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CLINICAL RESEARCH / KLİNİK ARAŞTIRMA

Effects of RDW and MPV on Mortality in Patients with Pulmonary Thromboembolism

Pulmoner Tromboemboli Hastalarında RDW ve MPV'nin Mortalite Üzerine Etkileri

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Abstract

Objective: Pulmonary thromboembolism (PTE) is an important cause of mortality. This condition, which is increasing in frequency, needs early diagnosis and prognostic indicators. The present study showed the importance of mean platelet volume (MPV) and distribution width (RDW) in its prognosis.

Methods: A total of 121 patients who were diagnosed with PTE and who were admitted to the emergency department between 2014 and 2017 were included in the present study. Vital signs, hemograms, biochemistry, and blood gas parameters of the patients were recorded. In hospital mortality status was determined and a prognostic comparison of the risk factors of survivors and those who died and MPV and RDW was made.

Results: The median age of the patients was 69 years, 57% of the patients were women, and 57.9% of the patients were tachycardic. The median saturation value was 90%. In hospital mortality occurred in 19 patients. The MPV value of the patients who died was significantly lower than that of the patients who survived. According to the receiver operating characteristic analysis, age, saturation, and MPV yielded significant p values. Age had the highest area under the curve (AUC) value of 0.723 and MPV had 0.655 AUC. Although the risk of mortality increased 7.048-fold in patients over the age of 76, MPV below 7.9 increased it 3.194-fold.

Conclusion: The results of the present study showed that there was no direct relationship between RDW and MPV as a prognostic indicator of PTE, but a decrease in MPV in patients with PTE increased the risk of mortality.

Keywords: Pulmonary thromboembolism, mean platelet volume, red cell distribution width, prognosis

Öz

Amaç: Pulmoner tromboembolizm (PTE) önemli ölüm nedenlerinden biridir. Sıklığı giderek artan bu durum erken tanı ve prognostik göstergelere ihtiyaç duymaktadır. Bu çalışmanın amacı, ortalama trombosit hacmi (MPV) ve dağıtım genişliğinin (RDW) prognozdaki önemini göstermektir.

Yöntem: Bu çalışmaya 2014-2017 yılları arasında acil servise başvuran PTE tanısı alan toplam 121 hasta dahil edildi. Hastaların vital bulguları, hemogramları, biyokimyaları ve kan gazı parametreleri kaydedildi. Hastane içi mortalite durumu belirlenerek, hayatta kalan ve ölenlerin risk faktörleri ile MPV ve RDW'nin prognostik karşılaştırması yapıldı.

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Öz

Bulgular: Hastaların ortanca yaşı 69 idi, hastaların %57'si kadındı ve hastaların %57,9'u taşikardikti. Ortanca satürasyon değeri %90 idi. Hastane içi mortalite 19 hastada meydana geldi. Ölen hastaların MPV değeri yaşayan hastalara göre anlamlı derecede düşüktü. Alıcı işletim karakteristiği analizine göre yaş, satürasyon ve MPV anlamlı p değerleri verdi. Yaş en yüksek eğri altındaki alan (AUC) değerine 0,723, MPV ise 0,655 AUC'ye sahipti. Yetmiş altı yaş üstü hastalarda mortalite riski 7.048 kat artarken, MPV'nin 7,9'un altında olması ise 3.194 kat artırdı.

Sonuç: Bu çalışmanın sonuçları, PTE'nin prognostik bir göstergesi olarak RDW ile MPV arasında doğrudan bir ilişki olmadığını, ancak PTE'li hastalarda MPV'deki düşüşün mortalite riskini artırdığını gösterdi.

Anahtar Kelimeler: Pulmoner tromboembolizm, ortalama trombosit hacmi, kırmız hücre dağılım genişliği, prognoz

Introduction

Pulmonary thromboembolism (PTE) is the third leading cause of cardiovascular death. The occlusion of the pulmonary artery and its branches by thrombus creates different clinical scenarios, causing diagnostic difficulties. Its prevalence is increasing over time. Therefore, early diagnosis and prognostic indicators of the disease must be determined[1-3].

