ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

The White Blood Cell Count to Mean Platelet Volume Ratio (WMR) is Associated With Syntax Score in Patients With ST-Segment Elevation Myocardial Infarction

Beyaz Kan Hücresi Sayısı/Ortalama Trombosit Hacmi Oranın ST-Segmenti Yükselmeli Miyokard Enfarktüslü Hastalarda SYNTAX Skoru ile İlişkisi

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ABSTRACT

Background: *ST-segment elevation myocardial infarction (STEMI) is the most common reason for mortality worldwide. Scoring systems such as Syntax score plays a significant role in risk stratification in these patients. Besides, as a simple and easily applicable marker, white blood cell count to mean platelet volume ratio (WMR), which could play a vital role in identifying risky patients, has emerged as an indicator of inflammation in atherosclerotic disease. In the current study, we aimed to investigate the predictive role of WMR for Syntax score in patients with STEMI.*

Material and Method: *Demographics, comorbidities, and laboratory results on the admission of hospitalized 335 patients with STEMI were analyzed. The study population was divided into two groups according to the syntax score median of the study population (Syntax score median=19). Findings were compared between Syntax score <19 and Syntax score ≥19 groups.*

Results: *The Pearson correlation value between WMR and Syntax score was 0.415 (p<0.001). One hundred and sixty four patients were assigned to the Syntax score <19 group, 171 patients were designated as Syntax score ≥19 group. White blood cell count to mean platelet volume ratio was significantly higher in the Syntax score ≥19 group than the Syntax score <19 group [median (IQR), 1.56 (1.28–1.81) vs 1.32 (1.16–1.5), p<0.001]. White blood cell count to mean platelet volume ratio was an independent predictor according to multivariate analysis [Odds ratio (95% CI), 1.26 (1.08–1.47), p=0.002].*

Conclusion: *In patients with STEMI, WMR is significantly correlated with high syntax score. It could provide supportive data for early risk stratification and optimized approach. Consequently, therapeutic methods may be wellplanned to avoid a poor outcome in these patients.*

Key words: *ST-segment elevation miyocardial infarction; syntax score; white blood cell; mean platelet volume*

ÖZET

Amaç: *ST-segment yükselmeli miyokard enfarktüsü (STEMI) dünya çapında en yaygın ölüm nedenlerindendir. Syntax skoru gibi skorlama sistemleri, bu hastalarda risk sınıflandırmasında önemli bir rol oynar. Ayrıca, basit ve kolay uygulanabilir bir belirteç olarak, riskli hastaların belirlenmesinde hayati bir rol oynayabilecek beyaz kan hücresi sayısının ortalama trombosit hacmine oranı (WMR), aterosklerotik hastalıkta enflamasyonun bir göstergesi olarak ortaya çıkmıştır. Bu çalışmada, STEMI hastalarında WMR'nin Syntax skoru için prediktif rolünü araştırmayı amaçladık.*

Materyal ve Metot: *ST-segment yükselmeli miyokard enfarktüsü tanısı ile hastaneye yatırılan 335 hastanın demografik özellikleri, komorbiditeleri ve laboratuvar sonuçları incelendi. Çalışma popülasyonu, çalışma popülasyonunun syntax skor medyanına (Syntax skor medyan=19) göre iki gruba ayrıldı. Bulgular Syntax skoru <19 ve Syntax skoru ≥19 olan gruplar arasında karşılaştırıldı.*

Bulgular: *Beyaz kan hücresi sayısının ortalama trombosit hacmine oranı ile Syntax skoru arasındaki Pearson korelasyon değeri 0,415 (p<0,001) bulundu. Yüz altmış dört hasta Syntax skoru <19 grubuna, 171 hasta Syntax skoru ≥19 grubuna ayrıldı. Beyaz kan hücresi sayısının ortalama trombosit hacmine oranı, Syntax skoru ≥19 olan grupta Syntax skoru <19 olan gruptan anlamlı olarak daha yüksekti [ortanca (IQR), 1,56 (1,28–1,81) ve 1,32 (1,16–1,5), p<0,001]. Beyaz kan hücresi sayısının ortalama trombosit hacmine oranı, çok değişkenli analize göre bağımsız bir belirleyiciydi [Odds oranı (%95 GA), 1,26 (1,08–1,47), p=0,002].*

Sonuç: *ST-segment yükselmeli miyokard enfarktüsü hastalarında WMR, yüksek syntax skoru ile anlamlı şekilde ilişkilidir. Erken risk sınıflandırması ve optimize edilmiş yaklaşım için destekleyici veriler sağlayabilir. Sonuç olarak, bu hastalarda kötü bir sonlanımdan kaçınmak için terapötik yöntemler iyi planlanabilir.*

