were evaluated as numbers (percentages). Normality analysis was performed. The analysis of variance test was used for normally distributed data in the comparison of more than two independent groups and continuous variables. For the 2x2 comparisons between the categorical variables, the Pearson chi-square test was performed if the expected value was >5 , a chi-square test incorporating Yates' correction if this value was 3-5, and Fisher's exact test if <3 . For the comparisons larger than 2x2 between the categorical variables, the Pearson chi-square test was used when the expected value was >5 and the Fisher-Freeman-Halton test when it was <5 . A p value of <0.05 was considered significant in all statistical analyses.

Results

Of the 80 patients included in the study, seven had a low probability, 57 had an intermediate probability, and 16 had a high probability of pulmonary embolism according to the Wells scores. Concerning the demographic characteristics of the patients, 48.8% ($n = 39$) were female and 51.2% ($n = 41$) were male. The median age of the patients was 72 (IQR: 15) years (Table 2). The median Wells score of the patients was 4.5 (IQR: 3). Other clinical and demographic data of the patients are detailed in Table 2.

When examined according to the Wells scores, the PaO_2 value was 56.7 ± 8.0 mmHg for the low probability group, 56.1 ± 11.2 mmHg for the intermediate probability group, and 51.8 ± 9.9 mmHg for the high probability group. The comparison of the PaO_2 values between the groups did not show any statistically significant difference ($p = 0.353$). The FiO_2 scores were determined as 0.29 ± 0.07 , 0.29 ± 0.06 , and 0.28 ± 0.04 for the patients with a low, intermediate, and high probability of APE, respectively. There was no statistically significant difference in the FiO_2 scores between the groups ($p = 0.873$). Lastly, the P/F ratios of the low, intermediate, and high probability groups were calculated as 205.5 ± 72.2 , 198.5 ± 62.5 , and 183.5 ± 43.6 , respectively, indicating no statistically significant difference ($p = 0.620$) (Table 3).

It was also evaluated whether the Wells score and P/F ratio were correlated. There was an inverse correlation between the Wells score and P/F ratio, but this was not statistically significant ($p = 0.286$) (Table 4).

Discussion

On completion of this study, we determined that there was no correlation between the patients' Wells scores used to determine the risk of APE and their P/F ratios used to determine the degree of hypoxia. In the literature, it has been suggested that the P/F ratio can be used to grade hypoxia. However, this parameter is not included in the diagnostic criteria of APE. According to the results of a prospective study investigating the value of the ventilation/perfusion scan in the diagnosis of APE, hypoxia in patients with APE without a history of cardiopulmonary disease was not deeper compared to healthy people [10]. In contrast, there are also studies in the literature showing that hypoxia develops in patients diagnosed with APE as a result of obstruction in the pulmonary artery [11]. In our study, the PaO_2 levels were determined to be lower than normal in the patients diagnosed with APE. However, when the patients were classified according to the Wells criteria, there was no statistically significant difference between the probability groups. The P/F ratios of these patients indicated mild hypoxia (P/F in the range of 200-300) in the low-probability group and moderate hypoxia (P/F in the range of 100-200) in the intermediate- and high-probability groups. However, the differences in the P/F ratios between the groups were not statistically significant. Since we did not evaluate mortality in our study, we cannot present data on the relationship between hypoxia and mortality in our patients. However, there are researchers reporting the presence of a relationship between the P/F ratio and mortality in patients with APE [7,12]. Patients with suspected APE in the emergency department are usually those presenting with the complaint of acute dyspnea. During the clinical evaluation of these patients, clinical decision-making rules (such as the Wells criteria and Geneva clinical decision-making rules) and APE diagnosis probabilities of the patients are reviewed. In the presence of suspected APE, patient selection can be made according to clinical decision-making rules when deciding to take CTA for a definitive diagnosis. However, although the Wells criteria are beneficial in clinical decision-making in patients with APE, the use of this system in prognosis remains dubious [13]. In our review of the literature, we found no study investigating the correlation between the P/F ratio and the Wells criteria. This may be because the P/F ratio is associated with prognosis in patients diagnosed with APE while the Wells criteria are more associated with clinical decision-making in those suspected to have APE. Wells scoring is the most well-known diagnostic system used to reduce the frequency of CTA procedures in patients evaluated in the emergency department with the suspicion of APE [10,11]. In this scoring system, patients are classified as having a high probability (>6), intermediate probability (2-6), or low probability (<2) of APE. However, in a previous study, it was observed that the Wells scoring system was not adequate to diagnose APE, especially in patients with low scores [14]. In the current study, APE was detected using CTA in patients with a low and intermediate risk, and the diagnosis of APE was tried to be strengthened using the results of the D-dimer test together with the Wells criteria. In another study, it was recommended that patients with >2 points in the

Table 2. Demographic characteristics and vital signs of the patients according to their pulmonary embolism probability.

