RESEARCH ARTICLE / *Araştırma Makalesi*

Mean Platelet Volume in Patients with Subclavian Artery Stenosis

Subklavyen Arter Stenozu Olan Hastalarda Ortalama Trombosit Hacmi

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Abstract

Objective	Thrombocytes and mean platelet volume (MPV) are related to atherosclerosis. The purpose of the present study was to investigate the relationship between MPV and subclavian artery stenosis (SAS).
Materials and Methods	Patients who were diagnosed with SAS by an angiography performed in the catheter laboratory between September 2010 and September 2015 were included in this study. A control group with similar clinical and demographic characteristics as the patients with SAS in angiographic terms was formed. The MPV and other hemogram values for SAS patients (35 patients) and the patients in the control group (38 patients) were determined retrospectively from the registry system and then compared.
Results	The two groups were similar to each other in terms of demographic and clinical characteristics. When the hemogram parameters were compared between the groups, the MPV was detected as being significantly higher in patients with SAS (8.07 ± 1.41 vs 7.19 ± 0.52; p = 0.001).
Conclusion	In conclusion, this study was the first to find a higher MPV in patients with SAS. Considering both the effect of platelets on atherosclerosis and their close association with other risk factors, MPV level may be an important factor in pathogenesis of SAS.
Keywords	Atherosclerosis; subclavian arterial stenosis; mean platelet volume

Öz

Amaç	*Trombositler ve ortalama trombosit hacmi ateroskleroz ile ilişkilidir. Bu çalışmanın amacı, ortalama trombosit hacmi ile subklavyen arter darlığı arasındaki ilişkiyi araştırmaktır.*
Gereç ve Yöntemler	*Sakarya Üniversitesi Eğitim ve Araştırma Hastanesi kateter laboratuvarında Eylül 2010 - Eylül 2015 tarihleri arasında yapılan anjiyografi ile subklavyen arter darlığı tamısı alan hastalar retrospektif olarak çalışmaya dahil edildi. Subklavyen arter darlığı olan hastalar ile anjiyografik açıdan benzer klinik ve demografik özelliklere sahip bir kontrol grubu oluşturuldu. Subklavyen arter darlığı olan hastalar (35 hasta) ve kontrol grubundaki hastalar (38 hasta) için ortalama trombosit hacmi ve diğer hemogram değerleri kayıt sisteminden geriye dönük olarak belirlenmiş ve karşılaştırılmıştır.*
Bulgular	*İki grup yaş, cinsiyet, ateroskleroz risk faktörleri, koroner arter hastalığı öyküsü ve ilaç kullanımı açısından birbirine benzerdi. Gruplar arasında hemogram parametreleri karşılaştırıldığında, ortalama trombosit hacmi subklavyen arteriyel darlığı olan hastalarda kontrol grubuna göre anlamlı olarak yüksek saptandı (8,07 ± 1,41 vs 7,19 ± 0,52; p = 0,001).*
Sonuç	*Sonuç olarak, bu çalışma subklavyen arter darlığı olan hastalarda daha yüksek ortalama trombosit hacmi bulan ilk çalışma olmuştur. Hem trombositlerin ateroskleroz üzerindeki etkisi hem de diğer risk faktörleri ile yakın ilişkisi düşünüldüğünde MPV düzeyi subklavyen arter darlığının patogenezinde önemli bir factor olabilir.*
Anahtar Kelimeler	*Ateroskleroz; subklavyen arter darlığı; ortalama trombosit hacmi*

INTRODUCTION

Atherosclerosis development in the aortic arch and its branches is observed mostly in the subclavian arteries and is about 3–4 times more prevalent on the left side than the right.[1] The prevalence of subclavian artery stenosis or occlusion (SAS) is about 2%, and they have been demonstrated to be associated with age, hypertension, and smoking.[2] SAS is the specific and clinically significant form of peripheral artery disease and has been associated with widespread atherosclerosis and increased cardiovascular event risks.[3] The chronic events causing SAS are atherosclerosis, vasculitis, traumas, aneurism, congenital malformations, fibro muscular dysplasia, extrinsic pressure, thoracic outlet syndrome, and radiation exposure.[4] As stenosis progresses, end-organ ischaemia (upper-extremity ischaemia, posterior fossa ischaemia) may develop, and patients may experience pain or weakness in the arm, pulse deficit, significant blood pressure differences between the two arms, vertigo with arm exercises, fainting, and visual impairment.[5]

Thrombocytes play a role in atherosclerosis and arterial thrombosis development.[6] When they are bigger, or when they are heterogeneous in terms of size and density, thrombocytes have more pro-thrombotic activity in terms of enzymatic status and metabolism.[7] Mean platelet volume (MPV) indicates the average size of the thrombocytes in the blood and is associated with atherosclerotic diseases, such as increased vascular inflammation, acute thrombogenic events,[8] carotid artery disease,[9] coronary artery disease (CAD),[10] and transplant vasculopathy.[11] This study aimed to investigate whether a relationship between SAS and MPV and other hemogram parameters exists.

