ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA MAKALESİ

Comparison of WBC / MPV Ratio with the Well's Score in Patients with Pulmonary Embolism at Emergency Department

Acil Serviste Pulmoner Emboli Tanılı Hastalarda WBC/MPV Oranının Well's Skoru ile Karşılaştırılması

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ABSTRACT

Aim: This study aims to compare the WBC / MPV ratio with the Wells clinical probability score in patients admitted to the emergency department with the suspicion of Pulmonary Embolism (PE) and to investigate whether this ratio can be used as a marker in determining prognosis.

Material and Methods: A total of 111 patients who presented to the emergency department between 01 September 2019 and 31 August 2020 and met the criteria were included in the study. The Well's score was used to evaluate patients' clinical probability of PE. According to the Wells scores, patients were divided into 3 as low, moderate and high-risk groups. In addition, the WBC / MPV ratio (WMR) obtained from the patients' first admission hemograms were calculated.

Results: The median age of the patients in the study was 65 (IQR 25-75: 57-79). 56 of the patients (50.5%) were female and PE was detected in 68 (61.3%). It was observed that the mean WBC level was significantly different in the group with PE ($p < 0.05$). There was no statistically significant difference between MPV and WMR levels with PE groups. There was no statistically significant difference between the mean WBC, MPV, and WMR levels with the 28-day mortality. Additionally, there was no statistically significant difference between the Wells scores of the patients in the low, moderate and high-risk groups with WBC, MPV and WMR levels. In Pearson correlation analysis, there was no relationship between WBC, MPV and WMR levels with the Well's scores.

Conclusion: It was found that the WMR value, a simple, cheap and accessible test, is insufficient to predict the 28-day mortality in patients with PE. No correlation was identified between WMR values and Wells scores. WBC elevation was found to be significantly higher in those with a diagnosis of PE. It was determined that the use of WMR as a pre-test in the diagnosis of PE is not beneficial.

Keywords: Emergency department, pulmonary embolism, Wells score, mortality, D-dimer

ÖZ

Amaç: Bu çalışmanın amacı acil servise Pulmoner Emboli (PE) şüphesi ile başvuran olgularda WBC/MPV oranın Wells klinik olasılık skoru ile karşılaştırmak ve prognozu belirlemede bir belirteç olarak kullanılıp kullanılamayacağını araştırmaktır.

Gereç ve Yöntemler: 01 Eylül 2019 ile 31 Ağustos 2020 arasında acil servise başvuran ve kriterleri karşılayan toplam 111 hasta çalışmaya dâhil edildi. Hastaların PE klinik olasılık değerlendirilmesi için Wells skoru kullanıldı. Wells skorunda ise hastalar düşük, orta ve yüksek riskli olarak 3 gruba ayrıldı. Ayrıca hastaların ilk başvuru hemogramlarından elde edilen WBC/ MPV oranı (WMO) hesaplandı.

Bulgular: Çalışmaya dâhil edilen hastaların ortanca yaşı 65 (IQR 25-75: 57-79) yıldı. Hastaların 56'sı (%50.5) kadın olup, 68'inde (%61.3) PE saptandı. Ortalama WBC düzeyinin PE tanılı grupta anlamlı derecede farklı olduğu görüldü ($p<0.05$). MPV ve WMO düzeyleri ile PE grupları arasında istatistiksel olarak anlamlı bir fark bulunamadı. Ortalama WBC, MPV ve WMO düzeyleri ile 28 günlük mortalite arasında istatistiksel olarak anlamlı bir fark bulunamadı. Düşük, orta ve yüksek riskli Wells skorları ile WBC, MPV ve WMO düzeyleri arasında istatistiksel olarak anlamlı bir fark saptanmadı. Pearson korelasyon analizinde WBC, MPV ve WMO düzeyleri ile Wells skor değerleri arasında bir korelasyon saptanmadı.

