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# The association between red cell distribution width to total calcium ratio and syntax score in patients with acute coronary syndrome

Akut koroner sendromlu hastalarda kırmızı hücre dağılım genişliğinin total kalsiyuma oranının syntax skoru ile ilişkisi

Uğur Küçük <sup>1</sup>	
<sup>1</sup> Department of Cardiology, Numune State Hospital, Sivas, Turkey	Abstract Aim: The relationship of both red blood cell distribution width (RDW) and Syntax risk score with prognosis and mortality in patients
ORCID ID of the author(s) UK: 0000-0003-4669-7387	with acute coronary syndrome (ACS) has been shown. Besides, there is insufficient information about the use of red cell distribution width to total serum calcium (RDW-to-TSC) ratio in patients with ACS. We aimed to research the relationship between RDW-to-TSC and Syntax risk scores in our study. Methods: For our retrospective cohort study, 270 patients hospitalized in the cardiology intensive care unit with the diagnosis of myocardial infarction between January 2019 and December 2019 were screened. A total of 115 patients who were eligible were included
	in the study. The patients were classified into two groups: 58 had NSTE-ACS and 57 had STEMI. The included age range was 18-80 years. RDW-to-TSC was calculated as the ratio of red cell distribution width to total serum calcium count. By using Pearson's correlation analysis, the relationship between RDW-TAF ratio and Syntax score was obtained. Results: Among 115 patients, there were 50 males (43.5%), and 65 females (56.5%). The mean age was 58.09 (9.55) years. There were more hypertensive patients in the NSTE-ACS group ( <i>P</i> =0.003). There was no statistically significant difference in RDW-to-TSC ratio
	between the two groups ( $P=0.809$ ). The correlation of RDW and RDW / TSC ratio with syntax score were statistically significant ( $P<0.001$ ). ( $P<0.001$ ). Conclusions: RDW-to-TSC ratio is a simple, cost-effective, and readily available test in all health centers. This may be used as a risk
	calculation tool like the Syntax score for patients with ACS. <b>Keywords:</b> Acute coronary syndrome, Serum calcium, Red cell distribution width
Corresponding author/Sorumlu yazar:	Öz Amaç: Eritrosit dağılım genişliğinin (RDW) ve Syntax risk skorunun akut koroner sendrom (AKS) tanılı hastalarda prognoz ve mortalite ile ilişkileri gösterilmiştir. Bununla birlikte eritrosit dağılım genişliğinin serum kalsiyuma oranı (RDW/TSK) ile ilgili yeterli bilgiler yoktur. Bu çalışmanın amacı RDW-TSK oranının Syntax risk skoru ile ilişkisini araştırmayı hedefledik. Yöntemler: Çalışmamız retrospektif kohort çalışması olup, Ocak 2019-Aralık 2019 tarihleri arasında kardiyoloji yoğun bakım ünitesinde
Uğur Küçük Address/Adres: Numune Devlet Hastanesi Kardiyoloji Kliniği, Sivas, Türkiye E-mail: drugurkucuk@hotmail.com Ethics Committee Approval: All procedures in	miyokard enfarktüsü tanısı ile yatşı olan 270 hasta tarandı. Dışlama kriterlerinden sonra uygun olan 115 hasta çalışmaya alındı. Bu alınan hastaların 58 tanesi NSTE-AKS'li ve 57 tanesi STEMI olarak iki gruba sınıflandırıldı. Çalışmaya 18-80 yaş arası hastalar dahil edildi. RDW-TSK, eritrosit dağılım genişliğinin toplam serum kalsiyum sayısına oranı olarak hesaplandı. Pearson korelasyon analizi kullanılarak RDW-TSK oranı ile Syntax skoru arasındaki ilişki elde edildi. Bulgular: 115 hastanın 50 tanesi erkek (%43,5), 65 tanesi kadın (%56,5) ve ortalama yaşları 58,09 (9,55) yıldı. NSTE-AKS grubunda
this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments. Etik Kurul Onayı: İnsan katılımcıların katıldığı çalışmalardaki tüm prosedürler, 1964 Helsinki Deklarasyonu ve daha sonra yapılan değişiklikler uyarınca gerçekleştirilmiştir.	daha fazla hipertansiyon hastasi vardı ( $P$ =0,003). Gruplar arasında RDW / TSK oranında istatistiksel olarak anlamlı fark yoktu ( $P$ =0,809). RDW ve RDW / TSK oranı korelasyonu syntax skoru ile istatistiksel olarak anlamlı idi ( $P$ <0,001). Sonuç: RDW / TSK oranı, tüm sağlık merkezlerinde basit, uygun maliyetli ve kolay ulaşılabilir bir testtir. Bununla birlikte AKS hastalarında Syntax skoru gibi risk hesaplama aracı olabilir. <b>Anahtar kelimeler:</b> Akut koroner sendrom, Serum kalsiyum, Eritrosit dağılım dağıtım genişliği
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# Introduction