Mean platelet volume (MPV), which is one of the platelet indices, provides information about the production and function of platelets[4]. It was shown that elevated MPV values are associated with increased number of granules, thromboxane A2 level, faster aggregation, and increased presence of glycoprotein Ib and IIb/IIIa receptors. In brief, it means that larger platelets are in circulation[5]. Larger platelets are more active than platelets of normal volume. This was demonstrated with the level of p-selectin and increased platelet activity during acute thromboembolic events such as myocardial infarction, cerebrovascular accident, and venous thromboembolism, which were found to be associated with the severity of the clinical manifestation[6]. Although studies have reported that the increased MPV value, which is found to be related with cardiovascular diseases, is also associated with PTE, the results of some studies do not show any relation in PTE[7,8].

Although red cell distribution width (RDW) is an indicator of prothrombotic clinical processes, it is controversial[9]. In PTE, increased RDW value is associated with mortality. It is not clear why and how the inflammatory mechanisms occur during this process. It has been shown that some cytokines stimulate erythrocyte production and others inhibit the production of erythrocyte[10].

The present study showed the importance of MPV in prognosis because of the evaluation of risk factors in PTE.

Materials and Methods

The study was conducted retrospectively in patients who were diagnosed with PTE in our emergency department between 2014 and 2017. The study was approved by the University of Health Sciences Turkey, Dışkapı Yıldırım Beyazıt Education and Research Hospital, Ethics Committee (decision: 39/5, date: 12.06.2017) and was conducted following the Helsinki Rules and good clinical practices. Written informed consent was not obtained because the study was conducted retrospectively through the patient files and the identities of the patients were not disclosed.

Among the patients who were admitted to the emergency department with symptoms such as angina, dyspnea, hemoptysis, and syncope and were considered to have the diagnosis of PTE, 121 patients were diagnosed with PTE by computed tomography pulmonary angiography and were included in the study. Those who were under the age of 18 and pregnant and did not have PTE diagnosis were excluded. Age, gender, vital signs (i.e., blood pressure, pulse, fever, respiratory rate, and saturation % oxygen), hemogram parameters [white blood cell (WBC), platelet, RDW, MPV], biochemistry parameters (i.e., urea, creatinine, sodium, potassium, creatine kinase, creatinine kinase-MB) and blood gas values (pH, partial oxygen, partial carbon dioxide, bicarbonate, base deficit, and lactate) were recorded. The in-hospital mortality status of the patients was determined. The relationship between RDW and MPV values of the patients was examined.

Statistical Analysis

Statistical analyses of the data were made by using the SPSS 20.0 (SPSS Inc., Chicago, IL) package program. Normality analysis of the data was performed using the histograms and Kolmogorov-Smirnov test. Quantitative data that did not fit the normal distribution were reported as the median (25-75% quartiles), quantitative variables with normal

distribution were expressed as mean ± standard deviation, and the categorical variables were expressed as frequency (percentages). Differences between groups were investigated using the Mann-Whitney U test for quantitative variables with non-normal distribution and the student's t-test for quantitative variables with a normal distribution. The intergroup comparisons of the categorical variables were made by using the chi-square test. To assess the strength of in-hospital mortality, the quantitative factors that provided significant p values in the Mann-Whitney U test and student's t-test were included in the receiver-operating characteristic (ROC) analysis. The Youden Index was used to find appropriate cutoff values for the parameters. The sensitivity, specificity, positive predictive value, negative predictive value, and odds ratios were calculated by categorizing the parameters according to their cutoff values. A p-value of <0.05 was considered statistically significant.