MATERIALS and METHODS

This study was designed as a case control study. The patient group was comprised of 35 patients who had undergone peripheral angiography in the catheter laboratory in Sakarya University Training and Research Hospital between September 2010 and September 2015. The patients had symptomatic SAS, and 22 of them had been revascularized. A control group with similar clinical and demographic characteristics as the patients with SAS in angiographic terms was formed. This group included 38 patients without any known SAS diagnosis and without any symptoms or physical examination findings that would indicate SAS.

The inclusion criteria were symptomatic SAS stemming from atherosclerosis. The exclusion criteria were as follows: Acute coronary syndrome; hematologic, oncologic, or inflammatory diseases; white blood cells>10.400 mm3; a haemoglobin level <10 g/dl; medium-level serious valvular heart disease; a history of valvular heart disease surgery; an ejection fraction <40%; liver or kidney failure; thyroid function disorder; thrombocytopaenia; thrombocytosis and vasculitis; aneurism; thromboembolism; extrinsic pressure; thoracic outlet syndrome; dissection; trauma causing subclavian arterial stenosis; and occlusion except for atherosclerosis. The study was approved by the Sakarya University Faculty of Medicine Ethics Committee (Ethics committee number: 71522473/050.01.04/92, date: 02.05.2016).

Both groups were formed considering the risk factor rates for atherosclerosis, CAD frequency, age, gender, and drug use. Hypertension (HT) was considered as using antihypertensive drugs or having hypertension diagnosis (systolic blood pressure being >140mmHg, diastolic blood pressure >90mmHg). Diabetes mellitus (DM) was considered as using anti-diabetic agents or having a DM diagnosis (fasting blood glucose being ≥126mg/dl). Patients were considered to have hyperlipidaemia (HL) when using anti-hyperlipidaemic agents or having a hyperlipidaemia diagnosis (total cholesterol ≥200mg/dl, low-density cholesterol ≥160 mg/dl, triglyceride ≥200mg/dl). CAD was considered as having stenosis in one or more coronary arteries (proven angiographically) or having a history of coronary bypass surgery. Platelet counts, mean platelet volume, neutrophil, hemoglobin, hematocrit, lymphocites, were collected in all

patients as hematological indices. The angiography images and blood test parameters of the patients were received from the Patient Registry System.

Statistical analyses

Statistical analyses were performed using SPSS for Windows 18.0 (SPSS Inc., Chicago, IL). The data were presented as frequencies and percentages for categorical variables and mean ± standard deviation (SD) for continuous variables unless otherwise indicated. The Chi-square test was used to compare the categorical variables between the groups. The normality assumptions of continuous variables were examined using the Kolmogorov–Smirnov test. The normal distribution of the variables was verified with the Kolmogorov–Smirnov test. For numerical variables, an independent sample t-test was used for intergroup comparisons. A binary logistic regression test was used for statistical comparison of subclavian artery stenosis between white blood cells, thrombocytes, MPV, and neutrophil-lymphocyte ratio. A value of $p < 0.05$ was considered statistically significant.

RESULTS

The demographic characteristics of the patients are given in Table 1. No significant differences were found between the groups in terms of age, gender, atherosclerosis risk factors, CAD history, or drug use. The comparison of the groups in terms of haematological values is given in Table 2. All the values had similar rates in both groups; only the MPV results were significantly higher in the group with SAS than in the control group (8.07 ± 1.41 vs 7.19 ± 0.52; $p = 0.001$).

The effect of haematologic parameters on SAS was examined using binary logistic regression analysis, and the effects of high MPV were significant ($p = 0.05$; OR: 2.856; 95% confidence interval [CI]: 1.371–5.950). A high MPV caused a 2.85-fold increase in SAS (Table 3).

Table 1. Comparison of demographic and clinical characteristics between patients with subclavian artery stenosis and without subclavian artery stenosis

Variables	With SAS (n=35)	Without SAS (n=38)	p value
Age (years), mean±SD	61.77± 8,76	57.79± 9,29	0.060
Gender (female), n (%)	23 (65.71)	22 (57.89)	0.492
Hypertansion, n (%)	25 (71.42)	28 (73.68)	0.829
Diabetes mellitus, n (%)	11 (31.43)	14 (36.84)	0.626
Smoking, n (%)	15 (42.86)	14 (36.84)	0.600
Coronary artery disease, n (%)	18 (51.43)	19 (50.00)	0.903
Hyperlipidemia, n (%)	13 (37.14)	15 (39.47)	0.838
Previous CABG, n (%)	5 (14.29)	6 (15.79)	0.858
Medication usage			
Beta blocker, n (%)	14 (40.00)	19 (50.00)	0.391
Calcium channel blocker, n (%)	11 (31.43)	14 (36.84)	0.626
ACEI or ARB, n (%)	22 (62.86)	22 (57.89)	0.665
Statin, n (%)	13 (37.14)	15 (39.47)	0.205
Diuretic, n (%)	9 (25.71)	7 (18.42)	0.452
Antiplatelet, n (%)	19 (52.29)	15 (39.47)	0.838