Sonuç: Basit, ucuz ve ulaşılabilir bir test olan WMO değerinin, PE'li hastalarda 28 günlük mortaliteyi öngörmede yetersiz olduğunu saptadık. WMO değerleri ile Wells skorları arasında bir korelasyon saptayamadık. WBC yüksekliği PE tanısı olanlarda anlamlı olarak yüksek bulundu. WMO'nun PE tanısında ön test olarak kullanımının faydalı olmadığı tespit edildi.

Anahtar Kelimeler: Acil servis, pulmoner emboli, Well's skoru, mortalite, D-dimer

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Introduction

Pulmonary embolism (PE) is an acute and life-threatening disease. PE can occur as a complete or partial occlusion of the pulmonary artery or its branches with a clot (air, tumor, fat) originating from elsewhere in the body. In epidemiological studies, annual incidence rates for PE vary between 39 and 115 per 100,000 (1). There should be a clinical suspicion for the diagnosis of PE. There is no specific laboratory test. The most commonly used laboratory test is D-dimer. The sensitivity and negative predictive value (NPV) of D-dimer is high, whereas its specificity and positive predictive value (PPV) are low. Due to the simultaneous activation of coagulation and fibrinolysis, D-dimer levels in plasma increase in the presence of acute thrombosis. While a normal D-dimer level eliminates the possibility of acute PE or DVT, the PPV of an elevated D-dimer level is low. Thus, the D-dimer test is not useful for confirming PE(2). Various risk scores to help the diagnosis of PE have been developed (Pulmonary Embolism Rule out Criteria [PERC], the Well's Score and Geneva Score) (3, 4).Leukocytes (White blood cell (WBC)) mediate inflammation, cause proteolytic and oxidative damage to endothelial cells, clog micro vessels, and induce hyper coagulability. Since leukocytes are larger than red blood cells and thrombocytes, they migrate to the microvascular damaged area following necrotic damage in diseases with acute ischemia, trigger ischemia, and enlarge the infarct area by occluding the tiny vessels (5).

Among the hemogram parameters, the mean platelet volume (MPV) is a parameter that is particularly used in the follow-up of inflammation. MPV indicates the size of platelets and is associated with platelet function and activation. MPV increases with the elevation in the diameter of thrombocytes. New platelet synthesis occurs in the bone marrow. Thus, platelets become more functional, younger, and larger; MPV increase is detected. There are many studies regarding the role of MPV in carrying important information in cardiovascular diseases and in inflammation. High MPV increases the risk of stroke as well as coronary artery disease (CAD) (6-8).

This study aims to investigate whether WBC / MPV level can be used as a marker in determining prognosis and whether there is a relationship between WBC / MPV level with the Well's and other scoring.

Material and Methods

This single-center, prospective, cross-sectional, and descriptive case study was conducted in the Emergency Department of University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital between 01.09.2019 and 31.08.2020. The approval was obtained from the Clinical Research Ethics Committee of the aforementioned hospital with the protocol number 2011-KAEK-25 2019 / 10-09. Patients who were over 18, had Computed Thoracic Tomography (CTTA) and signed a consent form were included in the study. Patients with a history of pregnancy, those under the age of 18, those who did not sign a consent form, and those who could not undergo CTTA due to various reasons (such as allergy, chronic kidney disease, etc.) were excluded.

A total of 131 patients participated in the study. 6 were excluded due to pregnancy and 14 were excluded as CT angiography could not be performed. To sum up, a total of 111 patients who met the criteria were included.

According to the information obtained from the patients presenting to the emergency department with the suspicion of PE, the complaints during admission, age, gender, vital signs, comorbidities, and ECG findings were recorded. The Well's score was used for the clinical probability assessment of PE. Patients were divided into 3 as low, moderate and high risk groups according to the Well's score. When D-dimer levels were high in patients in low and moderate risk groups, CT angiography was performed for the definitive diagnosis. In the high-risk group, CTTA was performed regardless of D-dimer levels. In addition, WMR was calculated from the ratio of WBC and MPV values obtained from the first admission hemograms of the patients.