		Low probability	Intermediate probability	High probability	Total
Gender	Female	2 (28.6%)	27 (47.4%)	10 (62.5%)	39 (48.8%)
	Male	5 (71.4%)	30 (52.6%)	6 (37.5%)	41 (51.2%)
Age (median, IQR)		70 (22)	73 (13)	69 (13)	72 (15)
Systolic blood pressure (mmHg)		136.8 ± 20.5	121.8 ± 21.9	113.5 ± 22.7	121.4 ± 22.4
Diastolic blood pressure (mmHg)		78.4 ± 9.1	74.0 ± 14.3	71.1 ± 9.7	73.8 ± 13.1
Pulse (/min)		98.1 ± 18.3	99.6 ± 17.8	107.3 ± 12.1	101 ± 17
Saturation (%)		84.4 ± 6.1	84.4 ± 7.6	83.5 ± 6.4	84 ± 7.2
Amount of oxygen support (h)		2.1 ± 1.7	2.1 ± 1.6	1.9 ± 1.1	2 ± 1.5
Total Wells score (median, IQR)		1.2 ± 0.5	4.2 ± 1.2	7.2 ± 0.8	4.5 (3)

IQR: interquartile range.

Table 3. Comparison of the PaO₂, FiO₂, and P/F values between the Wells score probability groups.

	Low probability	Intermediate probability	High probability	P*
PaO ₂ (mmHg)	56.7 ± 8.0	56.1 ± 11.2	51.8 ± 9.9	0.353
FiO ₂	0.29 ± 0.07	0.29 ± 0.06	0.28 ± 0.04	0.873
P/F ratio	205.5 ± 72.2	198.5 ± 62.5	183.5 ± 43.6	0.620

*analysis of variance PaO₂: partial oxygen pressure, FiO₂: inspired oxygen concentration, P/F: PaO₂/FiO₂.

Table 4. Correlation of the total Wells score and P/F ratio.

	Total Wells score	P/F ratio
Pearson correlation	1	-.121
P		0.286
N		80

P/F: partial oxygen pressure/inspired oxygen concentration.

Wells score should be evaluated with the D-dimer test, and the CTA decision should be taken according to the results [15]. However, in the APE diagnosis and treatment guideline published in 2019, it was recommended that patients with a high probability of having this condition should be evaluated with CTA regardless of the D-dimer value [1]. In light of these findings, it can be concluded that low-probability patients can be evaluated with the D-dimer test. However, a study showed that the low specificity of the D-dimer test could not prevent CTA procedures in patients with a low probability of APE [16]. The use of the D-dimer test together with Wells scoring was also not effective in reducing the need for CTA in patients with a low clinical probability of APE. In our study, although seven patients had a low probability and 57 had an intermediate probability of APE according to the Wells scores, these patients were diagnosed with APE based on the CTA findings. In addition to Wells scoring, another scoring system that is considered to support clinical suspicion of APE is the revised Geneva score. However, in a study conducted to evaluate the diagnosis of APE with the revised Geneva and Wells criteria, it was observed that the former was less diagnostic than the latter when used alone [3]. However, the fact that the “no alternative diagnosis” criterion in the Wells scoring system depends on the subjective judgment of the physician evaluating the patient can also be con-

sidered as a limitation of the Wells scoring system [17]. Furthermore, it has been recommended that the Wells criteria and the revised Geneva criteria be applied together to achieve more definitive diagnoses in patients with suspected APE [18]. The APE diagnosis treatment guideline also states that the analysis of D-dimer together with the evaluation of clinical scoring systems may be useful in identifying patients that require CTA [1]. However, despite all these recommendations, there is still no decrease in the use of CTA in clinical practice.

Conclusion

Although we observed a negative correlation between the Wells criteria and the P/F ratio, this correlation was statistically non-significant. It seems that the Wells score is more associated with clinical decision-making while the P/F ratio concerns mortality. Therefore, although these parameters can be negatively correlated with each other at the diagnosis stage, they are not suitable for clinical use.

Limitations

In our study, the clinical follow-up of the patients was not undertaken, and mortality was not evaluated. Therefore, the relationship between the Wells criteria or the P/F ratio with mortality or prognosis was not investigated in our patients. The small number of patients included in the study can be considered as another limitation. If the study is repeated with larger patient populations, the results may provide more significant results concerning the correlation between the Wells score and P/F ratio.

Ethics approval

Ethical approval for the this study was obtained from the Ataturk University Clinical Research Ethics Committee, (Number: 31/06, Date: 30/06/2022).

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