SAS: Subclavian artery stenosis; CABG: Coronary artery bypass grafting; ACEI: Angiotensin-converting enzyme inhibitor; ARB: Angiotensin receptor blocker; SD: Standard deviation

Table 2. Comparison of hematological parameters between patients with subclavian artery stenosis and without subclavian artery stenosis

Variables	With SAS (n=35)	Without SAS (n=38)	p value
Hemoglobin (g/dL), mean±SD	13.36 ± 1.38	13.28 ± 1.33	0.805
Hematocrit %, mean±SD	40.15 ± 3.89	39.68 ± 3.68	0.598
White blood cell count (x 103/L), mean±SD	7.85 ± 1.54	7.81 ± 1.40	0.950
Neutrophil count (x 103/L), mean±SD	4.90 ± 1.24	4.57 ± 1.24	0.258
Lymphocyte count (x 103/L), mean±SD	2.23 ± 0.66	2.28 ± 0.66	0.600
Platelet count (x 103/L), mean±SD	269.06 ± 72.21	278.53 ± 89.00	0.621
Mean platelet volume (fL), mean±SD	8.07 ± 1.41	7.19 ± 0.52	**0.001**
Neutrophil-lymphocyte ratio, mean±SD	2.37 ± 0.92	2.16 ± 0.95	0.341

SAS: Subclavian artery stenosis; SD: Standard deviation

Table 3. Binary logistic regression with hematological parameters

Variables	**B**	**S.E**	**Wald**	**p**	**Exp(B)**	**95 % C.I for EXP(B)**	
						Lower	**Upper**
White blood cell count (x 103/L)	0,054	0,371	0,021	0,885	1,055	0,510	2,183
Platelet count (x 103/L)	0,002	0,009	0,053	0,817	1,002	0,985	1,020
Mean platelet volume (fL)	1,050	0,374	7,857	**0,005**	2,856	1,371	5,950
Neutrophil-lymphocyte ratio	0,032	0,764	0,002	0,967	1,032	0,231	4,616

DISCUSSION

By comparing the hemogram parameters between two groups with similar clinical characteristics, this study found that the MPV values were high in the group with SAS. No significant differences were found between the groups in terms of the other values.

In SAS, the left side is influenced more than the right side. The symptoms are frequently associated with upper extremity ischaemia (10–92%) and vertebrobasilar insufficiency (51–84%).[12,13] While proximal stenosis occurs especially due to atherosclerosis, the causes of distal stenosis may be atherosclerosis, trauma, arteritis, or the compression or adhesion of the extrinsic tissues.[14] All of this study's patients had proximal atherosclerotic SAS.

Recent studies have focused on new risk factors, such as fibrinogen, apolipoprotein A-1, and homocysteine, as well as already-known risk factors, such as age, HT, DM, HL, and smoking.[15] Recent studies have examined MPV, which is considered a new atherosclerosis risk factor.[16] A strong connection has been found between MPV and the inflammation of the thrombocytes, atherogenesis, and thrombosis development. Platelet factor IV, platelet-related growth factors, and chemokines have been found in atherosclerotic plaques.[17] Furthermore, the diameter of thrombocytes increases with HT, DM, obesity, and smoking, which are prognostic risk factors.[18] As the diameter of the thrombocytes increases, their activation also increases, and they become more pro-thrombotic.[19] Işık et al. reported that a high MPV value was associated with slow coronary flow development,[20] and Sayın et al. showed that atherosclerotic renal artery stenosis was associated with high MPV.[16] The present study investigated the relationship between SAS and hemogram parameters; there is no study examining this relationship in the literature before. The study found that MPV was significantly higher in the group with SAS. This finding supports a relationship between high MPV and atherosclerosis.

Study limitations

The retrospective, single-centred design was one of the

limitations of this study. Furthermore, SAS, which develops due to progressed and widespread atherosclerosis, is clinically rare. To the best of our knowledge, this is the first study to investigate the relationship between MPV and SAS, and it needs to be supported with multi-centred studies with a wider patient population.

CONCLUSION

In conclusion, we have shown that MPV was significantly elevated in patients with SAS compared with controls. Considering both the effect of platelets on atherosclerosis and their close association with other risk factors, MPV level may be an important factor in pathogenesis of SAS. However, especially given that the MPV level can be affected by a wide range of factors, multicentred, large-scale, randomised, and prospective studies are needed to corroborate these findings.

Authors; declares that the manuscript has not been sent to another journal simultaneously and has not been previously published in another journal.

Declaration of Conflicting Interests

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Ethical approval

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation in Turkey and with the Helsinki Declaration of 1975, as revised in 2008. Ethics committee approval was given for this study from the Faculty of Medicine of Sakarya University (Ethics committee number: 71522473/050.01.04/92, date: 02.05.2016).

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