Despite advances in technology and medicine, coronary artery diseases (CAD) have significant mortality and morbidity rates. Acute coronary syndromes (ACS) are responsible for the largest proportion of deaths worldwide. ACS is examined under two groups, ST elevated acute coronary syndrome (STEMI) and Non-ST elevated acute coronary syndrome (NSTE-ACS) [1].

In cardiology practice, risk and lesion classification of the coronary artery disease and life expectancy are the most significant problems in patients diagnosed with ACS. There are many related invasive and noninvasive tests. Many cardiac risk classification tests such as Grace, Syntax, Gensini provide information on mortality and morbidity [2-4]. Unfortunately, many parameters are needed to calculate such risk scoring tests in patients diagnosed with ACS, and for some scores, images obtained from coronary angiography (CAG) are used. There are recent studies showing the relationship between the cost effective and easy-to-calculate tests such as the red cell distribution width (RDW) blood test. C-reactive protein (CRP), Neutrophil/lymphocyte ratio (NLR), Monocyte/lymphocyte ratio (MLR) with cardiac risk scores [5]. Although there are enough studies on both cardiac and noncardiac diseases associated with RDW, studies on the ratio of the red cell distribution width (RDW) to total serum calcium (RDW-to-TSC) are insufficient.

The studies conducted with RDW in the literature showed an association of RDW-to-TSC with mortality, morbidity and cardiac risk scores in cardiovascular diseases, however, data related to whether RDW-to-TSC rate could be used as a risk score in patients with ACS are limited [6]. Syntax score is associated with increased mortality and morbidity in patients with ACS, and in our study, we aimed to investigate the relationship between the RDW-TSC ratio and Syntax risk scores.

### Materials and methods

Our retrospective cohort study consists of 115 patients who were hospitalized in the coronary intensive care unit between January 2019 and December 2019. It includes patients older than 18 years and younger than 80 years of age. In the STEMI and NSTE-ACS groups, there were 57 and 58 patients, respectively. Out of 270 patients who were admitted to the emergency department of our hospital with chest pain and diagnosed with ACS, 115 underwent coronary angiography (CAG) after meeting the appropriate criteria. Stenoses of 50% and above were considered significant in at least one coronary artery. Consent form was obtained from all patients before the procedure.

The study excluded patients who underwent coronary artery bypass graft (CABG) surgery but did not want to receive further CAG, patients with renal insufficiency (serum creatinine level >1.5 mg/dL), moderate to severe valvular disease, liver failure (liver function values greater than twice the upper limit of the 'normal' value), hypertrophy, chronic obstructive pulmonary disease (COPD), septic manifestations, and diagnosis of malignancy.

The patients were diagnosed with STEMI and NSTE-ACS in accordance with current guidelines and treatment was initiated accordingly [7]. STEMI was defined as ST-segment elevation of 0,1 mV in all leads in both genders at the J- point in two continuous leads except for in V2–V3, where 0.2 mV was required for males older than 40 years old, 0.25 mV was required for males younger than 40 years old and 0.15 mV was required for females, new-onset left bundle-branch block, new-onset wall motion abnormalities and troponin elevation. NSTE-ACS was defined as troponin levels above the 99<sup>th</sup> percentile of the upper normal reference limit, ischemic symptoms such as chest pain lasting longer than 20 minutes and the absence of ST- segment elevation on ECG.