Statistical Analysis

IBM SPSS Statistics for Windows, Version21.0 (IBM Corp. Armonk, NY: USA. Released 2012) package program was used for statistical analysis. In descriptive statistics, the categorical variables were expressed as the number of cases and percentage (%), while the numerical variables were expressed as mean ± standard deviation (minimum - maximum), median and range and / or interquartile range (IQR). Kolmogorov-Smirnov test was used for the normality distribution of the data. Whether the assumption of homogeneity of variances was achieved was investigated by Levene's test. The significance of the difference between the groups in terms of continuous numerical variables where parametric test statistics assumptions were met was examined with Student's t test, whereas the significance of the difference in terms of continuous numerical variables where parametric test statistics assumptions were not met was evaluated with the Mann Whitney U test. One-Way ANOVA test was used to compare three or more normally distributed groups. Pearson correlation analysis was also used to evaluate the relationships between variables showing parametric distribution. Chi-square and Fisher's exact test were used to analyze whether there was a relationship between categorical variables. $p < 0.05$ was considered statistically significant.

Results

A total of 111 patients were included in the study. The median age of the patients was 65 (IQR 25-75: 57-79) and 56 (50.5%) of them were females. PE was found in 68 (61.3%) of the patients, while it was not detected in 43 (38.7%). The median systolic blood pressure (SBP) of the patients was 128 mm / Hg (IQR 25-75: 110-140) and the median heart rate was 100 / minute (IQR 25-75: 88-112). The mean WBC value of the patients was found to be 10.64 ± 4.22, the mean MPV value as 9.72 ± 1.30 and the mean WMR value as 1.11 ± 0.46. The clinical and laboratory findings of the patients are shown in Table 1.

Variables	Total	PE (+)	PE(-)
Age, median (IQR25-75)	65 (57-79)	70 (57.25-80)	63 (51-73)
GCS, median (IQR25-75)	15 (15-15)	15 (15-15)	15 (15-15)
CBP,median (IQR25-75)	128 (110-140)	120 (110-136,75)	130 (116-151)
DBP, median (IQR25-75)	80 (70-86)	80 (70-80)	80 (70-91)
Pulse, median (IQR25-75)	100 (88-112)	102,50 (90-113,50)	96 (84-112)
SPO_2 median (IQR25-75)	94 (90-97)	94 (88-97)	95 (90-97)
Respiratory Rate, median (IQR25-75)	18 (16-20)	17 (15-20)	18 (16-20)
Shock index, mean ± (Std dv)	0,88 ± 0,53	0,95 ± 0,39	0,76 ± 26
Fever, mean ± (Std dv)	36,56 ± 0,57	36,56 ± 0,52	36,54 ± 0,65
D-dimer, mean ± (Std dv)	11,70 ± 16,73	13,56 ± 18,03	8,765 ± 2,65
WBC, mean ± (Std dv)	10,64 ± 4,22	11,30 ± 4,10	9,61 ± 8,98
MPV, mean ± (Std dv)	9,72 ± 1,30	9,77 ± 1,17	9,65 ± 9,40
WMR, mean ± (Std dv)	1,11 ± 0,46	1,17 ± 0,46	1,01 ± 1,02
pH, mean ± (Std dv)	7,38 ± 0,08	7,37 ± 0,06	7,393 ± 7,39
Lactate, mean ± (Std dv)	2,29 ± 1,79	2,39 ± 1,76	2,13 ± 1,40
Troponin, mean ± (Std dv)	56,92 ± 100,32	60,81 ± 102,52	50,76 ± 12,79

GKS: Glaskow Coma Scale, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure SPO2: Finger Tip Oxygen Saturation

Table 1. Clinical and Laboratory Variables

The most common complaint of patients presenting to the emergency department was dyspnea in 57 (51.4%). Additionally, the most common complaint was found to be dyspnea in patients diagnosed with PE. 96 (86.5%) of the patients had a history of comorbidities. In the Well's scoring of the patients, it was observed that 52.3% of the patients had a moderate risk. Additionally, of patients diagnosed with PE, 54.4% had a moderate risk. Mortality was seen in 8 (7.2%) of the patients within a period of 28 days. Moreover, mortality occurred in 7 (10.3%) of the patients with a diagnosis of PE within a period of 28 days (Table 2.)