Anahtar kelimeler: *ST-segment elevasyonlu miyokard infarktüsü; syntax skoru; lökosit; ortalama trombosit hacmi*

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Introduction

Acute coronary syndrome (ACS) is a disease characterized by rupture of atherosclerotic plaque in most cases followed by complete or incomplete thrombosis of the coronary arteries[1]. Despite the ongoing amelioration in related mortality rates, ACS remains the most common cause of death worldwide[2]. In parallel, ST-segment elevation myocardial infarction (STEMI), a life-threatening complication of coronary artery disease (CAD), is among the leading causes of morbidity and mortality worldwide[3].

The SYNTAX [Synergy (SYNergy) between Taksus (TAXus) and percutaneous coronary intervention and cardiac surgery] scoring system is an anatomical scoring system that measures the complexity of a coronary lesion in addition toits features such as its morphology and location in the coronary vascular system[4]. It has been shown that the SYNTAX score can predict short- and long-term mortality in patients who were operated on due to CAD[4]. It has been reported that the severity of CAD, which is commonly graded based on SYNTAX scores calculated from coronary angiography, was closely correlated with poor prognosis in ACS[4].

To date, the relationship between the SYNTAX score and various hematological and biochemical parameters in ACS patients has been investigated in many studies[5–7]. White blood cells (WBCs) play a crucial role in the progression of atherosclerosis and in the destabilization and rupture of a plaque, leading to thrombotic events. Additionally, WBCs and platelets have potential roles in the pathogenesis of STEMI[1,8]. The mean platelet volume (MPV), which is a highly sensitive marker of platelet activity, can be used to correlate the pathophysiology of thrombosis and inflammatory diseases[9]. The platelet size, which is expressed as MPV, has also been shown to predict cardiac deaths or major adverse cardiac events (MACEs) following percutaneous coronary intervention (PCI)[10]. The WMR value, which is the ratio of WBC count to MPV, is used as an indicator of inflammation in patients with atherosclerotic disease[9,10]. In this context, the objective of this study is to investigate the relationship between WMR, clinical prognosis and SYNTAX score in patients with STEMI.

Methods

The study population consisted of patients hospitalized between 2016 and 2020 with the diagnosis of STEMI. Among the patients whose demographic characteristics, comorbidities, and laboratory results were reviewed retrospectively, 37 patients who did not give consent, who received steroid or non-steroidal anti-inflammatory therapy, and who had blood diseases that could affect blood parameters, including cytopenia, were excluded from the study. The remaining 335 patients were included in the study sample. The study protocol was approved by the local ethics committee (Ethics Committee of the Dean of the Faculty of Medicine of Kafkas University-80576354-050-99/197 numbered ethics committee approval). The study was conducted according to the principles of the Declaration of Helsinki. Written informed consent was obtained from all patients included in the study sample.

SYNTAX scores were calculated from the angiographic images of the patients. Blood parameters of all patients were evaluated. Biochemical and complete blood count (CBC) data were obtained from venous blood samples taken from patients at admission. Blood samples were collected in standard tubes containing EDTA (ethylenedinitrilotetraacetic acid). All samples were processed in the XE 5000 (Sysmex, Norderstedt, Germany) device for 60 minutes, and the relevant blood values were obtained. White blood cell count to mean platelet volume ratio was calculated using WBC and MPV values. The diagnosis of STEMI was made based on the criteria available in the most recent guidelines[11]. The study sample was divided into two groups of 171 patients with a SYNTAX score ≥19 and 164 patients with a SYNTAX score <19. The groups were analyzed comparatively on the basis of the variables examined within the scope of the study. Evaluation of cineangiographic imaging results was performed by two experienced cardiologists blinded to study data using the Axiom (Siemens Medical Solution, Erlangen, Germany) workstation. Each lesion with a diameter stenosis ≥50% in coronary vessels ≥1.5 mm in diameter was scored using the online SYNTAX score calculator. In cases where two cardiologists could not reach a consensus on the coronary lesions, the final score was determined by averaging the scores calculated by each cardiologist.

Statistical Analysis

Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) program version 23.0 (Social Science Statistical Program for Windows Program, version 23.0, IBM Company, Armonk, NY, USA, 2015) software package. Descriptive statistics were expressed as mean ± standard deviation or median (0.25–0.75 percentiles) depending on whether the respective data were determined to conform to the normal distribution in the case of numerical variables and as number (n) and percentage (%) values in the case of categorical variables.

