Predictive value of mean platelet volume in young patients with non-ST-segment elevation acute coronary syndromes: a retrospective observational study

ST-yükselmesiz akut koroner sendromlu genç hastalarda ortalama trombosit hacminin öngördürücü değeri: Geriye dönük gözlemsel bir çalışma

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ABSTRACT

Objective: Platelets play an important role in both initiation and propagation of acute coronary syndromes. We sought to evaluate the predictive value of mean platelet volume (MPV) in young patients with non-ST-segment elevation acute coronary syndromes (NSTE-ACS).

Methods: This is a retrospective observational study; evaluating the MPV values of 79 NSTE-ACS patients aged under 45 years and 45 control subjects having normal coronary anatomy. NSTE-ACS group was composed of 41 non-ST elevation myocardial infarction (NSTEMI) and 38 unstable angina pectoris (USAP) patients. MPV was measured using an automated hematologic analyzer called Coulter counter. The predictive value of MPV was evaluated using logistic regression analysis and comparison of MPV between NSTE-ACS and control groups was performed by Mann-Whitney U test.

Results: The MPV was found to be significantly higher in the NSTE-ACS compared with control group (8.49±1.22 versus 7.78±0.65 fL, p=0.001). In logistic regression analysis, MPV was found to be an independent predictor of NSTE-ACS (OR=3.1, 95% CI 1.2-8.2, p=0.022). The MPV values of NSTEMI group were not significantly different from USAP group (8.78±1.38 versus 8.17±0.95 fL, p=0.66). Similarly, the MPV values of the 3 groups (Control, USAP and NSTEMI) were found to be significantly different (7.78±0.65, 8.18±0.95, 8.78±1.38 fL respectively, p=0.001).

Conclusion: In conclusion, MPV was found to be elevated in NSTE-ACS patients compared with control subjects in young population. In addition, increased MPV was established to be an independent predictor of NSTE-ACS. *(Anadolu Kardiyol Derg 2013; 13: 57-61)*

Key words: Young patients, acute coronary syndrome, mean platelet volume, regression analysis

ÖZET

Amaç: Trombositler akut koroner sendromların oluşumu ve ilerlemesinde önemli bir rol oynamaktadır. Bu çalışmada ST yükselmesi olmayan akut koroner sendromlu (NSTE-AKS) genç hastalarda ortalama trombosit hacminin öngördürücü değerini araştırmayı amaçladık.

Yöntemler: Bu, 45 yaş altındaki 79 NSTE-AKS hastasının ve normal koroner anatomiye sahip 45 kontrol bireyinin MPV değerlerini karşılaştıran geriye dönük gözlemsel bir çalışmadır. NSTE-AKS grubunu 41 ST yükselmesi olmayan miyokart enfarktüsü (NSTEMI) ve 38 kararsız angina pektoris (USAP) hastası oluşturmuştur. MPV, Coulter Sayaç adı verilen otomatik bir hematolojik tahlil cihazı kullanılarak ölçülmüştür. MPV'nin prediktif değeri lojistik regresyon analizi kullanılarak ve NSTE-AKS ve kontrol grupları arasında MPV karşılaştırılması Mann-Whitney U testi ile değerlendirilmiştir.

Bulgular: NSTE-AKS grubundaki MPV değerleri kontrol grubuna göre anlamlı olarak yüksek bulundu (8.49±1.22'a karşılık 7.78±0.65 fL, p=0.001). Lojistik regresyon analizinde, MPV'nin NSTE-AKS'nin bağımsız bir belirleyicisi olduğu bulunmuştur (OR=3.1, %95 CI 1.2-8.2, p=0.022). NSTEMI grubunda MPV değerleri USAP grubundan anlamlı olarak farklı değildi (8.78±1.38 versus 8.17±0.95 fL, p=0.66). Benzer

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Accepted Date/Kabul Tarihi: 29.08.2012 **Available Online Date/Çevrimiçi Yayın Tarihi:** 19.10.2012

doi:10.5152/akd.2013.007

şekilde, 3 grubun (Kontrol, USAP ve NSTEMI) MPV değerleri arasında anlamlı derecede farklılık olduğu tespit edilmiştir (7.78±0.65, 8.18±0.95, 8.78±1.38 fL respectively, p=0.001).

Sonuç: Sonuç olarak, kontrol grubu ile karşılaştırıldığında genç NSTE-AKS hastalarında MPV değerleri daha yüksek bulunmuştur. Aynı zamanda artmış MPV, NSTE-AKS'ın bağımsız bir belirleyicisi olarak bulunmuştur.