The Independent Samples T test was performed to investigate whether there was a difference between WBC, MPV and WMR levels with PE diagnosis and 28-day mortality. As a result of this test, it was seen that the mean WBC level was significantly different in the group with PE ($p < 0.05$). No statistically significant difference was found between MPV and WMR levels with PE diagnosis. In addition there was no statistically significant difference between WBC, MPV and WMR levels with 28-day mortality ($p > 0.05$) (Table 3).

In the One-Way ANOVA test conducted to see whether there was a significant difference between low, moderate and high risk Well's scores with WBC, MPV and WMR levels, no statistically significant difference was found between the groups ($p > 0.05$) (Table 4).

In the Pearson correlation analysis conducted to determine whether there was a relationship between WBC, MPV and WMR levels with the Well's scores, no correlation was found between WBC, MPV and WMR levels with the Well's scores ($p > 0.05$) (Table 5).

Discussion

PE is a disease with high morbidity and mortality. As there are no clinical and physical examination findings specific to the disease, clinicians may experience difficulties in the diagnosis and treatment phase. Therefore, rapid diagnosis and treatment is vital in patients with clinical suspicion of PE in emergency departments.

PE is more common in middle-aged and female population. In a study by Keller et al., the mean age was found to be 68.5 ± 15.3 years and the rate of women was 61.5% (9). Similarly, in a study conducted by Hassine et al., the mean age was found to be 58 and the rate of females was 53%(10). Additionally, in a study conducted in our country by Mangal et al. the mean age was determined to be 68.54 and the rate of females was 65.1% (11).In our study, the median age of patients diagnosed with PE was 70, and the rate of the female population was also relatively high. These findings are consistent with the results of studies in the literature. PE has atypical clinical signs and symptoms.

Variables		Total n (%)	PE(+) n(%)	PE(-) n(%)
Admissions complaints	Dyspnea	57 (51,4)	46 (67,6)	11(25,6)
	Chest Pain	23 (20,7)	11 (16,2)	12 (27,8)
	Syncope	1 (0,9)	1 (1,5)	0 (0)
	Palpitation	10 (9)	6 (8,8)	4 (9,3)
	Other	20 (18)	4 (5,9)	16 (37,3)
Comorbidities	No	15 (13,5)	6 (8,8)	9 (20,9)
	Yes	96 (86,5)	62 (91,2)	34 (79,1)
HT	No	66 (59,5)	40 (58,8)	26 (60,5)
	Yes	45 (40,5)	28 (41,2)	17 (39,5)
DM	No	94 (84,7)	58 (85,3)	36 (83,7)
	Yes	17 (15,3)	10 (14,7)	7 (16,3)
COPD / Asthma	No	91 (82)	57 (83,8)	34 (79,1)
	Yes	20 (18)	11(16,2)	9 (20,9)
CAD	No	76 (68,5)	52 (76,5)	23 (53,5)
	Yes	35 (31,5)	16 (23,5)	20 (45,5)
Malignancy	No	94 (84,7)	59 (86,8)	35 (81,4)
	Yes	17 (15,3)	9 (13,2)	8 (18,6)
CVD	No	96 (86,5)	59 (86,8)	37 (86)
	Yes	15 (13,5)	9 (13,2)	6 (14)
Other	No	107 (96,4)	64 (94,1)	43 (100)
	Yes	4 (3,6)	4 (5,9)	0 (0)
Normal sinus rythm	No	57 (51,4)	37 (54,4)	20 (46,5)
	Yes	54 (48,6)	31 (45,6)	23 (53,5)
Sinus Tachycardia	No	76 (68,5)	46 (67,6)	30 (69,8)
	Yes	35 (31,5)	22 (32,4)	13 (30,2)
AF	No	100 (90,1)	61 (89,7)	39 (90,7)
	Yes	11 (9,9)	7 (10,3)	4 (9,3)
Right Bundle Branch Block	No	102 (91,9)	61 (89,7)	41 (95,3)
	Yes	9 (8,1)	7 (10,3)	2 (4,7)
S1Q3T3	No	101 (91)	61 (89,7)	40 (93)
	Yes	10 (9)	7 (10,3)	3 (7)
Other	No	105 (94,6)	64 (94,1)	41 (95,3)
	Yes	6 (5,4)	4 (5,9)	2 (4,7)
The Wells Risk Scoring	0-1 Low	45 (40,5)	23 (33,8)	22 (51,2)
	2-6 Moderate	58 (52,3)	37 (54,4)	21 (48,8)
	6<High	8 (7,2)	8 (11,8)	0 (0)
Status	Ex	3 (2,7)	2 (2,9)	1 (2,3)
	Leaving without permission	1 (0,9)	1 (1,5)	0 (0)
	Hospitalization	79 (71,2)	57 (83,8)	22 (51,2)
	Dispatch	6 (5,4)	6 (8,8)	0 (0)
	Discharge	16 (14,4)	0 (0)	16 (37,2)
	İntensive care	6 (5,4)	2 (2,9)	4 (9,3)
28-Day Mortality	No	103 (92,8)	61 (89,7)	42 (97,7)
	Yes	8 (7,2)	7 (10,3)	1 (2,3)
Total		**111 (100)**	**68 (100)**	**43 (100)**