Normality assumptions in the case of numerical variables were analyzed with the Shapiro-Wilk test. Categorical data were analyzed with Pearson's chi-squared and Fisher's exact tests. The differences between the two groups were evaluated with the student's t-test in the case of data that were determined to conform to the normal distribution, and with the Mann-Whitney U test for data that did not conform to the normal distribution. Spearman's correlation coefficient was used to evaluate the relationships between continuous variables. Univariate and multivariate logistic regression analyses were used to identify independent risk factors associated with an in-hospital MACE.

The receiver operating characteristic curve (ROC) analysis was used to evaluate the predictive power of the SYNTAX scores and WMR values for MACEs and the area under the curve (AUC) within a 95% confidence interval (CI), and the sensitivity and specificity of these markers. Maximum Youden index values were determined as optimal cut-off points. Univariate and multivariate analyses of independent predictors of MACEs were performed using the Cox proportional hazards regression model. The variables significantly associated with MACEs in univariate analyses were further subjected to multivariate analysis. The corresponding 95% CI and odds ratio (OR) values were reported. Probability (p) values ≤0.05 were deemed to indicate statistical significance.

Results

A total of 335 STEMI patients with a mean age of 56.4±11 years were retrospectively included in the study sample. The patients' baseline demographic, clinical and laboratory data were analyzed and compared between groups. The results of the comparative analysis are given in Table 1. There was no significant difference between the patient group with a SYNTAX score <19 and the patient group with a SYNTAX

Table 1. *Demographic, clinical, and laboratory characteristics*

	Overall (n=335)	Syntax Score <19 (n=164)	Syntax Score ≥19 (n=171)	P-value
Male, n (%)	275 (82.1)	134 (48.7)	141 (51.3)	0.887
Age (years), mean ± SD	56.4±11	55.1±11	57.7±10	0.035
WMR	1.41 (1.20–1.64)	1.32 (1.16–1.5)	1.56 (1.28–1.81)	<0.001
Killip class 2–4, n (%)	64 (19.1)	15 (9.1)	49 (28.7)	<0.001
Ejection Fraction (%) median [IQR]	45 (40–50)	45 (41.5–52)	44 (35–50)	<0.001
Initial Vital Signs				
SBP (mmHg), median [IQR]	135 (120–147)	130 (119–140)	135 (121–161)	0.015
Heart Rate, median [IQR]	80 (70–88)	78 (70–85)	82 (71–92)	0.016
Laboratory findings at admission				
Hgb (g/dL), median [IQR]	13.9 (13–15.1)	13.8 (12.9–14.9)	14 (13.1–15.2)	0.223
WBC (× 10^3/μL), median [IQR]	12.8 (11.1–14.5)	11.9 (10.4–13.6)	13.8 (12.1–16.2)	<0.001
PLT (× 10^3/μL), median [IQR]	260 (222–298)	257 (216–290)	261 (225–301)	0.201
MPV	9 (8.2–9.8)	9 (8.2–10)	9 (8.2–9.8)	0.816
Neutrophil	10 (8–11.9)	8.87 (7.55–10.73)	11 (9.15–13.35)	<0.001
Lymphocyte	1.8 (1.28–2.5)	1.8 (1.29–2.41)	1.7 (1.26–2.5)	0.878
eGFR (mL/min), mean ± SD	85±23	89±23	81±23	0.002
Comorbidities				
Hypertension, n (%)	153 (45.7)	63 (38.4)	90 (52.6)	0.012
Diabetes, n (%)	78 (23.3)	30 (18.3)	48 (28.1)	0.039
Cigarette smoking, n (%)	190 (56.7)	94 (57.3)	96 (56.1)	0.912
COPD, n (%)	19 (5.7)	8 (4.9)	11 (6.4)	0.639
CKD (eGFR <60 mL/min/m^2), n (%)	34 (10.1)	12 (7.3)	22 (12.9)	0.105

WMR: white cell blood count to mean platelet volume; SBP: systolic blood pressure; Hgb: hemoglobin; WBC: white blood cell count; PLT: platelet; MPV: mean platelet volume; eGFR: estimated glomerular filtration rate; BNP: B type natriuretic peptide; CRP: C-reactive protein; CK: creatine kinase; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; SBP: systolic blood pressure; WBC: white blood cell count.