Hypertension was defined as antihypertensive medication use or systolic blood pressure above 140 mmHg and diastolic blood pressure above 90 mmHg. Diabetes mellitus was defined as fasting blood glucose  $\geq$ 126 mg / dL or drug use for glucose regulation.

# Calculation of coronary angiography and Syntax Score

Coronary angiography (CAG) was performed via the femoral or radial arteries using standardized Judkins technique. Each coronary artery was evaluated with at least two different images. Percutaneous coronary intervention was performed using the standardized technique. The Syntax score was calculated using the most up-to-date system for vessels with a stenosis over p value and a diameter of  $\geq 1.5$  mm (www.syntaxscore.com) [8]. Based on the calculated Syntax score, patients were divided into two groups - those having a score of 22 and below (considered low), and those having a score of 23 and above (considered moderate- high).

#### Laboratory measurements

A hematology analyzer was used to calculate hemogram parameters and other biochemical measurements (Abbott Cell-Dyn 3700; Abbott Laboratory, Abbott Park, Illinois, US And Abbott Architect C16000 auto-analyzer (Architect C16000 autoanalyzer; Abbott Laboratory, Abbott Park, Illinois, USA), which were located in the laboratory of our institution. RDW-to-TSC ratio was calculated as RDW count divided by TSC.

### Statistical analysis

SPSS 21.0 (IBM 1989, 2012) package program was used for all statistical analyses. Kolmogorov-Smirnov test was used for normal distribution assumptions of continuous variables. Continuous variables were presented as mean (standard deviation) and comparison was made with the Student's t-test. Correlation analysis was performed using Pearson test. *P*-value <0.05 was considered statistically significant.

### Results

The study included 115 patients with acute coronary syndrome. Mean age of the patients was 58.09 (9.55) years. Sixty-one (53%) patients were male and 54 (47%) were female. Fifty-seven patients were assigned to the STEMI group and 58 patients, to the NSTE-ACS group.

Demographic, clinical and laboratory information of the patients are summarized in Tables 1 and 2. Except for hypertension and age, there was a numerical difference between the demographic, clinical and laboratory values between the groups, which was not statistically significant (P>0.05 for each). RDW-to-TSC ratios were 1.49 (0.18) in the STEMI group, and 1.48 (0.16) the NSTE-ACS group.

Syntax scores were 14.63 (2.03) and 14.75 (1.77) in the STEMI and NSTE-ACS groups, respectively (Table 2). There was a positive correlation between SYNTAX score and RDW and RDW-to-TSC ratio (r=0.670, P<0.001 and r=0.939, P<0.001, respectively) (Table 3).

Table 1: Baseline clinical, demographic	features and laboratory findings
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	STEMI	NSTE-ACS	P-value
	(n=57)	(n=58)	
Age, mean (SD)	59.94 (9.66)	45.94 (14.96)	0.039
Glucose (mg/dL) mean (SD)	119.62 (31.12)	123.19 (13.17)	0.374
Creatinine, mg/dL	0.82 (0.15)	0.78 (0.16)	0.192
Hypertension, (n)	28	44	0.003
Diabetes mellitus, (n)	14	20	0.244
Hemoglobin, g/L	13.24 (1.23)	13.50 (1.42)	0.298
Platelet count, x103/µL	235.24 (44.73)	237.98 (49.14)	0.755
WBC count, x10 <sup>3</sup> /µL	11.73 (2.24)	12.00 (2.42)	0.527
Total serum calcium (mg/dl)	8.99 (0.72)	9.05 (0.75)	0.676

NSTE-ACS: Non-ST elevated acute coronary syndrome, STEMI: ST elevated acute coronary syndrome, WBC: white blood cell