PE: Pulmonary Embolism, HT: Hypertension, DM: Diabetes Melitus, COPD: Chronic Obstructive Pulmonary Disease, CAD: Coronary Artery Disease, CVD: Cerebrovascular Disease, AF: Atrial Fibrillation

Table 2. Clinical Findings of Variables

In a study by Yoon et al., The most common symptoms were dyspnea (63.7%) and chest pain (19.9%) (12).In another study conducted by Pollack et al. with 1880 patients, it was found that the two most common symptoms were dyspnea and pleuritic chest pain (13).

		Variables	n	Mean	SD	Independent Samples Test
Pulmonary Embolism	No	WBC	43	9,61	4,25	p<0.05
	Yes		68	11,3	4,1	
	No	MPV	43	9,65	1,5	p>0.05
	Yes		68	9,77	1,17	
	No	WMO	43	1,01	0,44	p>0.05
	Yes		68	1,17	0,47	
28-Day Mortality	No	WBC	103	10,61	4,24	p>0.05
	Yes		8	11,13	4,18	
	No	MPV	103	9,68	1,29	p>0.05
	Yes		8	10,33	1,43	
	No	WMO	103	1,12	0,48	p>0.05
	Yes		8	1,09	0,41	

WBC: White Blood Cell, MPV: Mean Platelet Volume, WMR: WBC/MPV Ratio

Table 3. Pulmonary Embolism and 28-Day Mortality Analysis of Variables

In a study conducted in our country by Acar et al., it was found that the most common symptoms were dyspnea and chest pain (14). Similarly in our study, the most common symptoms observed in patients were dyspnea and chest pain. These findings are also consistent with the literature.

PE is an acute emergency with high mortality and morbidity rates. In the study conducted by Tanabe et al., the 30-day mortality was found to be 6.1%. In another study by Dahhan et al., this rate was found to be 20.2% (15, 16). In a multi-center study conducted by Pollack et al., in-hospital 30-day mortality rate in patients with PE was found to be 3.4% (13). In the study conducted by Jimenez et al., the 30-day mortality rate was found to be 5.7% (17). In another study conducted by Hajizadeh et al., in-hospital short-term mortality rates of patients with PE were found to be 9.3% (18). In our study, the 28-day mortality rate was found to be 10.3%. This rate is consistent with the other publications in the literature.

					95% Confidence Interval		
	The Well's Risk	n	Mean	SD	Lower Limit	Upper Limit	One-Way ANOVA Test
WBC	Low	45	10,4	4,46	9,06	11,74	p>0.05
	Moderate	58	10,9	4,15	9,8	11,98	
	High	8	10,28	3,75	7,15	13,41	
MPV	Low	45	9,65	1,3	9,26	10,03	p>0.05
	Moderate	58	9,73	1,37	9,37	10,1	
	High	8	10,14	0,85	9,43	10,85	
WMO	Low	45	1,11	0,52	0,95	1,26	p>0.05
	Moderate	58	1,13	0,42	1,02	1,24	
	High	8	1,03	0,42	0,68	1,38	
Total		111	1,11	0,46	1,03	1,2	