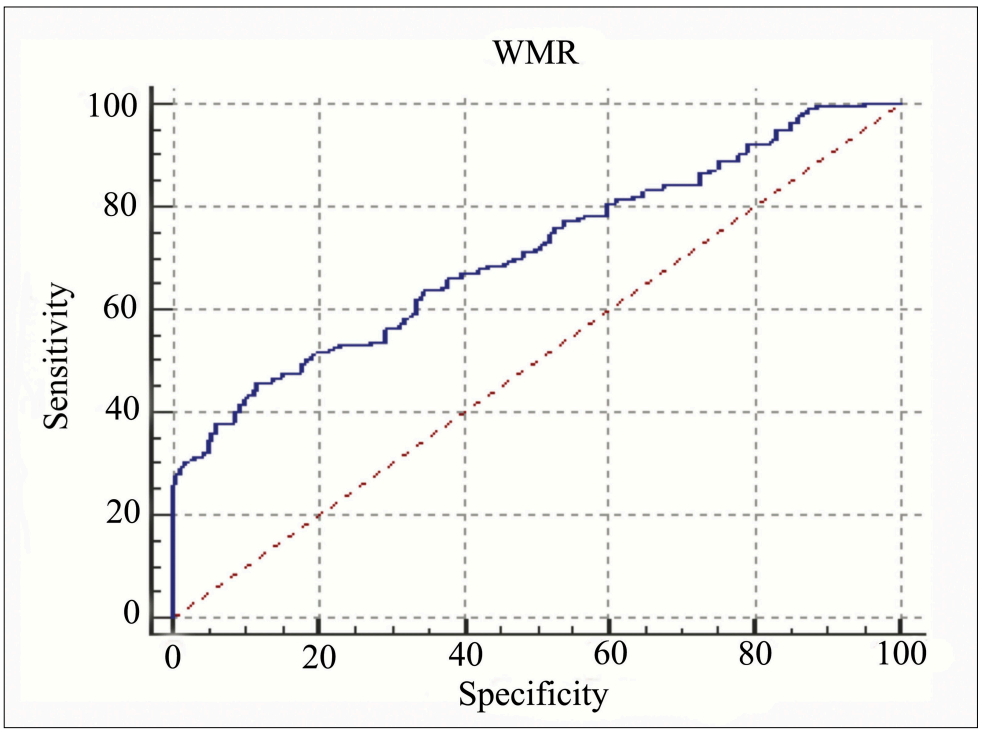

Figure 1. *Receiver operating characteristic (ROC) curve analysis of the WMR for Syntax Score ≥19.*

Table 2. *Univariable and multivariable predictors of syntax score*

	Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	P value	OR (95% CI)	P-value
Age	1.02 (1.00–1.04)	0.034	1.03 (1.00–1.06)	0.031
WMR	20 (8.46–51.68)	<0.001	1.26 (1.08–1.47)	0.002

OD: odds ratio; WMR: white cell blood count to mean platelet volume; SBP: systolic blood pressure; WBC: white blood cell count; eGFR: estimated glomerular filtration rate; CK: creatine kinase.

score ≥19 in terms of gender, smoking status, presence of chronic obstructive pulmonary disease (COPD), and chronic kidney disease (CKD), and hemoglobin (Hgb), platelet (Plt), MPV, and lymphocyte values. The number of patients with Hypertension (HT) and Diabetes Mellitus (DM) was significantly higher in the patient group with a SYNTAX score ≥19 than in the patient group with a SYNTAX score <19. In addition, the mean age of the patient group with a SYNTAX score ≥19 was also significantly higher than the patient group with a SYNTAX score <19 (55.1±11 years vs. 57.7±10 years, p=0.035). White blood cell count to mean platelet volume ratio value was statistically significantly higher in the patient group with SYNTAX score ≥19 (OR: 1.56; 95% CI: 1.28–1.81) compared to the patient group with SYNTAX score <19 (OR: 1.32; 95% CI: 1.16–1.5) (p<0.001). Additionally, according to the Killip classification, the number of patients with class 2–4 symptoms was higher in the patient group with a SYNTAX score ≥19 compared to the patient group with a SYNTAX score <19.

The ejection fraction (EF) was significantly higher in the patient group with a SYNTAX score <19 compared to the patient group with a SYNTAX score ≥19 [45% (min: 41.5, max: 52) vs 44% (min: 35, max: 50), p<0.001].

A comparison of patients' vital signs values at admission revealed that the number of patients with low systolic blood pressure (SBP) and high heart rate was significantly higher in the patient group with a SYNTAX score of ≥19 compared to the patient group with a SYNTAX score of <19.

Additionally, the mean glomerular filtration rate (GFR) of the patient group with a SYNTAX score <19 was significantly higher than the patient group with a SYNTAX score of ≥19 (89±23 vs. 81±23, p=0.002).