(Anadolu Kardiyol Derg 2013; 13: 57-61)

Anahtar kelimeler: Genç hastalar, akut koroner sendromlar, ortalama trombosit hacmi, regresyon analizi

Introduction

Platelets play a key role in both initiation and propagation of acute coronary syndromes (ACS) (1, 2). Mean platelet volume (MPV) is an important hematologic variable and indicator of platelet function (3, 4). Larger platelets are more active and have higher thrombotic potential (5, 6). They are also denser (7), have higher thromboxane A2 levels (8), and express more glycoprotein Ib and IIb/IIIa receptors (9), thus, larger platelets are aggregate more rapidly with collagen than smaller platelets (10). In a recent trial, high MPV was found to be an independent predictor of ST-segment elevation myocardial infarction (STEMI) in young patients (11).

Non-ST-segment elevation acute coronary syndrome (NSTE-ACS) differs from STEMI with a pathophysiological background involving mainly platelets rather than the Şbrin pathway (1). Thus, platelets play a central role in the pathogenesis of NSTE-ACS.

Young persons with ACS display a unique risk profile compared with older patients (12, 13). ACS are most frequently seen in older population; only a little part of acute coronary syndromes occurs among young population. Although its prevalence is increasing among young people, there are limited numbers of studies about the predictors of ACS in young patients (12, 13).

In this regard, we hypothesized that an increased mean platelet volume predicts development of NSTE-ACS and we evaluated the MPV of young patients with NSTE-ACS and control subjects in this study.

Methods

Study design

This is a retrospective observational study.

Study population

Overall, 79 patients, younger than 45 years old, with the diagnosis of NSTE-ACS (41 NSTEMI, 38 USAP) were included in the study. The control group was comprised of 45 subjects, who were younger than 45 years old with normal coronary arteries. All the NSTE-ACS patients had been hospitalized within the first 24 hour of their chest pain between May 2009 and February 2011. Only patients with the first acute coronary event were assessed. Permission for the study was obtained from local ethics committee of Abant İzzet Baysal University.

Data collection and definitions

Hospital medical records were retrospectively analyzed. Diagnosis of NSTEMI or USAP was made by assessing unstable chest pain, typical electrocardiographic changes and/or elevation of cardiac enzymes (1). Also medical history, drug use, body mass index (BMI) and the other risk factors like diabetes mellitus, hypertension, hyperlipidemia, and cigarette smoking were recorded. Hypertension was diagnosed according to the Joint National Committee (JNC) 7 report as blood pressure above 140/90 mmHg or having anti-hypertensive therapy (14). Diabetes mellitus was diagnosed as one of these criteria; Symptoms of diabetes plus any time plasma glucose concentration ≥200 mg/dL, FPG ≥126 mg/dL, 2-h post load glucose ≥200 mg/dL (11.1 mmol/l) during an OGTT or active use of anti-diabetic treatment (15) Family history of CAD was diagnosed if patients had a first degree male relative under 55 years of age or a female relative less than 65 years of age with CAD (1). Patients who were smoking before hospitalization were accepted as smokers. Coronary angiography was performed by the Judkin's technique.

Laboratory analysis

Blood samples were obtained into blood collection tubes with ethylenediaminetetraacetic acid from all patients on admission in all cases. Hemoglobin, platelet count and MPV measurements were performed within approximately 60 minutes after blood sampling with Coulter LH 780 Analyzer and Coulter Hmx Hematology Analyzer (Beckman Coulter, Inc. CA, USA) with original method and reagents. LDL-C was calculated using the Friedewald formula. The other laboratory parameters were determined with standard methods.

Statistical analysis

Statistical analyses were performed the SPSS software version 15.0 (SPSS Inc. IL, USA). Continuous variables were presented as mean±standard deviation. Nominal variables were presented as the percentage. As the MPV was not normally distributed, shown by Kolmogorov-Smirnov test, Mann-Whitney U test was conducted in the comparison of MPV of NSTE-ACS and control group. The MPV values of the 3 groups (Control, USAP and NSTEMI) were compared with Kruskal-Wallis tests. The univariate analyses to identify variables associated with patient outcome (NSTE-ACS) was investigated using Chi-square, Fisher exact, Student's t and Mann-Whitney U tests, where appropriate. For the multivariate analysis, the possible factors identified with univariate analyses were further entered into logistic regression analysis to determine the independent pre-

dictors of NSTE-ACS. Hosmer-Lemeshow goodness of fit statistics was used to assess model fit. A 5% type-I error level was used to infer statistical significance.