Results

A total of 121 patients who were diagnosed with PTE were included in the study. The median age of the patients was 69 (55-80.5). When the distribution of gender was evaluated, female gender was found to be more prevalent. The male-gender ratio was 43% (52 patients). When vital signs were evaluated, tachycardia was detected in 70 (57.9%) patients. The patients' median saturation value was found to be 90 (85.5-95.5), and the median pulse value was 101 (88.5-118.5). When the laboratory findings were evaluated, the median RDW value of the patients was found to be 15.5 (14.35-17.7), and the median MPV value was 8.2 (7.5-9.05). The detailed characteristics of the participants are summarized in Table 1.

In hospital mortality occurred in 19 (15.7%) of the patients who were included in the study. The parameters of the deceased and surviving patients were compared, and it was found that the median age of patients who died was statistically significantly higher than those who survived [79 (72.25-83.25), 67 (54-80), 0.001]. The median systolic blood pressure values of the patients who died were statistically significantly lower than those who survived [110 (100-127.75), 120 (110-140), 0.04]. The median saturation values of the patients who died were statistically significantly lower than those who survived [86.5 (80-90.75), 91.5 (86.75-96), 0.028]. The median MPV value of the patients who died was found to be statistically significantly lower than those who survived [7.65 (7.27-8.42), 8.3 (7.5-9.22), 0.037]. The median urea value of the patients who died was found to be statistically significantly higher than those who survived [57.5 (36-62.5), 44 (30-55), 0.025]. The data of the compared parameters are presented in detail in Table 2.

Age, systolic blood pressure, saturation, MPV, and urea parameters were included in the ROC analysis, which was performed to evaluate the predictive power of in-hospital mortality. Age, saturation, and MPV was the only parameters with significant p values. Age had the highest AUC value of 0.723, and MPV had 0.655 AUC (Figure 1). Although the risk of mortality increased 7.048-fold in patients over the age of 76, MPV below 7.9 increased it 3.194-fold. Detailed

Table 1. General characteristics of participants

The number of participants		121 (100%)
Age		69 (55-80.5)
Gender	Male	52 (43%)
	Female	69 (57%)
Vital findings	Fever (ºC)	36.7 (36.6-37)
	Pulse	101 (88.5-118.5)
	Systolic blood pressure (mmHg)	120 (102.5-135)
	Diastolic blood pressure (mmHg)	80 (62-80)
	Saturation (%)	90 (85.5-95.5)
	Respiration rate	20 (20-22)
	Tachycardia	70 (57.9%)
Laboratory results	WBC	10.2 (8.15-13.7)
	Platelet	230 (189-299)
	RDW	15.5 (14.35-17.7)
	MPV	8.2 (7.5-9.05)
	Urea	45 (31.5-58)
	Creatine	0.97 (0.82-1.12)
	Sodium	136.86±4.91
	Potassium	4.28±0.57
	CK	62 (39.5-104)
	CK-MB	17 (12-24)
	pH	7.43 (7.39-7.45)
	PO_2	52.9±22.92
	PCO_2	34 (30.5-40)
	HCO_3	22.6 (21-24)
	BE	-0.75±3.06
	Lactate	2 (1.45-2.55)
In hospital mortality	Yes	19 (15.7%)
	No	102 (84.3%)

RDW: Red cell distribution width, MPV: Mean platelet volume, WBC: white blood cell

ROC analysis results of the parameters are summarized in Table 3.

Discussion

The results of the study showed that there was no direct relationship between RDW and MPV as a prognostic indicator of PTE, but a decrease in MPV in patients with PTE increased the risk of mortality.

In previous studies, prognostic evaluations between RDW and PTE showed an association between increased RDW value and mortality. However, this mechanism has not yet been fully elucidated[10]. Ren et al.[11] showed a correlation between RDW and inflammatory markers such as PCT, CRP, and WBC in community-acquired pneumonia. Another indication that RDW is an inflammatory marker is that it has been linked to an increase in cancer and cardiovascular disease[10] . Pehlivanlar Küçük et al.[12] showed that a high level of RDW can be an auxiliary parameter as an independent predictor of mortality in acute PTE. This study showed that RDW was not statistically significant between deceased and surviving patients. However, as in the literature, their findings revealed that RDW levels were higher in patients who died. This difference might be attributed to our study's short-term in-hospital mortality. Most other studies evaluated 30-day mortality, which created a difference between the mortality rate of our study and other studies. A situation that causes an increase in RDW may also be induced by hypoxia, which