WBC: White Blood Cell, MPV: Mean Platelet Volume, WMR: WBC/MPV Ratio

Table 4. Analysis of Variables with the Well's Score

Clinical probability calculation scores were developed by combining symptoms, signs and history characteristics in patients with PE. The most commonly used clinical prediction rule was proposed by Well's et al. (19). In the study by Wong et al., the sensitivity of the Well's score was found to be 46.7% and the specificity was 62% (20). In the study of Martinez et al., the sensitivity of the Well's score was found to be 65% and the specificity was 81% (21). In our study, the moderate risk (52.3%) was found to be the most common in the Well's scoring of the patients. Additionally, 63.8% of the patients with moderate risk were diagnosed with PE. In the high risk group, PE was detected in all 8 patients (100%) while this rate was 51.1% in the low-risk group. Our study supports the effectiveness of Well's scores in showing the presence of PE. Accordingly, clinical findings and risk scoring systems should be carefully examined before performing invasive tests for diagnostic purposes.

WBC and MPV are the hemogram parameters that are quickly accessible in the emergency departments.

		WBC	MPV	WMR	The Wells Score
WBC	r	1	0,005	,935**	0,11
	p		0,957	0	0,249
MPV	r	0,005	1	-,325**	0,151
	p	0,957		0,001	0,113
WMO	r	,935**	-,325**	1	0,046
	p	0	0,001		0,633
The Well's Score	r	0,11	0,151	0,046	1
	p	0,249	0,113	0,633	

WBC: White Blood Cell, MPV: Mean Platelet Volume, WMR: WBC/MPV Ratio

Table 5. Pearson's Correlation Analysis of the Variables

The leukocyte increase in PE was first shown by Afzal et al. They stated that neutrophils particularly play an important role in the inflammatory response in the atherosclerotic background. Leukocytes are associated with both thrombogenesis and increased levels of fibrinogen, factor VII, factor VIII (22).

In recent studies, the relationship between WBC and MPV has been examined and the WBC / MPV ratio has been called as WMR. In studies with NSTEMI and STEMI patients, the relationship between WBC / MPV with major adverse cardiac events and long-term mortality has been observed to be stronger than other hematological parameters, which has recently attracted more attention (23, 24). In a retrospective study by Cannon et al., it was found that WBC above 10,000 increased mortality in AMI and UA patients (25).According to the study conducted by Hilal E. et al., there was no significant difference between MPV values of the study and control groups(26). In the study by Kostrubiec et al., there was no difference in MPV values between the groups with and without acute PE(27). According to the study by Çavuş et al., the high WBC values were found to be higher in the PE group than the control group, and it was shown that this value was the highest value in the study in those who could not survive after the disease (28).

There was no significant difference between the MPV and WMR values with the presence of PE in our study. However, WBC values were found to be significantly higher in patients with PE. In this study, it was found that the WBC, MPV and WMR values of the patients were not statistically significant in predicting 28-day mortality. Additionally, there was no statistically significant relationship between low, moderate and high risk well's scores with WBC, MPV and WMR levels of the patients.

The relatively low number of patients is the main limitation of this study. In addition, the COVID-19 pandemic was still ongoing during the study. We think that changes in complete blood count parameters in COVID-19 patients may have affected the study data and findings. The diagnosis of PE may also be overlooked due to similar symptoms and radiological and laboratory findings seen in COVID-19 patients.

As a result, we found that the WMR value obtained from the hemogram, which is a simple, cheap and accessible test, was insufficient to predict the 28-day mortality in patients with PE. We could not find a correlation between WMR values and well's scores. WBC elevation was found to be significantly higher in those diagnosed with PE. However, using WMR as a pre-test in the diagnosis of PE was not statistically significant.

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Authors' Contribution: All authors contrubuted for conception, design of the study, data collection, data analysis, and assembly. The manuscript was written and approved by all authors.

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All authors declared that they follow the rules of Research and Publication Ethics.

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