Results

Demographic, medical and biochemical characteristics of controls and patients with NSTE-ACS are shown in Table 1. Hypertension, diabetes mellitus, smoking and family history were significantly higher in NSTE-ACS patients. In addition, high-density lipoprotein levels were significantly lower and triglycerides were significantly higher in NSTE-ACS patients. There was no difference in platelet counts between the groups (p=0.874).

The MPV was found to be significantly higher in the NSTE-ACS compared with control group (8.49±1.22 versus 7.78±0.65, p=0.001) (Fig. 1). In addition, the MPV values of NSTEMI group were not significantly different from USAP group (8.78±1.38 versus 8.17±0.95, p=0.66). The mean of the MPV values were found to be significantly different among 3 groups (Control, USAP and NSTEMI) (7.78±0.65, 8.18±0.95, 8.78±1.38 respectively, p=0.001) (Fig. 1).

According to the logistic regression analysis, male gender, smoking, body mass index and MPV were found to be independent predictors of NSTE-ACS (Table 2). The fit of the developed model was tested using Hosmer-Lemeshow test. The p value of this test was found to be 0.28, meaning that the model had a high prediction value. Also, it was estimated that one unit increase in the MPV leads to 3.1 fold increased risk of NSTE-ACS.

Discussion

The main findings of the present study are; increased MPV was found to be an independent predictor of NSTE-ACS in young patients and MPV of the young patients with NSTE-ACS was found to be significantly higher than the MPV of the subjects of control group.

In acute coronary syndromes, a thrombogenic medium usually arises around the atherosclerotic plaque, and this can lead to adverse clinical outcomes. The thrombus formed on the disrupted endothelium can enlarge after plaque rupture or erosion. Platelet functions are very important, especially in the pathophysiology of arterial thrombosis. MPV is an important marker of platelet activity, which is measured as aggregation, vasoactive amine release, or the expression of specific receptors (16, 17).

The metabolic and enzymatic activity of the platelets increase as the platelet volume increases (18). The vasoactive mediators secreted by the platelets may contribute the inflammatory and atherogenesis process. So, increased risk of acute coronary syndromes in young patients with high MPV may be explained with the increased activity of platelets, increased inflammation and increased platelet aggregation (19).

Table 1. Demographic, medical and biochemical characteristics of controls and patients with NSTE-ACS

Variables	NSTE -ACS (n=79)	Control (n=45)	*p
Age, years	41.0±4.3	40.9±5.2	0.058
Gender, M/F, n	58/21	30/15	<0.0001
Smoking, n (%)	54 (68.3)	4 (8.2)	<0.0001
Hypertension, n (%)	27 (34.1)	3 (6.7)	<0.0001
Diabetes mellitus, n (%)	9 (11.3)	1 (2.2)	0.035
Family history, n (%)	38 (48.1)	5 (11.1)	0.001
Hemoglobin, g/dL	14.6±1.6	13.6±1.5	0.002
MPV, fL	8.49±1.22	7.78±0.65	0.001
Platelet count, x10^3	267±79	263±74	0.874
TC, mg/dL	182.8±36.2	173.1±34.1	0.136
LDL, mg/dL	107.5±32.3	102.8±27.2	0.319
HDL, mg/dL	32.8 ± 6.2	41.1±7.3	<0.0001
Triglyceride, mg/dL	213±98	126±58	<0.0001

Data are presented as mean±SD, median (interquartile range) and number (percentage)
*Independent sample t-test, Mann-Whitney U test and Chi-square tests
HDL- high- density lipoprotein, LDL-low-density lipoprotein, MPV- mean platelet volume, NSTE-ACS- non-ST elevation acute coronary syndromes, TC-total cholesterol

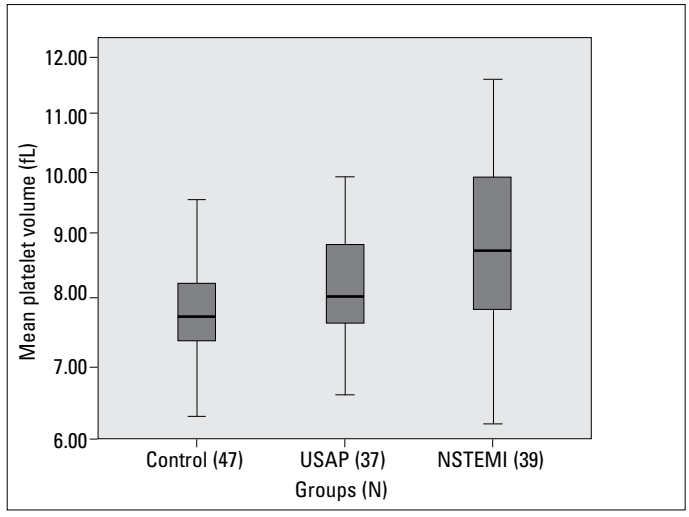

Figure 1. Mean platelet volumes of patients with NSTE-ACS and control subjects (Mean values; Control: 7.78 fL, USAP: 8.18 fL, NSTEMI: 8.78 fL)
*Kruskal-Wallis test Chi-square=15,134, p for trend <0.001