Table 2. General characteristics of differentiators between dead and living patients

		Deceased (19)	Survives (102)	p-value
Age		79 (72.25-83.25)	67 (54-80)	**0.001***
Gender	Male	12 (63.2%)	40 (39.2%)	0.053***
	Female	7 (36.8%)	62 (60.8%)	
Fever (ºC)		36.7 (36.55-37.25)	36.7 (36.57-37)	0.937*
Pulse		100.5 (89.75-112)	100 (87.75-119.25)	0.656*
Systolic blood pressure (mmHg)		110 (100-127.75)	120 (110-140)	**0.04***
Diastolic blood pressure (mmHg)		70 (60-80)	80 (68.75-80)	0.056*
Saturation (%)		86.5 (80-90.75)	91.5 (86.75-96)	**0.028***
Respiration rate		20 (20-25)	20 (20-22)	0.363*
tachycardia		14 (73.7%)	56 (54.9%)	0.128***
WBC		11.55 (6.97-15.77)	9.85 (8.17-13.32)	0.417*
Platelet		234 (183-321.75)	229 (189-300.25)	0.834*
RDW		16.45 (14.45-18.37)	15.5 (14.25-17.62)	0.379*
MPV		7.65 (7.27-8.42)	8.3 (7.5-9.22)	**0.037***
Urea		57.5 (36-62.5)	44 (30-55)	**0.025***
Creatine		0.96 (0.83-1.15)	0.97 (0.81-1.1)	0.656*
Sodium		135.26±5	137.16±4.85	0.141**
Potassium		4.48±0.71	4.24±0.53	0.101**
CK		48 (28.5-94.75)	64.5 (42.75-103.5)	0.161*
CK-MB		22 (15.25-26.25)	17 (12-24)	0.298*
pH		7.41 (7.38-7.43)	7.43 (7.38-7.46)	0.194*
PO_2		48.32±22.23	53.75±23.05	0.345**
PCO_2		35 (30.5-39)	34 (30-41)	0.817*
HCO_3		22 (20.75-23.47)	22.4 (21-24)	0.594*
BE		-1.33±2.22	-0.64±3.19	0.374**
Lactate		2.4 (1.7-3.02)	2 (1.5-2.5)	0.25*

Statistically significant p values are written in bold

*The Man-Whitney U test was used, **Student's t-test was used. ***The chi-square test was used, RDW: Red cell distribution width, MPV: Mean platelet volume, WBC: white blood cell

may accelerate erythropoietin production and result in the release of immature and varied sizes of erythrocytes into circulation. This can be accepted as a condition that causes an increased RDW in PTE[13]. It was shown in this study that the median oxygen saturation of our patients was low. In other words, the saturation values of the patients who died were lower than those who survived. This supports the pathophysiology in the literature.

Platelet activation is an expected condition in PTE. MPV is a simple hemogram parameter showing platelet activation. The MPV value increases as platelets get larger, implying that the platelet enzymatic and receptor activity will increase. Based on this mechanism, MPV is likely to increase in thrombotic events such as PTE. Previous research has found a link between MPV and prognostic factors such as mortality, massive submassive discrimination, and right ventricular dysfunction in PTE[14]. However, some studies did not support this relationship[15,16]. In our investigation, we discovered a link between low MPV values and in-hospital mortality. There are comparable studies in the literature that support this relation. Hilal et al.[8] showed that the MPV value increased in PTE survivors. Moharamzadeh et al.[17] reported that there was no relationship between MPV and patients without PTE. Lin et al.[18] showed that the MPV value is higher in patients with PTE who are mortal and it can be an easy indicator for predicting early death.