Table 2: Biochemical and Syntax score measurements of the two groups

	STEMI	NSTE-ACS	P-value
RDW (%)	13.30 (1.12)	13.34 (1.13)	0.877
RDW-to-TSC ratio	1.49 (0.18)	1.48 (0.16)	0.809
SYNTAX score	14.63 (2.03)	14.75 (1.77)	0.956

RDW: red cell distribution width, RDW-to-TSC ratio: red cell distribution width to total serum calcium ratio Table 3: Correlation of RDW and RDW-to-TSC ratio with Syntax score

	Syntax score	
	r	P-value
RDW	0.670	< 0.001
RDW-to-TSC ratio	0.939	< 0.001

RDW: red cell distribution width, RDW-to-TSC ratio: red cell distribution width to total serum calcium ratio

Correlation analysis revealed a significant relationship between the Syntax score and the RDW-to-TSC ratio, which is presented in Figure 1 (r=0.836, P < 0.001).

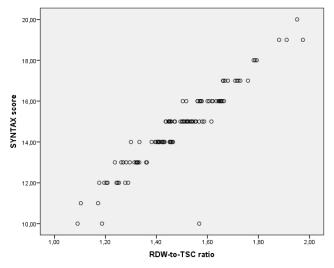


Figure 1: The relationship between RDW-to-TSC ratio and SYNTAX score in patients with acute coronary syndrome

#### Discussion

Atherosclerosis occurs at an early age and is seen as "fat lines" in the coronary arteries. ACS is one of the leading causes of death due to its onset at young ages. Identifying patients at risk will reduce costs, as well as mortality and morbidity [9]. The risk scores for patients with ACS allow us to identify patients at risk in clinical practice and to take important precautions such as lifestyle changes. There are many risk scores on this subject, including GRACE, SYNTAX, TIMI, and GENSINI.

Syntax risk score not only provides valuable information regarding the number, importance, and location of angiographic lesions, but it is also a predictor of elevated mortality and morbidity in patients with CAD [10]. Since the Syntax score is complex and time consuming, simpler tests are needed. Recently, RDW has been shown to be associated with risk scores in many domains and has established its place in clinical practice. RDW is a strong risk factor for mortality in patients with systemic inflammation, stroke, chronic kidney disease and coronary artery [11]. In their study, Nagula et al. [12] demonstrated that RDW is a marker that can be used in predicting coronary artery disease and severity of coronary artery stenosis. In another study, Magri et al. [13] demonstrated that RDW is an independent marker in predicting myocardial scar tissue and left ventricular functions. There are adequate number of studies regarding RDW in patients diagnosed with CAD; however, the studies on the RDW-to-TSC ratio are limited.

The study by Gravito-Soares et al. [14] demonstrated that RDW-to-TSC ratio is a good marker in predicting mortality in patients with acute pancreatitis.

As the syntax score increases in patients diagnosed with ACS, mortality and morbidity increase simultaneously. It is known that treatment alternatives that can be applied according to the severity of coronary artery disease determined by the score will contribute to the prognosis of the patient. Since calculating the syntax score is difficult and time-consuming, clinicians need a score that can be calculated quickly and easily. As a result of our study, we showed that RDW and Syntax scores were correlated in patients diagnosed with acute coronary syndrome, as in previous studies. In addition, we showed that there was a relationship between the RDW-to-TSC ratio and the Syntax risk score, on which there are few studies [15].

#### Limitations

The major limitations of our study include its retrospective nature and the small number of cases, since most of the patients' past information could not be reached. Multi-center studies will provide realistic and meaningful statistical results.

#### Conclusion

Syntax score has been proven to correlate with mortality and morbidity in CAD patients, and the RDW-to-TSC ratio is feasible for use in patients with ACS. As a result of our work, we showed that there is a positive relationship between RDW-to-TSC ratio and Syntax risk score. RDW-to-TSC ratio is a simple, cost-effective, and readily available test in all health centers, which we can use in clinical practice to learn about the patients' cardiac risk score and take necessary precautions to minimize risks.

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