Table 2. Independent predictors of NSTE-ACS

Risk factors	RR (95% CI)*	*p
Sex(male)	89.2 (4.6-1747.8)	0.003
Smoking	18.2 (3.5-93.0)	0.001
BMI	1.8 (1.2-2.7)	0.007
MPV	3.1 (1.2- 8.2)	0.022

* Logistic regression analysis
BMI - body mass index, MPV - mean platelet volume, NSTE-ACS - non-ST elevation acute coronary syndromes, RR - the estimated relative risk shown by odds ratio and 95% confidence interval

Many studies of MPV in ACS have been published. In one of them, MPV was found to be elevated in patients with STEMI (20). In another, Pereg et al. (21) found an association between unsuccessful thrombolytic therapy and an increased MPV in patients with STEMI. Also, Chu et al. (22) reported an association between MPV and acute myocardial infarction in a recent meta-analysis. Further, they reported that MPV is related with MI mortality and restenosis. However, none of these studies evaluated patients with ACS who were younger than 45 years old. In our study, MPV was evaluated in young patients with NSTE-ACS. Thrombogenic activity is known to be higher in NSTE-ACS, and it has been shown to play an essential role in the etiopathogenesis of NSTE-ACS (1, 23). Likewise, MPV were found to be higher in myocardial infarction patients with normal coronary arteries (24). This supports that the acute coronary syndromes comprises on the basis of increased thrombogenic activity shown by high MPV, rather than atherosclerotic basis. In our study there was no acute coronary syndrome patient with normal coronary arteries.

In a study of premature atherosclerosis, Kurrelmeyer et al. (25) evaluated the role of sex differences in platelet function among subjects with a family history of premature coronary artery disease (CAD). They found that platelets from females were more reactive than platelets from males with a family history of premature CAD. In our study, the proportion of females was low in both the NSTE-ACS and control groups; moreover, the proportion of women was higher in the control group. Despite the possible increased platelet activity among females, MPV was found to be higher in the NSTE-ACS group in our study.

As expected, cardiovascular risk factors, including smoking, family history, hypertension, and diabetes mellitus, were more prevalent in young patients with NSTE-ACS than in the control group. Varol et al. (26) found that the serum MPV was significantly higher in regular smokers than in controls. Similarly, we found that the MPV in NSTE-ACS patients who smoked was higher than those in non-smoking NSTE-ACS patients. In another study, platelet activity was reported to decrease with advancing age (27). This indicates that platelet activity is higher in young patients, as compared to older patients. The high MPV we found in young patients with NSTE-ACS may be associated with the increased level of platelet activity in this population. Therefore, MPV may be more important in premature atherosclerosis, and NSTE-ACS patients with a high MPV may be more prone to acute coronary events.

Study limitations

The major limitation of the study is the relatively low number of patients. In addition, MPV was evaluated only once; however, measurement of MPV after the acute phase could provide important data about the platelet functions and premature ACS.

Conclusion

In conclusion, MPV was found to be elevated in young patients with NSTE-ACS compared with control subjects. Also, increased MPV was found to be an independent predictor of NSTE-ACS. The platelet functions assessed by MPV may be more important in young patients with NSTE-ACS. Additional studies are needed to elucidate this relationship.

Conflict of interest: None declared.

Peer-review: Externally peer-reviewed.

Authorships contributions: Concept- M.F.Ö., S.Ö.; Design - S.Ö.; Supervision - S.S.A., M.Y.; Resource- A.E., M.T., M.Y.; Materials - A.A., M.T.; Data Collection&/or Processing - M.F.Ö., A.A., S.S.A., M.Y.; Analysis&/or Interpretation - M.T.; Literature Search - A.A., A.E.; Writing - F.Ö., A.E.; Critical Reviews - S.S.A., M.Y., A.Ö., A.E.

Acknowledgements

Thanks to Ass. Prof. Yalçın Karagöz from the numerical methods department of Abant İzzet Baysal University for the statistical analysis support.

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