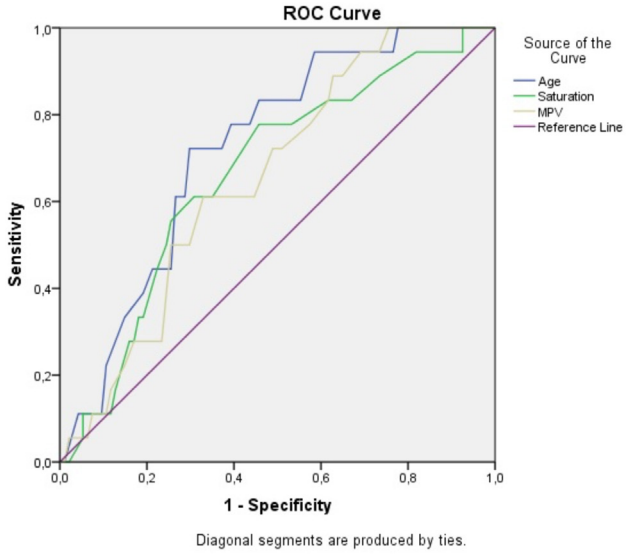

Figure 1. The ROC curve

ROC: Receiver-operating characteristic

Study Limitations

The retrospective nature of our study and the small number of patients with PTE were important limitations. Unlike most studies in the literature, this study; showed that the association of RDW with mortality was not statistically significant. The reason of this; may be due to the fact that our study was based on short-term in-hospital mortality. Most other studies have evaluated 30-day mortality.

We believe that simple, calculable and cost-effective hemogram parameters should be better known in the pathophysiology of PTE and multicenter, prospective studies are needed for their use in prognosis.

Conclusion

PTE patients who died were found to be statistically significantly older than those who survived, and the current study reported lower saturation and MPV levels. An MPV

Table 3. ROC analysis results according to in-hospital mortality

	Age	Saturation	MPV	Urea	SBP
AUC (95% CI)	0.723 (0.612-0.834)	0.664 (0.533-0.795)	0.655 (0.535-0.775)	0.642 (0.505-0.778)	0.634 (0.489-0.778)
P value	**0.003**	**0.028**	**0.038**	0.057	0.073
Cut-off level	>76	<91	<7.9	-	-
Odds ratio (95% CI)	7.048 (2.327-21.345)	3,277 (1.099-9.773)	3,194 (1.128-9.041)	-	-
Sensitivity	73.7%	73.7%	61.1%	-	-
Specificity	71.6%	53.9%	67%	-	-
PPV	32.6%	23%	26.2%	-	-
NPV	93.6%	91.7%	90%	-	-

CI: Confidence interval, AUC: Area under the curve, PPV: Positive predictive value, NPV: Negative predictive value, SBP: Systolic blood pressure, MPV: Mean platelet volume, ROC: Receiver-operating characteristic

value less than 7.9 results in an odds ratio of 3.194. No significant relationship was detected between RDW and PTE. The findings of this study showed different results compared to the MPV and RDW literature. This demonstrates that inflammatory events in PTE do not influence MPV and RDW levels in patients at the same rate and time. When the literature was reviewed, it was found that these values can be good or bad indicators of prognosis and diagnosis. This suggests that the pathophysiology of simple measurable hemogram parameters in PTE must be better.

Ethics

Ethics Committee Approval: The study was approved by the University of Health Sciences Turkey, Dışkapı Yıldırım Beyazıt Education and Research Hospital, Ethics Committee (decision: 39/5, date: 12.06.2017) and was conducted following the Helsinki Rules and good clinical practices.

Informed Consent: Retrospective study.

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Authorship Contributions

Surgical and Medical Practices: B.I., S.Ö., Concept: B.I., E.S., S.Ö., Design: B.I., E.S., K.K., Data Collection or Processing: B.I., S.Ö., M.S.Y., Analysis or Interpretation: B.I., E.S., S.Ö., K.K., Literature Search: B.I., E.S., M.S.Y., Writing: B.I., E.S.

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