The Pearson correlation coefficient between the WMR value and SYNTAX score was calculated as 0.415 (p<0.001). White blood cell count to mean platelet volume ratio was significantly higher in the patient group with a SYNTAX score ≥19 than in the patient group with SYNTAX score <19[median WMR (interquartile range (IQR): 1.56 (min: 1.28, max: 1.81) vs. 1.32 (min: 1.16, max: 1.5), p<0.001]. The results of the multivariate analysis indicated that WMR was an independent predictor [OR: 1.26 (min: 1.08, max: 1.47) (95% CI), p=0.002] (Table 2).

The results of the ROC analysis of WMR in the patient group with a SYNTAX score ≥19 are shown in Fig. 1. The cut-off value was determined as 1.6044×10^3/μL, with a sensitivity of 45.61% and a specificity of 88.41%. The AUC was calculated as 0.708.

Discussion

The findings of the study revealed a significant correlation between WMR values and high SYNTAX scores in patients who underwent angiography for STEMI. In addition, WMR was found to be an independent predictor based on the results of the multivariate analysis. It has long been recognized that inflammation contributes in a complex way to the development, progression and destabilization of atherosclerotic plaques. Platelets, leukocytes, and vascular endothelial cells trigger atherosclerotic plaque rupture in ACS by interacting with each other through a series of inflammatory mediators or markers that act simultaneously[12].

The SYNTAX scoring system is one of the most useful tools that objectively measures the severity of CAD in daily clinical and interventional practices. As is known, the SYNTAX scoring system is an anatomical scoring system that can measure the morphology, location and type of the lesion in patients with CAD[4]. The relationship between high SYNTAX scores and poor cardiovascular outcomes has also been reported[4].

It has been previously reported that several hematological indicators such as WBC, RDW, and MPV/lymphocyte ratio have prognostic value in predicting the SYNTAX score in ACS patients[7,9,13,14]. The MPV value, which refers to the mean platelet volume, is one of the parameters related to platelet activation. It is known that larger platelets are more active and thrombogenic[15]. On the other hand, it has been reported in different studies that an increase in the WBC count strongly predicts morbidity and mortality in addition to the SYNTAX score in ACS patients[16]. There are studies in the literature examining the relationship of WMR with SYNTAX scores or CAD severity in ACS patients[7,9].

The number of patients with HT and DM was significantly higher in the patient group with a SYNTAX score ≥19 compared to the patient group with a SYNTAX score <19 (p=0.012 and p=0.039, respectively). It is known that diabetes, especially DM or type 2 diabetes, is a risk factor for CAD[17]. The PROCAM (Prospective Cardiovascular Munster) study, in which myocardial infarction patients were followed for 4 years, revealed a strong correlation between HT and CAD[18].

The mean age of the patient group with a SYNTAX score ≥19 was higher than the patient group with a SYNTAX score <19. Indeed, in another study, age was found to be an independent predictor of the SYNTAX score[19].

The comparison of the GFR values of the two groups indicated that the mean GFR of the patient group with a SYNTAX score <19 was significantly higher than the patient group with a SYNTAX score of ≥19. Similarly, it was reported in another study that GFR was a strong predictor of high SYNTAX scores[19].

Given that steroid group drugs can affect the WBC subgroups of the patients, patients using these drugs were excluded from the study. The increase in the WBC count due to glucocorticosteroids (GCS) is referred to as "glucocorticoid-induced leukocytosis". Contrary to the said increase in the WBC count mainly in neutrophilic cells, the number of other circulating cells, especially eosinophils, decreases[20].

White blood cell count to mean platelet volume ratio values cannot replace clinical assessment, coronary angiography, and markers of myocardial injury. However, the results of this study demonstrated that WMR values can be used in the initial clinical evaluation of patients with STEMI in an integrated manner with other assessment tools.

Conclusion

The findings of this study revealed a significant correlation between the WMR values and high SYNTAX scores in STEMI patients. In this context, WMR can provide supportive data in predicting the severity of CAD in STEMI patients, in the early risk stratification of STEMI patients, and in determining an optimized

therapeutic approach. This way, the necessary therapeutic methods can be better planned to avoid a possible poor outcome in STEMI patients. However, large-scale studies are needed on using WMR values in clinical practice.

Exclusion Criteria from the Study

Exclusion criteria from the study were lack of patient consent, use of steroid or non-steroidal anti-inflammatory drugs, and the presence of blood disorders that could affect blood parameters, including cytopenia.

Limitations of the Study

As seen in comparable studies, the study's retrospective, observational, nonrandomized, single-center design inherently included limitations and biases.

Conflict of interest disclosure

All authors have no conflict of interest.

Statement of Ethics

The local ethics committee approved the study protocol (Ethics Committee of Kafkas University Faculty of Medicine) (Approval No: 80576354-050-99/197).

Informed consent was obtained from all patients.

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